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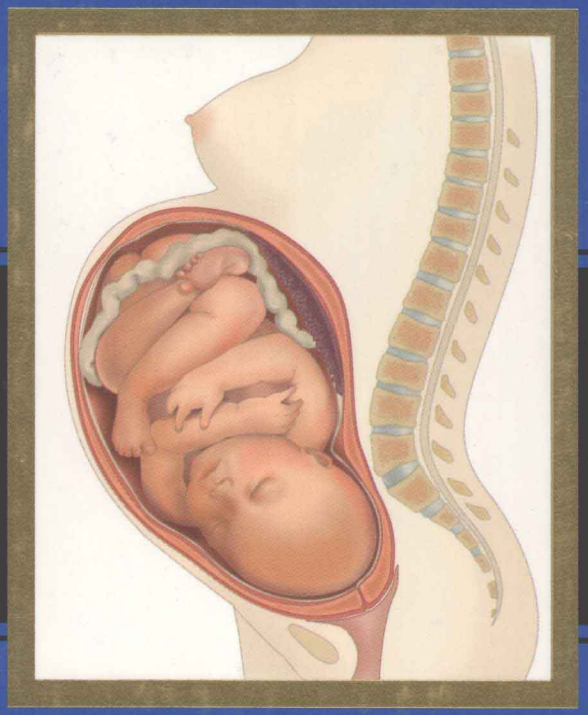


6th Edition MEDICAL COMPLICATIONS DURING PREGNANCY

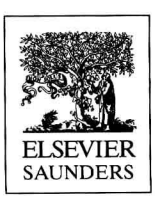
MEDICAL COMPLICATIONS DURING PREGNANCY

SIXTH EDITION

Gerard N. Burrow, M.D.
David Paige Smith Professor Emeritus of Medicine
Yale University School of Medicine
New Haven, Connecticut

Thomas P. Duffy, M.D.
Professor of Internal Medicine, Hematology
Yale University School of Medicine
New Haven, Connecticut

Joshua A. Copel, M.D.
Professor of Obstetrics, Gynecology &
Reproductive Sciences, and of Pediatrics
Yale University School of Medicine
New Haven, Connecticut



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Medical Complications During Pregnancy

FOR THE 500,000 WOMEN
IN DEVELOPING COUNTRIES
WHO DIE EACH YEAR
IN PREGNANCY OR CHILDBIRTH
BUT SHOULDN'T

CONTRIBUTORS

Jean T. Abbott, MD
Associate Professor, Division of Emergency Medicine, and Attending Physician, Emergency Department, University of Colorado Health Sciences Center; Denver, Colorado
Emergency Management of the Obstetric Patient

Phyllis August, MD, MPH
Professor of Medicine, Obstetrics and Gynecology in Medicine, and Public Health, Weill Medical College of Cornell University; Attending Physician, New York Presbyterian Hospital, New York, New York
Hypertensive Disorders in Pregnancy

Gerard N. Burrow, MD
David Paige Smith Professor Emeritus of Medicine, Department of Medicine, and Dean Emeritus, Yale University School of Medicine, New Haven, Connecticut
Thyroid Disease during Pregnancy
Pituitary and Adrenal Disorders of Pregnancy

Barbara Burtness, MD
Associate Professor and Director, Gastrointestinal Oncology, Department of Internal Medicine, Yale University School of Medicine; Attending Physician, Department of Internal Medicine, Yale-New Haven Hospital, New Haven, Connecticut
Neoplastic Diseases

Teresa Caulin-Glaser, MD
Associate Director of Preventive Cardiology, McConnell Heart Health Center-OhioHealth, Columbus, Ohio
Pregnancy and Cardiovascular Disease

Peter K. Chang, MD
Clinical Instructor, Gastroenterology, Mount Sinai School of Medicine, New York, New York
Gastrointestinal Complications

David A. Clark, MD, PhD
Professor Emeritus, Departments of Medicine, Molecular Medicine and Pathology, and Obstetrics and Gynecology, McMaster University, Hamilton; Professor of Medicine, Institute of Medical Sciences, University of Toronto, Toronto; Staff Physician, Department of Medicine, Hamilton Health Sciences, Hamilton, Ontario, Canada
Immunology of Pregnancy

Joshua A. Copel, MD
Professor of Obstetrics, Gynecology & Reproductive Sciences, and of Pediatrics, Yale University School of Medicine; Attending Physician, Yale-New Haven Hospital, New Haven, Connecticut
Obstetric Management of the High-Risk Patient

Kathryn Czarkowski, MA
Director of Clinical Services, Yale Behavioral Gynecology Program, Department of Psychiatry, Yale University School of Medicine, New Haven, Connecticut
Psychiatric Complications

James O. Donaldson, MD
Professor of Neurology, University of Connecticut School of Medicine, Farmington, Connecticut
Neurologic Complications

Thomas P. Duffy, MD
Professor of Internal Medicine, Hematology, Yale University School of Medicine; Attending Physician, Yale-New Haven Hospital, New Haven, Connecticut
Hematologic Aspects of Pregnancy
Neurologic Complications

C. Neill Epperson, MD
Assistant Professor of Psychiatry and Obstetrics/Gynecology and Director, Yale Behavioral Gynecology Program, Yale University School of Medicine; Attending Physician, Yale-New Haven Hospital and Connecticut Mental Health Center, New Haven, Connecticut
Psychiatric Complications

Harold J. Fallon, MD, MRCP
Dean Emeritus, University of Alabama School of Medicine, Birmingham, Alabama; Home Secretary, Institute of Medicine, Washington, D.C.
The Effects of Pregnancy on the Liver

Peter R. Garner, MD, FRCP(C) (deceased)
Professor of Obstetrics and Gynecology and Professor of Medicine, University of Ottawa, Ottawa, Ontario, Canada
Pituitary and Adrenal Disorders of Pregnancy

Lauren H. Golden, MD
Postdoctoral Fellow–Endocrinology, Section of Endocrinology, Department of Internal Medicine, Yale University School of Medicine, New Haven, Connecticut
Thyroid Disease during Pregnancy

John P. Hayslett, MD
Professor of Medicine (Nephrology) and Obstetrics and Gynecology, Department of Medicine, Yale University School of Medicine; Attending Physician, Yale–New Haven Hospital, New Haven, Connecticut
Renal Disease in Pregnancy

Debra Houry, MD, MPH
Assistant Professor, Department of Emergency Medicine, and Associate Director, Center for Injury Control, Emory University; Attending Physician, Emergency Department, Emory University Hospital and Grady Memorial Hospital, Atlanta, Georgia
Emergency Management of the Obstetric Patient

Karl L. Insogna, MD
Professor of Medicine, Yale University School of Medicine, New Haven, Connecticut
Calcium Homeostasis and Disorders of Calcium Metabolism during Pregnancy and Lactation

Anne B. Kenshole, MB, FRCPC, FACP
Professor Emeritus, Departments of Medicine and Obstetrics, University of Toronto; Staff Physician and Consultant to the South Central Ontario Regional High Risk Pregnancy Service, Sunnybrook and Women's Health Sciences Center, Toronto, Ontario, Canada
Diabetes and Pregnancy

Marie Louise Landry, MD
Professor, Department of Laboratory Medicine, Yale University School of Medicine; Director, Clinical Virology Laboratory, Yale–New Haven Hospital, New Haven, Connecticut
Viral Infections

Carl A. Laskin, MD, FRCPC
Associate Professor of Medicine, Obstetrics and Gynecology, and Immunology, Division of Rheumatology, Department of Medicine, University of Toronto; Consultant, Division of Rheumatology, Department of Medicine, University Health Network, and Department of Medicine and Obstetrics and Gynecology, Mount Sinai Hospital, Toronto, Ontario, Canada
Pregnancy and the Rheumatic Diseases

Richard V. Lee
Professor of Medicine, Pediatrics, and Obstetrics and Adjunct Professor of Anthropology, Social and Preventive Medicine, State University of New York at Buffalo School of Medicine, Buffalo, New York
Substance Abuse

Urania Magriples, MD
Associate Professor and Association Division Director, Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Yale University School of Medicine; Attending Physician, Yale–New Haven Hospital, New Haven, Connecticut
Obstetric Management of the High-Risk Patient

Jess Mandel, MD
Associate Professor of Medicine, Department of Medicine, Division of Pulmonary, Critical Care, and Occupational Medicine, and Assistant Dean, Office of Student Affairs and Curriculum, University of Iowa, Roy J. and Lucille A. Carver College of Medicine; Co-Director, Pulmonary Hypertension Program, University of Iowa Hospitals and Clinics, Iowa City, Iowa
Pulmonary Diseases

Urszula S. Masiukiewicz, MD
Assistant Professor, Department of Medicine, Yale University School of Medicine, New Haven, Connecticut
Calcium Homeostasis and Disorders of Calcium Metabolism during Pregnancy and Lactation

Ellen D. Mason
Internal Medicine Consultant, Department of Obstetrics and Gynecology, John H. Stroger, Jr., Hospital of Cook County, Chicago, Illinois
Substance Abuse

Mark R. Mercurio, MD
Associate Clinical Professor, Department of Pediatrics, Yale University School of Medicine, New Haven; Attending Neonatologist and Co-chair, Hospital Ethics Committee, Yale–New Haven Hospital, New Haven; Attending Neonatologist and Chair, Hospital Ethics Committee, Lawrence and Memorial Hospital, New London, Connecticut
Ethical Issues in Obstetrics

Peter McPhedran, MD
Professor of Laboratory Medicine and Internal Medicine, Yale University School of Medicine; Director, Clinical Hematology Laboratory, and Attending Physician, Yale–New Haven Hospital, New Haven, Connecticut
Venous Thromboembolism during Pregnancy

Caroline A. Riely, MD
Professor, Medicine and Pediatrics, and Attending Physician, Gastroenterology, University of Tennessee Health Science Center, Memphis, Tennessee
The Effects of Pregnancy on the Liver

Cheryl F. Rosen, MD, FRCPC
Associate Professor, Division of Dermatology, Department of Medicine, University of Toronto; Head, Division of Dermatology, Toronto Western Hospital, Toronto, Ontario, Canada
The Skin in Pregnancy

Maria C. Savoia, MD
Vice Dean for Medical Education and Professor of Medicine, University of California, San Diego, School of Medicine, La Jolla, California
Bacterial, Fungal, and Parasitic Disease

Margretta R. Seashore, MD
Professor of Genetics and Pediatrics, Yale University School of Medicine; Attending Physician, Department of Pediatrics, Yale-New Haven Hospital, New Haven, Connecticut
Clinical Genetics

John F. Setaro, MD
Associate Professor of Medicine and Director, Cardiovascular Disease Prevention Center, Section of Cardiovascular Medicine, Department of Internal Medicine, Yale University School of Medicine; Attending Physician, Department of Medicine, Yale-New Haven Hospital, New Haven, Connecticut
Pregnancy and Cardiovascular Disease

Adam F. Steinlauf, MD
Clinical Instructor, Gastroenterology, Mount Sinai School of Medicine; Clinical Assistant, Mount Sinai Medical Center, New York, New York
Gastrointestinal Complications

Morris Traube, MD, JD
Professor of Medicine and Director of Clinical Affairs, Section of Digestive Diseases, Yale University School of Medicine; Director, Gastrointestinal Procedure Center, Yale-New Haven Hospital, New Haven, Connecticut
Gastrointestinal Complications

Steven E. Weinberger, MD
Professor of Medicine and Faculty Associate Dean for Education, Harvard Medical School; Executive Vice Chair, Department of Medicine, Beth Israel Deaconess Medical Center, Boston, Massachusetts
Pulmonary Diseases

PREFACE

For the sixth edition of *Medical Complications During Pregnancy,* an obstetrician, Joshua A. Copel, has joined the Editors; this addition is long overdue. The basic concept of the book was based on the necessity for the internist and the obstetrician to care for the pregnant woman with medical problems together, often with, in addition, the neonatologist. As Vice Chair for Obstetrics in the Department of Obstetrics, Gynecology & Reproductive Sciences at Yale University School of Medicine, Dr. Copel is particularly well suited for such a role.

Another tenet of the book has been a commitment to keep the book as current as possible by adding new authors and new chapters to adequately cover the field. In the fifth edition, chapters on immunology and on emergency management of the obstetric patient were added to reflect concerns or progress in the field. As a consequence of the availability of new diagnostic and therapeutic modalities, obstetricians are increasingly asked to make difficult ethical decisions. A new chapter in bioethics has been added in the sixth edition, as has a chapter on the psychiatric consequences of pregnancy. New chapters have been written on obstetric care, calcium disorders, diabetes mellitus, rheumatic diseases, and dermatology.

Despite these changes, the basic purpose of the book continues to be to provide answers to clinical questions of physicians caring for pregnant women. Emphasis has been placed on evidence-based medicine, in which the effect of the disease process on pregnancy and the effect of the pregnancy on the disease are examined. There has also been an effort to provide the pathophysiologic foundation on which to base diagnostic and therapeutic measures.

Modern medicine has enabled more women to survive both acute and chronic illnesses that in the past would have resulted in death or such severe disability as to preclude childbearing. As more of these women become pregnant, the need for collaborative care by general obstetricians, specialists in high-risk pregnancy, and internists will only increase. Our purpose in this book is to provide a template for that care and some common ground: a set of information that is useful for physicians from different disciplines who join together to care for pregnant women with complex medical problems.

GERARD N. BURROW, MD
THOMAS P. DUFFY, MD
JOSHUA A. COPEL, MD

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Obstetric Management of the High-Risk Patient

Urania Magriples and Joshua A. Copel

Throughout the developed world in the 20th century, improvements in blood banking, antibiotics, the treatment of hypertension, and the advent of safe alternatives to general anesthesia have led to a reduction in maternal and fetal mortality and morbidity. Coupled with improvements in the understanding of maternal-fetal pathophysiology and with awareness of how changes in maternal physiology affect fetal growth and development, these developments have led to the awareness of high-risk pregnancy as the care of two patients: the mother and fetus. A pregnancy may be considered high risk because of maternal or fetal conditions, but the outcomes are often intimately linked.

Prenatal care in most of the 20th century was designed to identify hypertensive complications of pregnancy and to expedite the care of women with preeclampsia. In the 1980s and 1990s, there was an increased emphasis on early management of women at risk for prematurity, although efforts to delay preterm delivery have, as a whole, been disappointing. Also, since the mid-1970s, a new subspecialty of maternal-fetal medicine has emerged, attracting physicians trained in obstetrics with 2 to 3 years of additional education in the management of women and fetuses during complicated pregnancies.

The normal increase during pregnancy of both blood volume and cardiac output is well tolerated in normal women but may lead to heart failure in a patient with a fixed cardiac lesion or output, such as mitral stenosis or cardiomyopathy. Poor maintenance of cardiac output subsequently affects uterine and fetal perfusion and, therefore, fetal growth. The physiologic nadir of blood pressure in the first and second trimesters with physiologic elevation in the third trimester often makes it difficult to distinguish preeclampsia from exacerbation of chronic hypertension, and this dilemma is even more complicated for women with systemic lupus erythematosus, who may chronically have proteinuria, a hallmark of preeclampsia. Ultimately, if hypertension is not controlled by hospitalization and medication regardless of the diagnosis, it will lead to a need for delivery. The normal physiologic changes during pregnancy are profound but generally well tolerated by most pregnant women and are completely reversible. Those that are of primary interest are reviewed in Table 1–1. The objective of this chapter is to refine these concepts as well as review the obstetric management and recent technologic advances in the care of these complicated pregnancies.

PRECONCEPTION COUNSELING

The physician taking care of women has the opportunity to have an impact not only on the lives of women but also on the lives of their children. Preconception care is essential in minimizing exposure to drugs and teratogens, maximizing nutritional status, and identifying medical conditions that may either affect pregnancy or be influenced by it.[1–3]

In the United States, more than 150,000 birth defects and more than 500,000 infant deaths, spontaneous abortions, stillbirths, and miscarriages each year result from defective fetal development.[4] It is estimated that 1% to 5% of congenital anomalies may be drug or chemical related. Factors that determine a drug's effect on the fetus include dosage, duration, and time of exposure, as well as drug metabolism, concurrent use of other drugs, genetic susceptibility, and placental transfer. There is a critical period of embryonic development from the 3rd through 12th weeks, when the embryo is undergoing organogenesis. Before this time, exposures tend either to cause abortion or to have no effect at all (known as the "all-or-none phenomenon"). After the 12th week, effects are generally limited to growth and neural development.

Preconception counseling should be the mainstay of women's health care. Therefore, all physicians who care for women of reproductive age need to be aware of the potential influence of disease and medications on pregnancy and make their patients aware of this impact. The effect of teratogens often occurs prior to the recognition of pregnancy. Examples of recognized teratogens and their associated malformations are listed in Table 1–2. Infectious agents

TABLE 1–1 Physiologic Changes of Pregnancy

Organ System	Change	Clinical Correlate
Hematologic		
Blood volume	Increases by 45%	"Dilutional anemia"
Plasma volume	Increases	–
Red cell volume	Increases by 250-450 mL	–
Iron requirements	Increase	Iron deficiency common
White blood cell count	Increases to 12,000 cells/mm^3 (higher in stress or labor)	Diagnosis of infection difficult
Fibrinogen, plasminogen, factors VII, VIII, and X	Increase	Increased risk of venous thrombosis
Platelets	Increase turnover	Normal > 100,000
	Increase aggregation	More EDTA-induced clumping; manual platelet count needed to evaluate thrombocytopenia
C-reactive protein	Increases	Not useful as marker of acute infection
Sedimentation rate	Increases	Not useful as marker of acute infection
Cardiovascular		
ECG	Left axis deviation	Nonspecific T wave changes
Chest radiograph	Superior, lateral, and anterior displacement of heart by enlarging uterus	Enlarged cardiac silhouette straightened left heart border
Cardiac output	Increases by 30% to 50%	Systolic ejection murmurs common
	Increased end-diastolic dimensions	
	Myocardial hypertrophy	No long-term effect
Stroke volume	Increases	Increased cardiac work
Heart rate	Increases	Palpitations common; increase in premature atrial contractions; increase in arrhythmias
Blood pressure	Decreases in 1st and 2nd trimesters	Patient may need to decrease antihypertensive medications
	Increases to baseline in 3rd trimester	Increase in antihypertensive medication requirements
		Difficulty in distinguishing chronic hypertension from preeclampsia
Renal		
Kidney length	Increases by 1.5 cm	None
Ureters	Dilate	Right > left
Bladder	Relaxes	Increased dead space, increased risk of urinary tract infections and pyelonephritis
		Need for prophylaxis with recurrent urinary tract infections or pyelonephritis
		Frequent follow-up for women with history of urinary tract infections
Renal plasma flow	Increases by 50%	–
Glomerular filtration	Increases by 50%	Increased clearance of medications; difficulty attaining therapeutic levels, need to adjust dosing interval
Proteinuria	Increases	Underlying proteinuria worsens with pregnancy; symptoms from protein loss more common in pregnancy
Glycosuria	Increases	Poor indicator of diabetes in pregnancy
Alimentary		
Gastric emptying	Delayed	Heartburn, reflux
Sphincter tone	Decreases	Reflux
Motility	Decreases	Constipation, bloating
Gallbladder	Increase in residual volume	Increased risk of sludge and gallstones
	Decrease in emptying	Increase in symptoms with fatty diet
Cholesterol level	Doubles	Do not check in pregnancy
Binding protein levels	Increase	Increase in requirements of protein-bound medications
Transferrin level	Increases	–
Albumin level	Decreases	None
Alkaline phosphatase level	Increases (placental origin)	Unreliable test of liver disease
Transaminase levels	Unchanged	–
Drug metabolism	Increases	Close monitoring of drug levels

(*Continued*)

TABLE 1–1 Physiologic Changes of Pregnancy—cont'd

Organ System	Change	Clinical Correlate
Pulmonary		
Minute ventilation	Increases	Subjective shortness of breath Mild respiratory alkalosis
Total lung capacity	Decreases by 5%	None
Expiratory reserve volume	Decreases by 20%	Less dead space, more efficient ventilation
Tidal volume	Increases by 40%	—
Vital capacity	Unchanged	—
Inspiratory reserve volume	Unchanged	Unchanged
FEV_1	Unchanged	Decrease not explained by pregnancy
PaO_2	Unchanged	Hypoxemia abnormal
Integumentary		
Skin		
Hyperpigmentation	Increases	Linea nigra Mask of pregnancy Increase in nevi
Sweat glands	Increase production	Increase in sweating and acne

ECG, electrocardiogram; EDTA, ethylenediaminetetraacetic acid; FEV_1, forced expiratory volume in 1 second; PaO_2, partial pressure of arterial oxygen.

TABLE 1–2 Teratogenic Agents

Agent	Clinical Effect
Alcohol*	Fetal alcohol syndrome: cardiac abnormalities (ASD, VSD), characteristic facies, IUGR, maxillary hypoplasia, mental retardation, microcephaly
Methotrexate (antifolate)	Abnormal cranial ossification, cleft palate, hydrocephaly, IUGR and postnatal growth abnormalities, mental retardation, microcephaly, neural tube defects, reduction of derivatives of first branchial arch
Androgens	Masculinization of the female fetus
Angiotensin-converting enzyme inhibitors	Fetal and neonatal death, IUGR, neonatal anuria secondary to renal failure, oligohydramnios, pulmonary hypoplasia, skull hypoplasia (second and third trimester exposure)
Cocaine	Cardiac abnormalities, dislocated hip, facial clefts, musculoskeletal malformations, pyloric stenosis, respiratory malformations, ventriculomegaly
Cyclophosphamide	Cleft palate, eye abnormalities, skeletal and limb abnormalities (first trimester exposure)
Diethylstilbestrol	Cervical and uterine anomalies
Diphenylhydantoin	Cardiac abnormalities, cleft lip/palate, hypoplastic nails and distal phalanges, IUGR, mental retardation, microcephaly
External radiation (>5 rad)	Eye anomalies, IUGR, mental retardation, microcephaly
Hyperthermia	Neural tube defects
Indomethacin	Oligohydramnios, prenatal ductus arteriosus closure (reversible) (second and third trimester exposure)
Iodine deficiency and inorganic iodides	Deafness, fetal goiter, mental retardation
Isotretinoin	Cardiovascular, CNS and ear anomalies, cleft lip/palate
Lead	CNS abnormalities, microcephaly
Lithium carbonate	Ebstein anomaly of the tricuspid valve
Methimazole	Aplasia cutis
Methylmercury	Blindness, deafness, IUGR, microcephaly, neonatal seizures, poor muscle tone
Naphthalene	Hemolysis in G6PD-deficient infants
Nicotine	IUGR, increased incidence of sudden infant death syndrome
Penicillamine	Cutis laxa, joint hyperflexibility
Quinine (high dose)	Ototoxicity
Streptomycin	Ototoxicity
Tegretol	Cardiac abnormalities, developmental delay, fingernail hypoplasia, minor craniofacial defects
Tetracycline	Bone and tooth staining, dental enamel hypoplasia
Thalidomide	Cardiac defects, ear and nasal anomalies, gastrointestinal atresias and stenosis, limb reduction deformities
Trimethadione	Cardiac and CNS anomalies; developmental delay; high, arched palate; irregular teeth; IUGR; low-set ears; V-shaped eyebrows
Valproic acid	Cardiac abnormalities, dysmorphic facies, IUGR, neural tube defects
Warfarin	Anomalies of eyes, hands, and neck; CNS anomalies and hemorrhage; IUGR; nasal hypoplasia; stippling of secondary epiphyses

*Data are based on chronic use (10-12 drinks/day) associated with 30% incidence. Less known about lower amounts.
ASD, atrial septal defect; CNS, central nervous system; G6PD, glucose-6-phosphate dehydrogenase; IUGR, intrauterine growth restriction; VSD, ventricular septal defect.

can also cause maldevelopment in the human (Table 1–3). The lethal or developmental effects may be the result of mitotic inhibition, direct cytotoxicity, or necrosis. Inflammatory responses to infection can lead to metaplasia, scarring, or calcification, which lead to further damage.

Awareness of the need to optimize a medical condition before pregnancy is crucial, because many disease mechanisms are profoundly sensitive to the physiologic and hormonal changes in pregnancy. Routine health care maintenance for women with significant medical illnesses, such as pacemaker replacement and battery changes, stress testing, and appropriate medication changes and testing are best done before pregnancy.

Chronic maternal conditions are associated with an increased risk of teratogenicity. For example, diabetes increases the risk of a fetal abnormality by twofold to threefold.[5] There is still considerable controversy about whether the abnormalities are caused by only hyperglycemia or by the changes in pH and free fatty acids as well as the presence of hypoglycemia and ketosis.[6,7] Despite this debate, multiple studies have demonstrated that diabetic mothers with hemoglobin A_{1c} levels greater than 7.5 have a twofold increased risk of congenital malformations, and the risk is greater with increasing hemoglobin A_{1c} levels.[8,9] There are major cost savings associated with preconception diabetic care; these savings are secondary predominantly to a decrease in congenital anomalies.[10–13]

In mothers with phenylketonuria, levels of phenylalanine higher than 20 mg/dL are associated with a 90% incidence of congenital malformations in their fetuses, whereas levels lower than 16 mg/dL are associated with a 20% incidence.[14] Control of phenylalanine levels throughout the pregnancy is necessary to minimize the ongoing risk of abnormal fetal brain development throughout gestation. This often requires input from a nutritionist as well as close monitoring of blood levels.

In mothers with seizures, there is a twofold to threefold increased incidence of congenital anomalies in fetuses regardless of whether the mothers are taking antiseizure medications.[15] This baseline risk of teratogenicity is further increased by the medications used for treatment of the disorder. However, the risk of uncontrolled seizures for the mother and fetus far outweighs the potential medication risk. Phenylhydantoin is associated with an increased risk of cleft lip/palate and congenital heart disease, as well as a malformation sequence seen in up to 30% of exposed infants, known as the *fetal hydantoin syndrome.*[16,17] The disorder consists of growth restriction, mental retardation, nail hypoplasia, and a variety of craniofacial abnormalities. Trimethadione and carbamazepine have also been reported to produce similar defects, and valproic acid and carbamazepine exposure result in a significantly higher risk of neural tube defects.[18-21] The malformations seen are similar because the breakdown products of many of the medications and their interference with folate metabolism are the primary mechanisms of teratogenicity.[22,23] Elevated levels of oxidative metabolites, which are normally eliminated by the enzyme epoxide hydroxylase, have been associated with an increase in malformations. Unfortunately, predisposition to low enzyme levels may be genetically predetermined; thus, women who have one child with a malformation are more likely to have another affected child.[24] Studies have shown that exposure to higher doses, as well as to multiple medications, increases the fetal risk.[25] Barbiturates seem to have the least risk of teratogenicity and therefore may represent the safest medication to use if control of seizures can be obtained before conception. Folate requirements increase in pregnancy, and women taking antiepileptic medications who plan to become pregnant should begin taking supplemental folate. Careful monitoring of drug levels is necessary because protein binding, metabolism, and excretion of medications all increase in pregnancy.

ANTEPARTUM CARE

Routine obstetric care entails detailed medical, surgical, and family histories and a risk factor assessment based on the intake interview. In patients without risk factors, monthly visits are performed in the first and second trimesters with monitoring of blood pressure, weight,

TABLE 1–3 Fetal Effects of Infectious Agents in Humans

Agent	Clinical Effect
Cytomegalovirus	IUGR, mental retardation, microcephaly, chorioretinitis, deafness, hydrocephalus, intracranial hemorrhage and calcification, seizures, cerebral palsy, hepatosplenomegaly, chronic hepatitis, thrombocytopenia, anemia, death
Herpes simplex	IUGR, encephalitis, seizures, conjunctivitis, pulmonary disease, vesicular lesions, hepatosplenomegaly, hepatitis, anemia, thrombocytopenia, death
Parvovirus B19	Anemia secondary to bone marrow suppression, myocarditis, hydrops
Rubella	IUGR, mental retardation, microcephaly, deafness, cataracts, glaucoma, cardiovascular anomalies, hepatosplenomegaly, thrombocytopenia, purpura
Syphilis	Hepatosplenomegaly, hypotonia, rhinorrhea, periostitis, rash
Toxoplasmosis	IUGR, mental retardation, microcephaly, hydrocephalus, cerebral calcifications, seizures, chorioretinitis, hepatosplenomegaly, hydrops
Varicella	Mental retardation, seizures, cataracts, microphthalmia, optic atrophy, chorioretinitis, hepatosplenomegaly, cutaneous scars
Venezuelan equine encephalitis	Hydrocephalus, porencephaly, cataracts, microphthalmia

IUGR, intrauterine growth restriction.

an assessment of signs and symptoms of preterm labor, and evaluation of fetal growth by fundal height measurement. Monitoring is generally more frequent in the third trimester and in high-risk pregnancies, although standards have not been established. The basic laboratory tests recommended for all pregnant women are listed in Table 1–4. Monitoring of drug levels is performed more frequently in pregnancy because of the increase in liver metabolism, volume of distribution, and glomerular filtration rate, as well as changes in binding and binding proteins. Monitoring of thyroid function in the setting of thyroid disease is performed more frequently in pregnancy because of increased binding of thyroid hormone, increases in metabolism, and increases in hormone requirements. The need for thyroid hormone replacement in hypothyroidism almost doubles in pregnancy. Thyroid function also needs to be monitored closely in the postpartum period as hormone requirements return to baseline.

Thorough patient and family histories often reveal risk factors for genetically transmissible diseases. Women with a history of a stillbirth should receive genetic counseling because a stillborn fetus has a 6% to 11% risk of having a chromosomal abnormality. Couples with a history of three or more pregnancy losses or prolonged infertility have up to a 6% risk of a chromosomal abnormality. A previous child with a chromosomal abnormality or congenital malformation likewise puts the parents at increased risk with future pregnancies.[26]

Ethnicity is also important, because certain groups carry a higher risk for genetic diseases. Caucasians have a 1:20 risk of carrying a recessive gene for cystic fibrosis. Mutation analysis is informative in up to 90% of Caucasian carriers and should be offered to all patients.[27] Individuals of Mediterranean descent have a 1:12 risk of being carriers of the β-thalassemia gene.[28] The mean corpuscular volume is useful as a screening test for thalassemia trait. Ashkenazi Jews, who have a 1:30 risk of carrying the gene for Tay-Sachs disease and a 1:40 risk of carrying the gene for Canavan's disease, should be offered testing for these carrier states, preferably before pregnancy because the testing for Tay-Sachs is more complex during pregnancy as a result of changes in hexosaminidase A activity.[29] The carrier rate for sickle cell disease is 1:12 among African-Americans.[30] When both parents are carriers of any of these autosomal recessive diseases, the chance of having an affected child is 25%, and prenatal testing should be offered.

Although the risk of Down's syndrome (trisomy 21) is highest in women aged 35 or older, the majority of affected infants are born to women younger than 35, inasmuch as they represent a larger percentage of the childbearing population. Prenatal screening on the basis of age alone detects only 30% of these infants; thus screening for maternal serum markers has been used to increase detection.[31] Maternal serum α-fetoprotein (AFP) is the major early fetal serum protein. It enters the amniotic fluid via fetal renal excretion, transudation through skin, and open lesions such as spina bifida and ventral wall defects. An elevated maternal serum level is frequently found with open neural tube and ventral wall defects, twin gestations, intrauterine fetal demise, and pregnancies at risk for growth restriction and fetal demise.[32-34] In contrast, a low maternal serum level of AFP has been associated with an increased risk of trisomy 21 and other autosomal trisomies. Maternal serum AFP testing in women younger than 35 detects an additional 25% of

TABLE 1–4 Basic Laboratory Tests

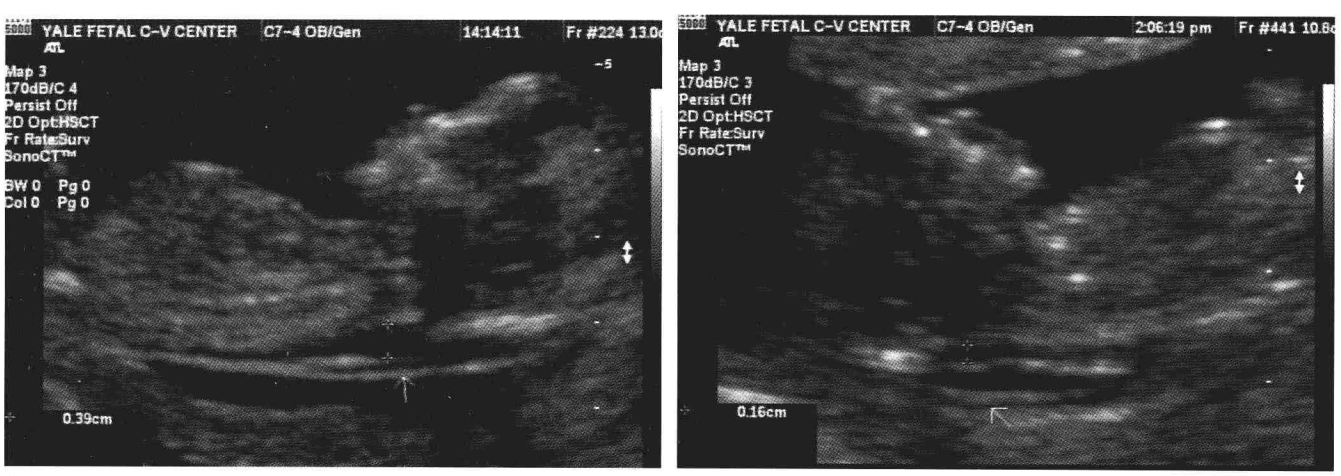
Complete blood cell count (registration and third trimester)
Blood type and antibody screen (indirect Coombs titer)
Hepatitis B surface antigen
Hemoglobin electrophoresis (need not be repeated if previously documented in record)
VDRL or RPR (if positive, test further with FTA-ABS)
Rubella titer
HIV*
Papanicolaou smear
Cervical cultures for gonorrhea and chlamydia (culture or PCR)
Urinalysis (culture if >5 WBCs/hpf or positive leukocyte esterase finding)
One hour 50 gram glucose challenge (28 weeks, or earlier if risk factors)
Three-hour 100-g glucose test (if 1-hour test result is abnormal)
Quadruple screen (maternal serum α-fetoprotein, human chorionic gonadotropin, estriol, and inhibin) (15-20 weeks)*
Genetic testing*
Ultrasonography*
Group B streptococcal swab from vagina and rectum (35-37 weeks)
Routine visit
Weight
Blood pressure
Urine dipstick tests for protein, glucose
Estimation of fetal growth and position by fundal height and palpation
Auscultation of fetal heart
Brief physical examination, including reflex testing and check for edema
Determination of symptoms of preterm labor (contractions, rupture of membranes, bleeding)
Cervical examination if necessary

*Tests generally recommended but necessitating patient counseling to determine appropriateness.
FTA-ABS, fluorescent treponemal antibody absorption (test); HIV, human immunodeficiency virus; hpf, high-power field; PCR, polymerase chain reaction; RPR, rapid plasma reagin (test); VDRL, Venereal Disease Research Laboratory (test); WBC, white blood cell.

pregnancies affected by Down's syndrome, with a 5% false-positive rate (i.e., in 5% of women with normal pregnancies, the risk of trisomy 21 is thought to be higher than the 1:270 risk in a 35-year-old woman). Maternal serum concentrations of human chorionic gonadotropin tend to be higher than normal, and those of unconjugated estriol are lower, in the presence of fetal Down's syndrome. The additional use of these markers along with maternal serum AFP ("triple screen") improves the detection rate of Down's syndrome to 67%, with a 7.2% false-positive rate.[35,36] The addition of the use of inhibin A ("quadruple test") has improved the detection of Down's syndrome to 74% with no change in the false-positive rate. In the first trimester, the combination of pregnancy-associated plasma protein A, free β-human chorionic gonadotropin, maternal serum AFP, and unconjugated estriol can yield a 70% detection rate, and an even higher rate is achieved when the nuchal thickness is measured between 11 and 14 weeks (Fig. 1–1).[37]

Ultrasonography has been used as a screening tool in the detection of neural tube and ventral wall defects in women with elevated maternal serum AFP; when performed by an experienced clinician, it has a very high sensitivity and specificity (Fig. 1–2).[38-40] Routine ultrasonography in all obstetric patients remains a controversial issue in the United States, but if the parents desire information on prenatal diagnosis of congenital anomalies, then second trimester ultrasonography at a facility with extensive experience in the identification of fetal anomalies is certainly advisable.[41-47] The addition of ultrasound detection of nuchal translucency to first trimester serum testing increases the detection of Down's syndrome to 88% and offers couples the best noninvasive screening available to date. Definitive testing for fetal karyotype requires an invasive procedure and can be obtained by chorionic villus sampling (CVS) or amniocentesis. CVS is essentially a placental biopsy and allows for determination of the fetal karyotype as well as extraction of DNA for detection of many genetic diseases.[48,49] It can be performed transcervically or transabdominally with ultrasound guidance of the biopsy catheter or needle, depending on the location of the placenta. Advantages of CVS are that it can be performed in the first trimester (10 to 12 weeks) and results are generally available in less than a week. Thus, pregnancy termination, if desired, is a less complicated and more private procedure. CVS has a procedure-related miscarriage rate of 0.5% to 1%. In some centers, concern was raised about an excess of transverse distal limb abnormalities; however, if there is any association, it is clustered primarily among procedures performed at less than 10 weeks' gestation.[50] Ultrasonographically guided amniocentesis can be performed after 15 weeks' gestation; the procedure-related miscarriage rate is estimated at 0.5%. Amniocytes are extracted from the amniotic fluid and can take 1 to 2 weeks to grow in culture in order to yield fetal DNA and a karyotype. Amniotic fluid can also be assessed for levels of AFP and acetylcholinesterase, both of which are increased when the integrity of the fetal integument is interrupted, as in spina bifida, anencephaly, or ventral wall defects. The availability of both polymerase chain reaction testing and culture of amniotic fluid has made the diagnosis of fetal viral and bacterial infections more accurate.[51-53] Because of the gestational age at which the procedure is performed, as well as the length of time necessary in tissue culture, termination of pregnancy after amniocentesis must be performed by either dilation and evacuation, a more complex procedure than in the first trimester, or induction of labor with prostaglandin. Fluorescent in situ hybridization specifically for chromosomes 21, 13, and 18 and for the sex chromosomes has allowed more rapid diagnosis of the more common trisomies.[54]

Amniocentesis is also used in the third trimester for verification of lung maturity. The predominant constituent of amniotic fluid is fetal urine, which the fetus swallows and "breathes." The phospholipids or surfactants in the lung act as the emulsifying agents that keep the alveoli open. Lung secretions exit the trachea into the amniotic fluid cavity, and therefore the assessment of the ratio of lecithin/sphingomyelin or the presence of phosphatidylglycerol by



A B

Figure 1–1. Screening for aneuploidy by nuchal translucency measurement. **A**, Normal nuchal translucency. Sagittal view of fetus with *calipers* on nuchal translucency. *Arrow* depicts normal unfused amniotic membrane. **B**, Abnormal nuchal translucency. Sagittal view of fetus with *calipers* on nuchal translucency. *Arrow* depicts normal unfused amniotic membrane.