

Williams Obstetrics, 25e >

CHAPTER 9: Prenatal Care

The borderline between health and disease is less distinctly marked during gestation, and therefore, it accordingly becomes necessary to keep pregnant patients under strict supervision, and to be constantly on the alert for the appearance of untoward symptoms.

—J. Whitridge Williams (1903)

INTRODUCTION

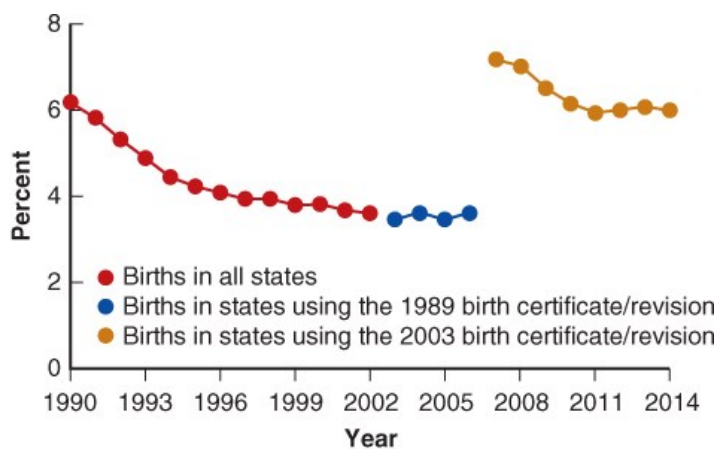
As emphasized above by Williams, prenatal care is important. According to the [American Academy of Pediatrics and the American College of Obstetricians and Gynecologists \(2017\)](#) a comprehensive antepartum program is defined as: “a coordinated approach to medical care, continuous risk assessment, and psychological support that optimally begins before conception and extends throughout the postpartum period and interconceptional period.”

PRENATAL CARE IN THE UNITED STATES

Almost a century after its introduction, prenatal care has become one of the most frequently used health services in the United States. In 2001, there were approximately 50 million prenatal visits. The median was 12.3 visits per pregnancy, and many women had 17 or more visits. Still, as seen from [Figure 9-1](#), 6 to 7 percent of women in this country have late or no prenatal care. In 2014, the percentages of non-Hispanic white, Hispanic, and African-American women who received inadequate or no prenatal care were 4.3, 7.5, and 9.7, respectively ([Child Trends, 2015](#)).

FIGURE 9-1

Percentage of births to mothers who received late or no prenatal care—United States, 1990–2014. (Data from [Child Trends, 2015](#).)



Source: F. Gary Cunningham, Kenneth J. Leveno, Steven L. Bloom, Catherine Y. Spong, Jodi S. Dashe, Barbara L. Hoffman, Brian M. Casey, Jeanne S. Sheffield. *Williams Obstetrics*, 25th Edition
 Copyright © McGraw-Hill Education. All rights reserved.

The [Centers for Disease Control and Prevention \(CDC\) \(2000\)](#) analyzed birth certificate data and found that half of women with delayed or no prenatal care wanted to begin care earlier. Barriers to care varied by social and ethnic group, age, and payment method. The most common reason cited was late recognition of pregnancy by the patient. The second most commonly cited obstacle was lack of money or insurance. The third was inability to obtain an appointment.

Prenatal Care Effectiveness

Care designed during the early 1900s focused on lowering the extremely high maternal mortality rate. Prenatal care undoubtedly contributed to the dramatic decline in this mortality rate from 690 deaths per 100,000 births in 1920 to 50 per 100,000 by 1955 (Loudon, 1992). And, the low current maternal mortality rate of 10 to 15 per 100,000 is likely associated with the high utilization of this care (Xu, 2010). Indeed, data from 1998 to 2005 from the Pregnancy Mortality Surveillance System identified a fivefold increased risk for maternal death in women who received no prenatal care (Berg, 2010).

Other reports also attest to prenatal care efficacy. In a study of almost 29 million births, the risk for preterm birth, stillbirth, early and late neonatal death, and infant death rose linearly with decreasing prenatal care (Partridge, 2012). Similarly, Leveno and associates (2009) found that a significant decline in preterm births at Parkland Hospital correlated closely with increased use of prenatal care by medically indigent women. Moreover, National Center for Health Statistics data showed that women with prenatal care had an overall stillbirth rate of 2.7 per 1000 compared with 14.1 per 1000 for women without this care (Vintzileos, 2002).

Evaluating the format of care, Ickovics and coworkers (2016) compared individual prenatal care and group prenatal care. The latter provided traditional pregnancy surveillance in a group setting with special focus on support, education, and active health-care participation. Women enrolled in group prenatal care had significantly better pregnancy outcomes. Carter and colleagues (2016) cited similar results. Childbirth education classes are also reported to result in better pregnancy outcomes (Afshar, 2017). Adolescent pregnancies carry special risk, and guidelines have been developed that focus on this subgroup (Fleming, 2015). Few data are available to recommend the practice of offering tangible incentives to improve prenatal care attendance (Till, 2015).

DIAGNOSIS OF PREGNANCY

Pregnancy is usually identified when a woman presents with symptoms and possibly a positive home urine pregnancy test result. Typically, these women receive confirmatory testing of urine or blood for human chorionic gonadotropin (hCG). Further, presumptive signs or diagnostic findings of pregnancy may be found during examination. Sonography is often used, particularly if miscarriage or ectopic pregnancy is a concern.

Symptoms and Signs

Amenorrhea in a healthy reproductive-aged woman who previously has experienced spontaneous, cyclical, predictable menses is highly suggestive of pregnancy. Menstrual cycles vary appreciably in length among women and even in the same woman (Chap. 5, Ovarian Cycle). Thus, amenorrhea is not a reliable pregnancy indicator until 10 days or more after expected menses have passed. Occasionally, uterine bleeding that mimics menstruation is noted after conception. During the first month of pregnancy, these episodes are likely the consequence of blastocyst implantation. Still, first-trimester bleeding should generally prompt evaluation for an abnormal pregnancy.

Of other symptoms, maternal perception of fetal movement depends on factors such as parity and habitus. In general, after a first successful pregnancy, a woman may first perceive fetal movements between 16 and 18 weeks' gestation. A primigravida may not appreciate fetal movements until approximately 2 weeks later. At about 20 weeks, depending on maternal habitus, an examiner can begin to detect fetal movements.

Of pregnancy signs, changes in the lower reproductive tract, uterus, and breasts develop early. These are described in detail in Chapter 4 (Reproductive Tract).

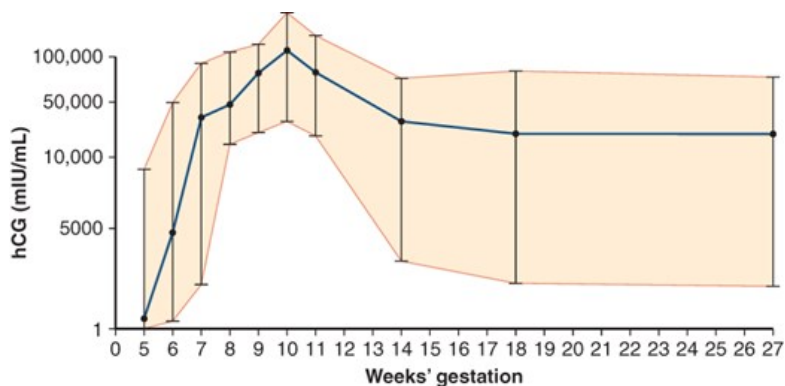
Pregnancy Tests

Detection of hCG in maternal blood and urine is the basis for endocrine assays of pregnancy. Syncytiotrophoblast produces hCG in amounts that increase exponentially during the first trimester following implantation. A main function of hCG is to prevent involution of the corpus luteum, which is the principal site of progesterone formation during the first 6 weeks of pregnancy.

With a sensitive test, the hormone can be detected in maternal serum or urine by 8 to 9 days after ovulation. The doubling time of serum hCG concentration is 1.4 to 2.0 days. As shown in Figure 9-2, serum levels range widely and increase from the day of implantation. They reach peak levels at 60 to 70 days. Thereafter, the concentration declines slowly until a plateau is reached at approximately 16 weeks' gestation.

FIGURE 9-2

Mean concentration (95% CI) of human chorionic gonadotropin (hCG) in serum of women throughout normal pregnancy.



Source: F. Gary Cunningham, Kenneth J. Leveno, Steven L. Bloom, Catherine Y. Spong, Jodi S. Dashe, Barbara L. Hoffman, Brian M. Casey, Jeanne S. Sheffield: *Williams Obstetrics*, 25th Edition
Copyright © McGraw-Hill Education. All rights reserved.

Measurement of hCG

This hormone is a glycoprotein with high carbohydrate content. The general structure of hCG is a heterodimer composed of two dissimilar subunits, designated α and β , which are noncovalently linked. The α -subunit is identical to those of luteinizing hormone (LH), follicle-stimulating hormone (FSH), and thyroid-stimulating hormone (TSH), but the β -subunit is structurally distinct among these. Thus, antibodies were developed with high specificity for the hCG β -subunit. This specificity allows its detection, and numerous commercial immunoassays are available for measuring serum and urine hCG levels. Although each immunoassay detects a slightly different mixture of hCG variants, its free subunits, or its metabolites, all are appropriate for pregnancy testing (Braunstein, 2014). Depending on the assay used, the sensitivity for the laboratory detection limit of hCG in serum is 1.0 mIU/mL or even lower (Wilcox, 2001).

False-positive hCG test results are rare (Braunstein, 2002). A few women have circulating serum factors that may bind erroneously with the test antibody directed to hCG in a given assay. The most common factors are heterophilic antibodies. These are produced by an individual and bind to the animal-derived test antibodies used in a given immunoassay. Thus, women who have worked closely with animals are more likely to develop these antibodies, and alternative laboratory techniques are available (American College of Obstetricians and Gynecologists, 2017a). Elevated hCG levels may also reflect molar pregnancy and its associated cancers (Chap. 20, Diagnosis). Other rare causes of positive assays without pregnancy are: (1) exogenous hCG injection used for weight loss, (2) renal failure with impaired hCG clearance, (3) physiological pituitary hCG, and (4) hCG-producing tumors that most commonly originate from gastrointestinal sites, ovary, bladder, or lung (Montagnana, 2011).

Home Pregnancy Tests

Over-the-counter pregnancy test kits have been available since the early 1970s, and millions are sold annually in the United States. More than 60 such tests are available in this country (Grenache, 2015). Unfortunately, many of these are not as accurate as advertised (Johnson, 2015). For example, Cole and associates (2011) found that a detection limit of 12.5 mIU/mL would be required to diagnose 95 percent of pregnancies at the time of missed menses, but they reported that only one brand had this degree of sensitivity. Two other brands gave false-positive or invalid results. In fact, with an hCG concentration of 100 mIU/mL, clearly positive results were displayed by only 44 percent of brands. Accordingly, only about 15 percent of pregnancies could be diagnosed at the time of the missed menses. Some manufacturers of even newer home urine assays claim >99-percent accuracy of tests done on the day of—and some up to 4 days before—the expected day of menses. Again, careful analysis suggests that these assays are often not as sensitive as advertised (Johnson, 2015).

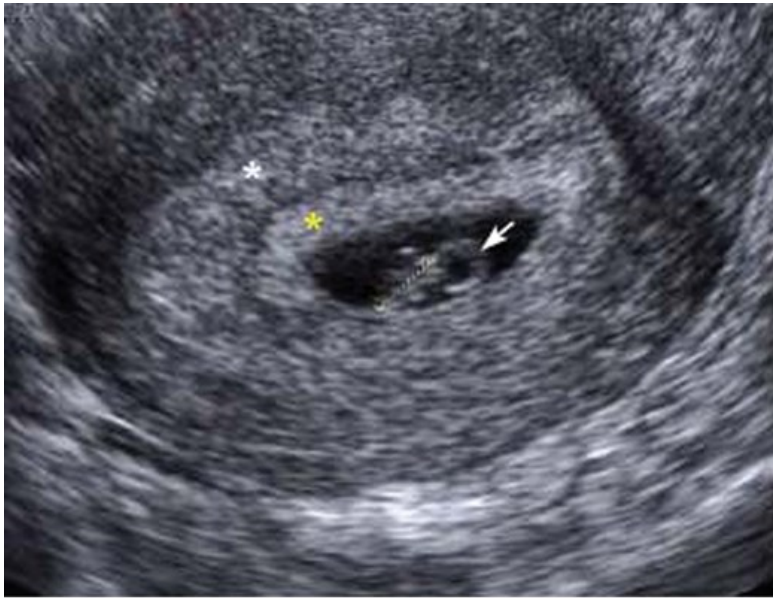
Sonographic Recognition of Pregnancy

Transvaginal sonography has revolutionized early pregnancy imaging and is commonly used to accurately establish gestational age and confirm pregnancy location. A *gestational sac*—a small anechoic fluid collection within the endometrial cavity—is the first sonographic evidence of pregnancy. It may be seen with transvaginal sonography by 4 to 5 weeks' gestation. A fluid collection, however, can also be seen within the endometrial cavity with an ectopic pregnancy and is termed a *pseudogestational sac* or *pseudosac* (Fig. 19-4). Thus, further evaluation may be warranted if this is the only sonographic finding, particularly in a woman with pain or bleeding. A normal gestational sac implants eccentrically in the endometrium, whereas a

pseudosac is seen in the midline of the endometrial cavity. Other potential indicators of early intrauterine pregnancy are an anechoic center surrounded by a single echogenic rim—the *intradecidual sign*—or two concentric echogenic rings surrounding the gestational sac—the *double decidual sign* shown in [Figure 9-3](#). If sonography yields equivocal findings, the term *pregnancy of unknown location (PUL)* is applied. In these cases, serial serum hCG levels and transvaginal sonograms can help differentiate a normal intrauterine pregnancy from an extrauterine pregnancy or an early miscarriage ([Chap. 19, Multimodality Diagnosis](#)).

FIGURE 9-3

Transvaginal sonogram of a first-trimester intrauterine pregnancy. The double decidual sign is noted surrounding the gestational sac and is defined by the decidua parietalis (*white asterisk*) and the decidua capsularis (*yellow asterisk*). The arrow notes the yolk sac, and the crown-rump length of the embryo is marked with measuring calipers. (Used with permission from Dr. Elysia Moschos.)



Source: F. Gary Cunningham, Kenneth J. Leveno, Steven L. Bloom, Catherine Y. Spong, Jodi S. Dashi, Barbara L. Hoffman, Brian M. Casey, Joanne S. Shuffatto, Melissa Chabros, 25th Edition. Copyright © McGraw-Hill Education. All rights reserved.

If the *yolk sac*—a brightly echogenic ring with an anechoic center—is seen within the gestational sac, an intrauterine location for the pregnancy is confirmed. The yolk sac can normally be seen by the middle of the fifth week. As shown in [Figure 9-3](#), after 6 weeks, an embryo is seen as a linear structure immediately adjacent to the yolk sac. Cardiac motion is typically noted at this point. Up to 12 weeks’ gestation, the crown-rump length is predictive of gestational age within 4 days ([Chap. 10, Gestational Age Assessment](#)).

INITIAL PRENATAL EVALUATION

Prenatal care is ideally initiated early. Major goals are to: (1) define the health status of the mother and fetus, (2) estimate the gestational age, and (3) initiate a plan for continued obstetrical care. Typical components of the initial visit are summarized in [Table 9-1](#). Subsequent care may range from relatively infrequent routine visits to prompt hospitalization because of serious maternal or fetal disease.

TABLE 9-1

Typical Components of Routine Prenatal Care

		Weeks			
Text Referral		First Visit	15–20	24–28	29–41
History					

Complete	Chap. 9, Normal Pregnancy Duration	•			
Updated			•	•	•
Physical examination					
Complete	Chap. 9, Clinical Evaluation	•			
Blood pressure	Chap. 40, Diagnosis of Hypertensive Disorders	•	•	•	•
Maternal weight	Chap. 9, Nutritional Counseling	•	•	•	•
Pelvic/cervical examination	Chap. 9, Clinical Evaluation	•			
Fundal height	Chap. 9, Subsequent Prenatal Visits	•	•	•	•
Fetal heart rate/fetal position	Chap. 9, Nutritional Counseling	•	•	•	•
Laboratory tests					
Hematocrit or hemoglobin	Chap. 56, Anemias	•		•	
Blood type and Rh factor	Chap. 15, Red Cell Alloimmunization	•			
Antibody screen	Chap. 15, Red Cell Alloimmunization	•		A	
Pap smear screening	Chap. 63, Epithelial Neoplasia	•			
Glucose tolerance test	Chap. 57, Screening and Diagnosis			•	
Fetal aneuploidy screening	Chap. 14, Screening for Aneuploidy	B ^a and/or	B		
Neural-tube defect screening	Chap. 14, Maternal Serum AFP Elevation: Neural-Tube Defect Screening		B		
Cystic fibrosis screening	Chap. 14, Cystic Fibrosis	B or	B		
Urine protein assessment	Chap. 4, Renal Function Tests	•			
Urine culture	Chap. 53, Urinary Tract Infections	•			
Rubella serology	Chap. 64, Rubella Virus	•			
Syphilis serology	Chap. 65, Diagnosis	•			C
Gonococcal screening	Chap. 65, Gonorrhea	D			D
Chlamydial screening	Chap. 65, Chlamydial Infections	•			C
Hepatitis B serology	Chap. 55, Pregnancy and Hepatitis B	•			D
HIV serology	Chap. 65, Human Immunodeficiency Virus	B			D

Group B streptococcus culture	Chap. 64, Bacterial Infections					E
Tuberculosis screening	Chap. 51, Diagnosis					

^aFirst-trimester aneuploidy screening may be offered between 11 and 14 weeks.

- A Performed at 28 weeks, if indicated.
- B Test should be offered.
- C High-risk women should be retested at the beginning of the third trimester.
- D High-risk women should be screened at the first prenatal visit and again in the third trimester.
- E Rectovaginal culture should be obtained between 35 and 37 weeks.

HIV = human immunodeficiency virus.

Prenatal Record

Use of a standardized record within a perinatal health-care system greatly aids antepartum and intrapartum management. Standardizing documentation allows communication and care continuity between providers and enables objective measures of care quality to be evaluated over time and across different clinical settings (Gregory, 2006). A prototype is provided by the American Academy of Pediatrics and the American College of Obstetricians and Gynecologists (2017) in their *Guidelines for Perinatal Care*, 8th edition.

Definitions

Several definitions are pertinent to establishment of an accurate prenatal record.

1. *Nulligravida*—a woman who currently is not pregnant and has never been pregnant.
2. *Gravida*—a woman who currently is pregnant or has been in the past, irrespective of the pregnancy outcome. With the establishment of the first pregnancy, she becomes a *primigravida*, and with successive pregnancies, a *multigravida*.
3. *Nullipara*—a woman who has never completed a pregnancy beyond 20 weeks' gestation. She may not have been pregnant or may have had a spontaneous or elective abortion(s) or an ectopic pregnancy.
4. *Primipara*—a woman who has been delivered only once of a fetus or fetuses born alive or dead with an estimated length of gestation of 20 or more weeks. In the past, a 500-g birthweight threshold was used to define parity. This threshold is now controversial because many states still use this weight to differentiate a stillborn fetus from an abortus (Chap. 1, Definitions). However, the survival of neonates with birthweights <500 g is no longer uncommon.
5. *Multipara*—a woman who has completed two or more pregnancies to 20 weeks' gestation or more. Parity is determined by the number of pregnancies reaching 20 weeks. It is not increased to a higher number if multiples are delivered in a given pregnancy. Moreover, stillbirth does not lower this number. In some locales, the obstetrical history is summarized by a series of digits connected by dashes. These refer to the number of term infants, preterm infants, abortuses younger than 20 weeks, and children currently alive. For example, a woman who is para 2–1–0–3 has had two term deliveries, one preterm delivery, no abortuses, and has three living children. Because these are nonconventional, it is helpful to specify the outcome of any pregnancy that did not end normally.

Normal Pregnancy Duration

The normal duration of pregnancy calculated from the first day of the last normal menstrual period is very close to 280 days or 40 weeks. In a study of 427,581 singleton pregnancies from the Swedish Birth Registry, Bergsjø and coworkers (1990) found that the mean pregnancy duration was 281 days

with a standard deviation of 13 days. However, menstrual cycle length varies among women and renders many of these calculations inaccurate. This, combined with the frequent use of first-trimester sonography, has changed the method of determining an accurate gestational age ([Duryea, 2015](#)).

The [American College of Obstetricians and Gynecologists \(2017e\)](#), the American Institute of Ultrasound in Medicine, and the Society for Maternal-Fetal Medicine have concluded that first-trimester ultrasound is the most accurate method to establish or reaffirm gestational age. For pregnancies conceived by assisted reproductive technology, embryo age or transfer date is used to assign gestational age. If available, the gestational ages calculated from the last menstrual period and from first-trimester ultrasound are compared, and this estimated date of delivery is recorded. This is discussed in further detail in [Chapter 7 \(Gestational Age\)](#) and in [Table 10-1 \(Gestational Age Assessment\)](#).

A quick estimate of a pregnancy due date based on menstrual data can be made as follows: add 7 days to the first day of the last period and subtract 3 months. For example, if the first day of the last menses was October 5, the due date is 10-05 minus 3 (months) plus 7 (days) = 7-12, or July 12 of the following year. This calculation is the *Naegle rule* ([American College of Obstetricians and Gynecologists, 2017e](#)).

Trimesters

It has become customary to divide pregnancy into three equal epochs or trimesters of approximately 3 calendar months. Historically, the first trimester extends through completion of 14 weeks, the second through 28 weeks, and the third includes the 29th through 42nd weeks of pregnancy. Thus, there are three periods of 14 weeks each. Certain major obstetrical problems tend to cluster in each of these time periods. For example, most spontaneous abortions take place during the first trimester, whereas most women with hypertensive disorders due to pregnancy are diagnosed during the third trimester.

In modern obstetrics, the clinical use of trimesters to describe a specific pregnancy is imprecise. For example, it is inappropriate in cases of uterine hemorrhage to categorize the problem temporally as “third-trimester bleeding.” Appropriate management for the mother and her fetus will vary remarkably depending on whether bleeding begins early or late in the third trimester ([Chap. 41, Risks](#)). Because precise knowledge of fetal age is imperative for ideal obstetrical management, the clinically appropriate unit is *weeks of gestation completed*. And more recently, clinicians designate gestational age using completed weeks and days, for example, 33^{4/7} weeks or 33 + 4, for 33 completed weeks and 4 days.

Previous and Current Health Status

As elsewhere in medicine, history taking begins with queries concerning medical or surgical disorders. Also, detailed information regarding previous pregnancies is essential as many obstetrical complications tend to recur in subsequent pregnancies. The *menstrual* and *contraceptive histories* are also important. Gestational or menstrual age is the number of weeks since the onset of the last menstrual period in women with menstrual cycles lasting 28 to 30 days. For those with irregular menses, sonography in early pregnancy will clarify gestational age. Last, some methods of birth control favor ectopic implantation following method failure ([Chap. 38, Method-Specific Adverse Effects](#) and [Progestin-Only Contraceptives](#)).

Psychosocial Screening

The [American Academy of Pediatrics and the American College of Obstetricians and Gynecologists \(2017\)](#) define psychosocial issues as nonbiomedical factors that affect mental and physical well-being. Women should be screened regardless of social status, education level, race, or ethnicity. Such screening should seek barriers to care, communication obstacles, nutritional status, unstable housing, desire for pregnancy, safety concerns that include intimate-partner violence, depression, stress, and use of substances such as tobacco, [alcohol](#), and illicit drugs. This screening is performed on a regular basis, at least once per trimester, to identify important issues and reduce adverse pregnancy outcomes. [Coker and colleagues \(2012\)](#) compared pregnancy outcomes in women before and after implementation of a universal psychosocial screening program and found that screened women were less likely to have preterm or low-birthweight newborns, as well as other adverse outcomes. Specific screens for depression are presented in [Chapter 61 \(The Puerperium\)](#).

Cigarette Smoking

Data on this practice have been included on the birth certificate since 1989. The number of pregnant women who smoke continues to decline. From 2000 to 2010, the prevalences were 12 to 13 percent ([Tong, 2013](#)). Based on the Pregnancy Risk Assessment Monitoring System, these women were more likely younger, had less education, and were either Alaska Natives or American Indians ([Centers for Disease Control and Prevention, 2013a](#)).

Numerous adverse outcomes have been linked to smoking during pregnancy (U.S. Department of Health and Human Services, 2000). Potential teratogenic effects are reviewed in [Chapter 12 \(Tobacco\)](#). Notable among these are greater rates of miscarriage, stillbirth, low birthweight, and preterm delivery (Man, 2006; Tong, 2013). There is also a twofold risk of placenta previa, placental abruption, and premature membrane rupture compared with nonsmokers. Thus, the U.S. Preventive Services Task Force recommends that clinicians offer counseling and effective intervention options to pregnant smokers at the first and subsequent prenatal visits (Siu, 2015). Although benefits are greatest if smoking ceases early in pregnancy or preferably preconceptionally, quitting at any stage of pregnancy can improve perinatal outcomes (Fiore, 2008).

Person-to-person psychosocial interventions are significantly more successful in achieving smoking abstinence in pregnancy than is simply advising the woman to quit (Fiore, 2008). One example is a brief counseling session covering the “5As” of smoking cessation ([Table 9-2](#)). This approach can be accomplished in 15 minutes or less and is effective when initiated by health-care providers ([American College of Obstetricians and Gynecologists, 2017i](#)).

TABLE 9-2

Five A’s of Smoking Cessation

ASK about smoking at the first and subsequent prenatal visits.

ADVISE with clear, strong statements that explain the risks of continued smoking to the woman, fetus, and newborn.

ASSESS the patient’s willingness to attempt cessation.

ASSIST with pregnancy-specific, self-help smoking cessation materials. Offer a direct referral to the smoker’s quit line (1-800-QUIT NOW) to provide ongoing counseling and support.

ARRANGE to track smoking abstinence progress at subsequent visits.

Adapted from [Fiore, 2008](#).

Behavioral interventions and nicotine replacement products are successful in reducing smoking rates ([Patnode, 2015](#)). That said, nicotine replacement has not been sufficiently evaluated to determine its effectiveness and safety in pregnancy. Trials evaluating such therapy have yielded conflicting evidence ([Coleman, 2015](#); [Pollak, 2007](#); [Spindel, 2016](#)). Two recent randomized trials also produced nonconclusive results. In the Smoking and Nicotine in Pregnancy (SNAP) trial, [Cooper and associates \(2014\)](#) reported a temporary cessation of smoking that may have been associated with improved infant development. In the Study of Nicotine Patch in Pregnancy (SNIPP) trial, [Berlin and coworkers \(2014\)](#) found no differences in smoking cessation rates or birthweights.

Because of limited available evidence to support pharmacotherapy for smoking cessation in pregnancy, the [American College of Obstetricians and Gynecologists \(2017i\)](#) has recommended that if nicotine replacement therapy is used, it should be done with close supervision and after careful consideration of the risks of smoking versus nicotine replacement.

Alcohol

Ethyl alcohol or *ethanol* is a potent teratogen that causes a fetal syndrome characterized by growth restriction, facial abnormalities, and central nervous system dysfunction. As discussed in [Chapter 12 \(Known and Suspected Teratogens\)](#), women who are pregnant or considering pregnancy should abstain from using any alcoholic beverages. The CDC analyzed data from the Behavioral Risk Factor Surveillance System from 2011 to 2013 and estimated that 10 percent of pregnant women used alcohol. It is estimated that 3.3 million women are at risk for such exposure ([Green, 2016](#)). The [American College of Obstetricians and Gynecologists \(2016b\)](#) in collaboration with the CDC has developed the *Fetal Alcohol Spectrum Disorders (FASD) Prevention Program*, which provides resources for providers and is available at: <http://www.acog.org/alcohol>.

Illicit Drugs

It is estimated that 10 percent of fetuses are exposed to one or more illicit drugs. Agents may include heroin and other opiates, cocaine, amphetamines, barbiturates, and marijuana ([American Academy of Pediatrics, 2017](#); [American College of Obstetricians and Gynecologists, 2015a, 2017d](#)). As discussed in [Chapter 12 \(Warfarin\)](#), chronic use of most of these in large quantities is harmful to the fetus ([Metz, 2015](#)). Well-documented sequelae include fetal-growth restriction, low birthweight, and drug withdrawal soon after birth. Adverse effects of marijuana are less convincing.

Women who use such drugs frequently do not seek prenatal care, which in itself is associated with risks for preterm and low-birthweight newborns (El-Mohandes, 2003; Eriksen, 2016).

For women who abuse heroin, methadone maintenance can be initiated within a registered methadone treatment program to reduce complications of illicit opioid use and narcotic withdrawal, to encourage prenatal care, and to avoid drug culture risks (American College of Obstetricians and Gynecologists, 2017f). Available programs can be found through the treatment locator of the Substance Abuse and Mental Health Services Administration at www.samhsa.gov. Methadone dosages usually are initiated at 10 to 30 mg daily and titrated as needed. In some women, careful methadone taper may be an appropriate option (Stewart, 2013). Although less commonly used, buprenorphine alone or in combination with naloxone may also be offered and managed by physicians with specific credentialing.

Intimate-Partner Violence

This term refers to a pattern of assault and coercive behavior that may include physical injury, psychological abuse, sexual assault, progressive isolation, stalking, deprivation, intimidation, and reproductive coercion (American College of Obstetricians and Gynecologists, 2012). Such violence has been recognized as a major public health problem. Unfortunately, most abused women continue to be victimized during pregnancy. With the possible exception of preeclampsia, domestic violence is more prevalent than any major medical condition detectable through routine prenatal screening (American Academy of Pediatrics and the American College of Obstetricians and Gynecologists, 2017). The prevalence during pregnancy is estimated to range between 4 and 8 percent. Intimate-partner violence is associated with an increased risk of several adverse perinatal outcomes including preterm delivery, fetal-growth restriction, and perinatal death (Chap. 47, Trauma).

The American College of Obstetricians and Gynecologists (2012) has provided methods for domestic violence screening and recommends their use at the first prenatal visit, then again at least once per trimester, and again at the postpartum visit. Such screening should be done privately and away from family members and friends. Patient self-administered or computerized screenings appear to be as effective for disclosure as clinician-directed interviews (Ahmad, 2009; Chen, 2007). Physicians should be familiar with state laws that may require reporting of intimate-partner violence. Coordination with social services can be invaluable in these cases. The National Domestic Violence Hotline (1-800-799-SAFE [7233]) is a nonprofit telephone referral service that provides individualized information regarding city-specific shelter locations, counseling resources, and legal advocacy.

Clinical Evaluation

A thorough, general physical examination should be completed at the initial prenatal encounter. Pelvic examination is performed as part of this evaluation. The cervix is visualized employing a speculum lubricated with warm water or water-based lubricant gel. Bluish-red passive hyperemia of the cervix is characteristic, but not of itself diagnostic, of pregnancy. Dilated, occluded cervical glands bulging beneath the ectocervical mucosa—*nabothian cysts*—may be prominent. The cervix is not normally dilated except at the external os. To identify cytological abnormalities, a Pap test is performed according to current guidelines noted in Chapter 63 (Epithelial Neoplasia). Specimens for identification of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* are also obtained when indicated.

Bimanual examination is completed by palpation, with special attention given to the consistency, length, and dilatation of the cervix; to uterine and adnexal size; to the bony pelvic architecture; and to any vaginal or perineal anomalies. Later in pregnancy, fetal presentation often can also be determined. Lesions of the cervix, vagina, or vulva are further evaluated as needed by colposcopy, biopsy, culture, or dark-field examination. The perianal region is visualized, and digital rectal examination performed as required for complaints of rectal pain, bleeding, or mass.

Gestational Age Assessment

Precise knowledge of gestational age is one of the most important aspects of prenatal care because several pregnancy complications may develop for which optimal treatment will depend on fetal age. As discussed earlier and in Chapter 7 (Gestational Age), first-trimester sonographic assessment is best correlated with menstrual history. That said, gestational age can also be estimated with considerable precision by carefully performed clinical uterine size examination that is coupled with knowledge of the last menses. Uterine size similar to a small orange roughly correlates with a 6-week gestation; a large orange, with an 8-week pregnancy; and a grapefruit, with one at 12 weeks (Margulies, 2001).

Laboratory Tests

Recommended routine tests at the first prenatal encounter are listed in Table 9-1. Initial blood tests include a complete blood count, a determination

of blood type with Rh status, and an antibody screen. The Institute of Medicine recommends universal human immunodeficiency virus (HIV) testing, with patient notification and right of refusal, as a routine part of prenatal care. The CDC ([Branson, 2006](#)) as well as the American Academy of Pediatrics and the [American College of Obstetricians and Gynecologists \(2016f, 2017\)](#) continue to support this practice. If a woman declines testing, this is recorded in the prenatal record. All pregnant women are also screened for hepatitis B virus infection, syphilis, and immunity to rubella at the initial visit. Based on their prospective investigation of 1000 women, [Murray and coworkers \(2002\)](#) concluded that in the absence of hypertension, routine urinalysis beyond the first prenatal visit was not necessary. A urine culture is recommended by most because treating bacteruria significantly reduces the likelihood of developing symptomatic urinary tract infections in pregnancy ([Chap. 53, Urinary Tract Infections](#)).

Cervical Infections

Chlamydia trachomatis is isolated from the cervix in 2 to 13 percent of pregnant women. The [American Academy of Pediatrics and the American College of Obstetricians and Gynecologists \(2017\)](#) recommend that all women be screened for chlamydia during the first prenatal visit, with additional third-trimester testing for those at increased risk. Risk factors include unmarried status, recent change in sexual partner or multiple concurrent partners, age younger than 25 years, inner-city residence, history or presence of other sexually transmitted diseases, and little or no prenatal care. For those testing positive, treatment described in [Chapter 65 \(Chlamydial Infections\)](#) is followed by a second testing—a *test of cure*—3 to 4 weeks after treatment completion.

Neisseria gonorrhoeae typically causes lower genital tract infection in pregnancy. It also may cause septic arthritis ([Bleich, 2012](#)). Risk factors for gonorrhea are similar to those for chlamydial infection. The [American Academy of Pediatrics and the American College of Obstetricians and Gynecologists \(2017\)](#) recommend that pregnant women with risk factors or those living in an area of high *N gonorrhoeae* prevalence be screened at the initial prenatal visit and again in the third trimester. Treatment is given for gonorrhea and simultaneously for possible coexisting chlamydial infection ([Chap. 65, Chlamydial Infections](#)). Test of cure is also recommended following treatment.

Pregnancy Risk Assessment

Many factors can adversely affect maternal and fetal well-being. Some are evident at conception, but many become apparent during the course of pregnancy. The designation of “high-risk pregnancy” is overly vague for an individual woman and probably is best avoided if a more specific diagnosis can be assigned. Some common risk factors for which consultation is recommended by the [American Academy of Pediatrics and the American College of Obstetricians and Gynecologists \(2017\)](#) are shown in [Table 9-3](#). Some conditions may require the involvement of a maternal-fetal medicine subspecialist, geneticist, pediatrician, anesthesiologist, or other medical specialist in the evaluation, counseling, and care of the woman and her fetus.

TABLE 9-3

Conditions for Which Maternal-Fetal Medicine Consultation May Be Beneficial

Medical History and Conditions
Cardiac disease—moderate to severe disorders Diabetes mellitus with evidence of end-organ damage or uncontrolled hyperglycemia Family or personal history of genetic abnormalities Hemoglobinopathy Chronic hypertension if uncontrolled or associated with renal or cardiac disease Renal insufficiency if associated with significant proteinuria (≥ 500 mg/24 hour), serum creatinine ≥ 1.5 mg/dL, or hypertension Pulmonary disease if severe restrictive or obstructive, including severe asthma Human immunodeficiency virus infection Prior pulmonary embolus or deep-vein thrombosis Severe systemic disease, including autoimmune conditions Bariatric surgery Epilepsy if poorly controlled or requires more than one anticonvulsant Cancer, especially if treatment is indicated in pregnancy
Obstetrical History and Conditions
CDE (Rh) or other blood group alloimmunization (excluding ABO, Lewis) Prior or current fetal structural or chromosomal abnormality Desire or need for prenatal diagnosis or fetal therapy Periconceptual exposure to known teratogens Infection with or exposure to organisms that cause congenital infection Higher-order multifetal gestation Severe disorders of amniotic fluid volume

SUBSEQUENT PRENATAL VISITS

These are traditionally scheduled at 4-week intervals until 28 weeks, then every 2 weeks until 36 weeks, and weekly thereafter. Women with complicated pregnancies—for example, with twins or diabetes—often require return visits at 1- to 2-week intervals (Luke, 2003; Power, 2013). In 1986, the Department of Health and Human Services convened an expert panel to review the content of prenatal care. This report was subsequently reevaluated and revised in 2005 (Gregory, 2006). The panel recommended, among other things, early and continuing risk assessment that is patient specific. It also endorsed flexibility in clinical visit spacing; health promotion and education, including preconceptional care; medical and psychosocial interventions; standardized documentation; and expanded prenatal care objectives—to include family health up to 1 year after birth.

The World Health Organization conducted a multicenter randomized trial with almost 25,000 women comparing routine prenatal care with an experimental model designed to minimize visits (Villar, 2001). In the new model, women were seen once in the first trimester and screened for certain risks. Those without anticipated complications—80 percent of those screened—were seen again at 26, 32, and 38 weeks. Compared with routine prenatal care, which required a median of eight visits, the new model required a median of only five. No disadvantages were attributed to the regimen with fewer visits, and these findings were consistent with other randomized trials (Clement, 1999; McDuffie, 1996).

Prenatal Surveillance

At each return visit, the well-being of mother and fetus are assessed (see Table 9-1). Fetal heart rate, growth, and activity and amniotic fluid volume are evaluated. Maternal blood pressure and weight and their extent of change are examined. Symptoms such as headache, altered vision, abdominal pain,

nausea and vomiting, bleeding, vaginal fluid leakage, and dysuria are sought. After 20 weeks' gestation, uterine examination measures size from the symphysis to the fundus. In late pregnancy, vaginal examination often provides valuable information that includes confirmation of the presenting part and its station, clinical estimation of pelvic capacity and configuration, amniotic fluid volume adequacy, and cervical consistency, effacement, and dilatation ([Chap. 22, Identification of Labor](#)).

Fundal Height

Between 20 and 34 weeks' gestation, the height of the uterine fundus measured in centimeters correlates closely with gestational age in weeks ([Jimenez, 1983](#)). This measurement is used to monitor fetal growth and amniotic fluid volume. It is measured along the abdominal wall from the top of the symphysis pubis to the top of the fundus. Importantly, the bladder must be emptied before fundal measurement ([Worthen, 1980](#)). Obesity or the presence of uterine masses such as leiomyomas may also limit fundal height accuracy. Moreover, using fundal height alone, fetal-growth restriction may be undiagnosed in up to a third of cases ([American College of Obstetricians and Gynecologists, 2015b](#); [Haragan, 2015](#)).

Fetal Heart Sounds

Instruments incorporating Doppler ultrasound are often used to easily detect fetal heart action, and in the absence of maternal obesity, heart sounds are almost always detectable by 10 weeks with such instruments ([Chap. 10, Doppler](#)). The fetal heart rate ranges from 110 to 160 beats per minute and is typically heard as a double sound. Using a standard nonamplified stethoscope, the fetal heart is audible by 20 weeks in 80 percent of women, and by 22 weeks, heart sounds are expected to be heard in all ([Herbert, 1987](#)). Because the fetus moves freely in amniotic fluid, the site on the maternal abdomen where fetal heart sounds can be heard best will vary.

Additionally, with ultrasonic auscultation, one may hear the *funic souffle*, which is a sharp, whistling sound that is synchronous with the fetal pulse. It is caused by the rush of blood through the umbilical arteries and may not be heard consistently. In contrast, the *uterine souffle* is a soft, blowing sound that is synchronous with the maternal pulse. It is produced by the passage of blood through the dilated uterine vessels and is heard most distinctly near the lower portion of the uterus.

Sonography

Sonography provides invaluable information regarding fetal anatomy, growth, and well-being, and most women in the United States have at least one prenatal sonographic examination during pregnancy ([American College of Obstetricians and Gynecologists, 2016h](#)). Continuing trends suggest that the number of these examinations performed per pregnancy is increasing. [Siddique and associates \(2009\)](#) reported that the average number rose from 1.5 in 1995 through 1997 to 2.7 almost 10 years later. This trend was noted in both high- and low-risk pregnancies. The actual clinical utility of this increased use in pregnancy has not been demonstrated, and it is unclear that the cost-benefit ratio is justified ([Washington State Health Care Authority, 2010](#)). The [American College of Obstetricians and Gynecologists \(2016h\)](#) has concluded that sonography should be performed only when there is a valid medical indication and under the lowest possible ultrasound exposure setting. The College further states that a physician is not obligated to perform sonography without a specific indication in a low-risk patient, but that if she requests sonographic screening, it is reasonable to honor her request.

Subsequent Laboratory Tests

If initial results were normal, most tests need not be repeated. Hematocrit or hemoglobin determination, along with serology for syphilis if it is prevalent in the population, is repeated at 28 to 32 weeks ([Hollier, 2003](#); [Kiss, 2004](#)). For women at increased risk for HIV acquisition during pregnancy, repeat testing is recommended in the third trimester, preferably before 36 weeks ([American College of Obstetricians and Gynecologists, 2016f](#)). Similarly, women who engage in behaviors that place them at high risk for hepatitis B virus infection are retested at the time of hospitalization for delivery. Women who are D (Rh) negative and are unsensitized should have an antibody screening test repeated at 28 to 29 weeks, and anti-D immunoglobulin is given if they remain unsensitized ([Chap. 15, Prevention of Anti-D Alloimmunization](#)).

Group B Streptococcal Infection

The [CDC \(2010b\)](#) recommends that vaginal and rectal group B streptococcal (GBS) cultures be obtained in all women between 35 and 37 weeks' gestation, and the [American College of Obstetricians and Gynecologists \(2016g\)](#) has endorsed this recommendation. Intrapartum antimicrobial

prophylaxis is provided to those whose culture results are positive. Women with GBS bacteriuria or a previous infant with invasive disease are given empirical intrapartum prophylaxis. Trials are in progress to test an investigational vaccine (Donders, 2016; Schrag, 2016). These infections are described further in [Chapter 64 \(Bacterial Infections\)](#).

Gestational Diabetes

All pregnant women are screened for gestational diabetes mellitus, whether by history, clinical factors, or routine laboratory testing. Although laboratory testing between 24 and 28 weeks' gestation is the most sensitive approach, there may be pregnant women at low risk who are less likely to benefit from testing ([American College of Obstetricians and Gynecologists, 2017c](#)). Gestational diabetes is discussed in [Chapter 57 \(Gestational Diabetes\)](#).

Neural-Tube Defect and Genetic Screening

Serum screening for neural-tube defects is offered at 15 to 20 weeks. Fetal aneuploidy screening may be performed at 11 to 14 weeks' gestation and/or at 15 to 20 weeks, depending on the protocol selected ([Rink, 2016](#)). Additionally, screening for certain genetic abnormalities is offered to women at increased risk based on family history, ethnic or racial background, or age ([American College of Obstetricians and Gynecologists, 2017h](#)). These are discussed in greater detail in [Chapter 14 \(Historical Perspective\)](#). Some examples include testing for Tay-Sachs disease for persons of Eastern European Jewish or French Canadian ancestry; β -thalassemia for those of Mediterranean, Southeast Asian, Indian, Pakistani, or African ancestry; α -thalassemia for individuals of Southeast Asian or African ancestry; sickle-cell anemia for people of African, Mediterranean, Middle Eastern, Caribbean, Latin American, or Indian descent; and trisomy 21 for those with advanced maternal age.

NUTRITIONAL COUNSELING

Weight Gain Recommendations

In 2009, the Institute of Medicine and National Research Council revised guidelines for weight gain in pregnancy and continued to stratify suggested weight gain ranges based on prepregnancy body mass index (BMI) ([Table 9-4](#)). The new guidelines included a specific, relatively narrow range of recommended weight gains for obese women. Also, the same recommendations apply to adolescents, short women, and women of all racial and ethnic groups. The [American College of Obstetricians and Gynecologists \(2016i\)](#) has endorsed these measures.

TABLE 9-4

Recommendations for Total and Rate of Weight Gain During Pregnancy

Category (BMI)	Total Weight Gain Range (lb) ^a	Weight Gain in 2nd and 3rd Trimesters Mean in lb/wk (range)
Underweight (<18.5)	28–40	1 (1–1.3)
Normal weight (18.5–24.9)	25–35	1 (0.8–1)
Overweight (25.0–29.9)	15–25	0.6 (0.5–0.7)
Obese (\geq 30.0)	11–20	0.5 (0.4–0.6)

^aEmpirical recommendations for weight gain in twin pregnancies include: normal BMI, 37–54 lb; overweight women, 31–50 lb; and obese women, 25–42 lb.

BMI = body mass index.

Modified from the [Institute of Medicine and National Research Council, 2009](#).

When the Institute of Medicine guidelines were formulated, concern focused on low-birthweight newborns, however, current emphasis is directed to

the obesity epidemic (Catalano, 2007). This explains renewed interest in *lower* weight gains during pregnancy. Obesity is associated with significantly greater risks for gestational hypertension, preeclampsia, gestational diabetes, macrosomia, cesarean delivery, and other complications (Chap. 48, *Maternal Morbidity*). The risk appears “dose related” to prenatal weight gain. In a population-based cohort of more than 120,000 obese pregnant women, those who gained <15 lb had the lowest rates of preeclampsia, large-for-gestational age neonates, and cesarean delivery (Kiel, 2007). Among 100,000 women with normal prepregnancy BMI, DeVader and colleagues (2007) found that those who gained <25 lb during pregnancy had a lower risk for preeclampsia, failed induction, cephalopelvic disproportion, cesarean delivery, and large-for-gestational age neonates. This cohort, however, had an increased risk for small-for-gestational age newborns. Lifestyle intervention during pregnancy can result in less weight gain (Sagedal, 2017).

There is irrefutable evidence that maternal weight gain during pregnancy influences birthweight. Martin and coworkers (2009) studied this using birth certificate data for 2006. Approximately 60 percent of women gained 26 lb or more during pregnancy, and maternal weight gain positively correlated with birthweight. Moreover, women with the greatest risk—14 percent—for delivering a newborn weighing <2500 g were those with weight gain <16 lb. Nearly 20 percent of births to women with such low weight gains were preterm.

Severe Undernutrition

Meaningful studies of nutrition in human pregnancy are exceedingly difficult to design because experimental dietary deficiency is not ethical. In those instances in which severe nutritional deficiencies have been induced as a consequence of social, economic, or political disaster, coincidental events have often created many variables, the effects of which are not amenable to quantification. Some past experiences suggest, however, that in otherwise healthy women, a state of near starvation is required to establish clear differences in pregnancy outcome.

During the severe European winter of 1944 to 1945, nutritional deprivation of known intensity prevailed in a well-circumscribed area of The Netherlands occupied by the German military (Kyle, 2006). At the lowest point during this Dutch Hunger Winter, rations reached 450 kcal/d, with generalized rather than selective malnutrition. Smith (1947) analyzed the outcomes of pregnancies that were in progress during this 6-month famine. Median neonatal birthweights declined approximately 250 g and rose again after food became available. This indicated that birthweight can be influenced significantly by starvation during later pregnancy. The perinatal mortality rate, however, was not altered. Moreover, the incidence of fetal malformations or preeclampsia did not rise significantly. Parenthetically, weight loss in obese women during pregnancy is also associated with an increased risk for low-birthweight neonates (Cox Bauer, 2016).

Evidence of impaired brain development has been obtained in some animal fetuses whose mothers had been subjected to intense dietary deprivation. Subsequent intellectual development was studied by Stein and associates (1972) in young male adults whose mothers had been starved during pregnancy in the aforementioned Hunger Winter. The comprehensive study was made possible because all males at age 19 underwent compulsory examination for military service. It was concluded that severe dietary deprivation during pregnancy caused no detectable effects on subsequent mental performance.

Several studies of the long-term consequences to this cohort of children born to nutritionally deprived women have been performed and have been reviewed by Kyle and Pichard (2006). Progeny deprived in mid to late pregnancy were lighter, shorter, and thinner at birth, and they had a higher incidences of subsequent hypertension, reactive airway disease, dyslipidemia, diminished glucose tolerance, and coronary artery disease. Early pregnancy deprivation was associated with greater obesity rates in adult women but not men. Early starvation was also linked to higher rates of central nervous system anomalies, schizophrenia, and schizophrenia-spectrum personality disorders.

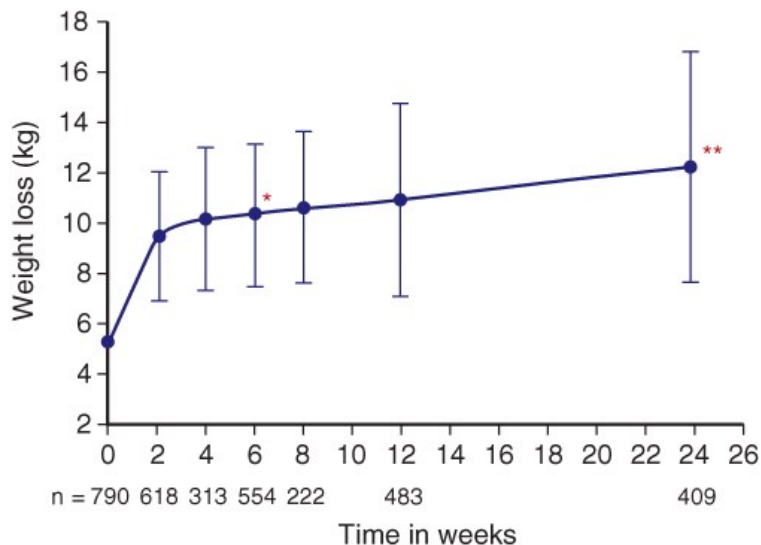
These observations and others have led to the concept of *fetal programming* by which adult morbidity and mortality are related to fetal health. Known widely as the *Barker hypothesis*, as promulgated by Barker and colleagues (1989), this concept is discussed in Chapter 44 (*Placental Abnormalities*).

Weight Retention after Pregnancy

Not all the weight gained during pregnancy is lost during and immediately after delivery. Schaubeger and coworkers (1992) studied prenatal and postpartum weights in 795 women. Their average weight gain was 28.6 lb or 12.9 kg. As shown in Figure 9-4, most maternal weight loss was at delivery—approximately 12 lb or 5.4 kg—and in the ensuing 2 weeks—approximately 9 lb or 4 kg. An additional 5.5 lb or 2.5 kg was lost between 2 weeks and 6 months postpartum. Thus, average retained pregnancy weight was 2.1 lb or 1 kg. Excessive weight gain is manifest by accrual of fat and may be partially retained as long-term fat (Berggren, 2016; Widen, 2015). Overall, the more weight that was gained during pregnancy, the more that was lost postpartum. Interestingly, there is no relationship between prepregnancy BMI or prenatal weight gain and weight retention.

FIGURE 9-4

Cumulative weight loss from last antepartum visit to 6 months postpartum. *Significantly different from 2-week weight loss; **Significantly different from 6-week weight loss. (Redrawn from Schauberger CW, Rooney BL, Brimer LM: Factors that influence weight loss in the puerperium. *Obstet Gynecol* 79:424, 1992.)



Source: F. Gary Cunningham, Kenneth J. Leveno, Steven L. Bloom, Catherine Y. Spong, Jodi S. Dashe, Barbara L. Hoffman, Brian M. Casey, Jeanne S. Sheffield: *Williams Obstetrics*, 25th Edition. Copyright © McGraw-Hill Education. All rights reserved.

Dietary Reference Intakes—Recommended Allowances

Periodically, the Institute of Medicine (2006, 2011) publishes recommended dietary allowances, including those for pregnant or lactating women. The latest recommendations are summarized in Table 9-5. Certain prenatal vitamin–mineral supplements may lead to intakes well in excess of the recommended allowances. Moreover, the use of excessive supplements, which often are self-prescribed, has led to concern regarding nutrient toxicities during pregnancy. *Those with potentially toxic effects include iron, zinc, selenium, and vitamins A, B₆, C, and D.*

TABLE 9-5

Recommended Daily Dietary Allowances for Pregnant and Lactating Women

	Pregnant	Lactating
Fat-Soluble Vitamins		
Vitamin A	770 µg	1300 µg
Vitamin D _a	15 µg	15 µg
Vitamin E	15 mg	19 mg
Vitamin K _a	90 µg	90 µg
Water-Soluble Vitamins		
Vitamin C	85 mg	120 mg

Thiamine	1.4 mg	1.4 mg
Riboflavin	1.4 mg	1.6 mg
Niacin	18 mg	17 mg
Vitamin B ₆	1.9 mg	2 mg
Folate	600 µg	500 µg
Vitamin B ₁₂	2.6 µg	2.8 µg
Minerals		
Calciuma	1000 mg	1000 mg
Sodiuma	1.5 g	1.5 g
Potassiuma	4.7 g	5.1 g
Iron	27 mg	9 mg
Zinc	11 mg	12 mg
Iodine	220 µg	290 µg
Selenium	60 µg	70 µg
Other		
Protein	71 g	71 g
Carbohydrate	175 g	210 g
Fibera	28 g	29 g

^aRecommendations measured as adequate intake.

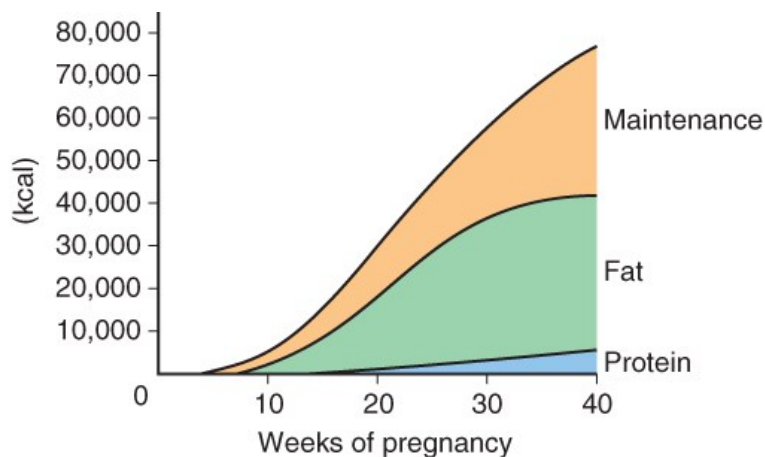
From the [Institute of Medicine, 2006, 2011](#).

Calories

As shown in [Figure 9-5](#), pregnancy requires an additional 80,000 kcal, mostly during the last 20 weeks. To meet this demand, a caloric increase of 100 to 300 kcal/d is recommended during pregnancy ([American Academy of Pediatrics and the American College of Obstetricians and Gynecologists, 2017](#)). This greater intake, however, should not be divided equally during the course of pregnancy. The [Institute of Medicine \(2006\)](#) recommends adding 0, 340, and 452 kcal/d to the estimated nonpregnant energy requirements in the first, second, and third trimesters, respectively. The addition of 1000 kcal/d or more results in fat accrual ([Jebeile, 2015](#)).

FIGURE 9-5

Cumulative kilocalories required for pregnancy. (Redrawn from Chamberlain G, Broughton-Pipkin F (eds): *Clinical Physiology in Obstetrics*, 3rd ed. Oxford, Blackwell Science, 1998.)



Source: F. Gary Cunningham, Kenneth J. Leveno, Steven L. Bloom, Catherine Y. Spong, Jodi S. Dashe, Barbara L. Hoffman, Brian M. Casey, Jeanne S. Sheffield: *Williams Obstetrics*, 25th Edition
Copyright © McGraw-Hill Education. All rights reserved.

Calories are necessary for energy. Whenever caloric intake is inadequate, protein is metabolized rather than being spared for its vital role in fetal growth and development. Total physiological requirements during pregnancy are not necessarily the sum of ordinary nonpregnant requirements plus those specific to pregnancy. For example, the additional energy required during pregnancy may be compensated in whole or in part by reduced physical activity (Hyttén, 1991).

Protein

Protein requirements rise to meet the demands for growth and remodeling of the fetus, placenta, uterus, and breasts, and for increased maternal blood volume (Chap. 4, [Protein Metabolism](#)). During the second half of pregnancy, approximately 1000 g of protein are deposited, amounting to 5 to 6 g/d (Hyttén, 1971). To accomplish this, protein intake that approximates 1 g/kg/d is recommended (see [Table 9-5](#)). Data suggest this should be doubled in late gestation (Stephens, 2015). Most amino-acid levels in maternal plasma fall markedly, including ornithine, glycine, taurine, and proline (Hyttén, 1991). Exceptions during pregnancy are glutamic acid and alanine, the concentrations of which rise.

Preferably, most protein is supplied from animal sources, such as meat, milk, eggs, cheese, poultry, and fish. These furnish amino acids in optimal combinations. Milk and dairy products are considered nearly ideal sources of nutrients, especially protein and calcium, for pregnant or lactating women. Ingestion of specific fish and potential methylmercury toxicity are discussed in [Common Concerns](#).

Minerals

The intakes recommended by the [Institute of Medicine \(2006\)](#) for various minerals are listed in [Table 9-5](#). With the exception of iron and iodine, practically all diets that supply sufficient calories for appropriate weight gain will contain enough minerals to prevent deficiency.

Iron requirements are greatly increased during pregnancy, and reasons for this are discussed in [Chapter 4 \(Iron Metabolism\)](#). Of the approximately 300 mg of iron transferred to the fetus and placenta and the 500 mg incorporated into the expanding maternal hemoglobin mass, nearly all is used after midpregnancy. During that time, iron requirements imposed by pregnancy and maternal excretion total approximately 7 mg/d (Pritchard, 1970). Few women have sufficient iron stores or dietary intake to supply this amount. Thus, the [American Academy of Pediatrics and the American College of Obstetricians and Gynecologists \(2017\)](#) endorse the recommendation by the National Academy of Sciences that at least 27 mg of elemental iron be supplemented daily to pregnant women. This amount is contained in most prenatal [vitamins](#).

[Scott and coworkers \(1970\)](#) established that as little as 30 mg of elemental iron, supplied as ferrous gluconate, sulfate, or fumarate and taken daily throughout the latter half of pregnancy, provides sufficient iron to meet pregnancy requirements and protect preexisting iron stores. This amount will also provide for iron requirements of lactation. The pregnant woman may benefit from 60 to 100 mg of elemental iron per day if she is large, has a multifetal gestation, begins supplementation late in pregnancy, takes iron irregularly, or has a somewhat depressed hemoglobin level. The woman who is overtly anemic from iron deficiency responds well to oral supplementation with iron salts. In response, serum ferritin levels rise more than the

hemoglobin concentration (Daru, 2016).

Iodine is also needed, and the recommended iodine allowance is 220 µg/d (see [Table 9-5](#)). The use of iodized salt and bread products is recommended during pregnancy to offset the increased fetal requirements and maternal renal losses of iodine. Despite this, iodine intake has declined substantially in the past 15 years, and in some areas it is probably inadequate (Casey, 2017). Severe maternal iodine deficiency predisposes offspring to endemic cretinism, which is characterized by multiple severe neurological defects. In parts of China and Africa where this condition is common, iodide supplementation very early in pregnancy prevents some cretinism cases (Cao, 1994). To obviate this, many prenatal supplements now contain various quantities of iodine.

Calcium is retained by the pregnant woman during gestation and approximates 30 g. Most of this is deposited in the fetus late in pregnancy (Pitkin, 1985). This amount of calcium represents only approximately 2.5 percent of total maternal calcium, most of which is in bone and can readily be mobilized for fetal growth. As another potential use, routine calcium supplementation to prevent preeclampsia has not proved effective (Chap. 40, [Antihypertensive Drugs](#)).

Zinc deficiency if severe may lead to poor appetite, suboptimal growth, and impaired wound healing. During pregnancy, the recommended daily intake approximates 12 mg. But, the safe level of zinc supplementation for pregnant women has not been clearly established. Vegetarians have lower zinc intakes (Foster, 2015). The bulk of studies support zinc supplementation only in zinc-deficient women in poor-resource countries (Nossier, 2015; Ota, 2015).

Magnesium deficiency as a consequence of pregnancy has not been recognized. Undoubtedly, during prolonged illness with no magnesium intake, the plasma level might become critically low, as it would in the absence of pregnancy. We have observed magnesium deficiency during pregnancies in some with previous intestinal bypass surgery. As a preventive agent, Sibai and coworkers (1989) randomly assigned 400 normotensive primigravid women to 365-mg elemental magnesium supplementation or placebo tablets from 13 to 24 weeks' gestation. Supplementation did not improve any measures of pregnancy outcome.

Trace metals include copper, selenium, chromium, and manganese, which all have important roles in certain enzyme functions. In general, most are provided by an average diet. Selenium deficiency is manifested by a frequently fatal cardiomyopathy in young children and reproductive-aged women. Conversely, selenium toxicity resulting from oversupplementation also has been observed. Selenium supplementation is not needed in American women.

Potassium concentrations in maternal plasma decline by approximately 0.5 mEq/L by midpregnancy (Brown, 1986). Potassium deficiency develops in the same circumstances as in nonpregnant individuals—a common example is hyperemesis gravidarum.

Fluoride metabolism is not altered appreciably during pregnancy (Maheshwari, 1983). Horowitz and Heifetz (1967) concluded that no additional offspring benefits accrued from maternal ingestion of fluoridated water if the newborn ingested such water from birth. Sa Roriz Fonteles and associates (2005) studied microdrill biopsies of deciduous teeth and concluded that antenatal fluoride provided no additional fluoride uptake compared with postnatal fluoride alone. Finally, supplemental fluoride ingested by lactating women does not raise the fluoride concentration in breast milk (Ekstrand, 1981).

Vitamins

The increased requirements for most vitamins during pregnancy shown in [Table 9-5](#) usually are supplied by any general diet that provides adequate calories and protein. The exception is folic acid during times of unusual requirements, such as pregnancy complicated by protracted vomiting, hemolytic anemia, or multiple fetuses. That said, in impoverished countries, routine multivitamin supplementation reduced the incidence of low-birthweight and growth-restricted fetuses, but did not alter preterm delivery or perinatal mortality rates (Fawzi, 2007).

Folic acid supplementation in early pregnancy can lower neural-tube defect risks (Chap. 13, [Genetic Tests](#)). Namely, the CDC (2004) estimated that the number of affected pregnancies had decreased from 4000 pregnancies per year to approximately 3000 per year after mandatory fortification of cereal products with folic acid in 1998. Perhaps more than half of all neural-tube defects can be prevented with daily intake of 400 µg of folic acid throughout the periconceptional period. Evidence also suggests that folate insufficiency has a global effect on brain development (Ars, 2016). Putting 140 µg of folic acid into each 100 g of grain products may increase the folic acid intake of the average American woman of childbearing age by 100 µg/d. Because nutritional sources alone are insufficient, however, folic acid supplementation is still recommended (American College of Obstetricians and

Gynecologists, 2016e). Likewise, the U.S. Preventive Services Task Force (2009) recommends that all women planning or capable of pregnancy take a daily supplement containing 400 to 800 µg of folic acid.

A woman with a prior child with a neural-tube defect can reduce the 2- to 5-percent recurrence risk by more than 70 percent with a daily 4-mg folic acid supplement taken during the month before conception and during the first trimester. As emphasized by the American Academy of Pediatrics and the American College of Obstetricians and Gynecologists (2017), this dose should be consumed as a separate supplement and not as multivitamin tablets. This practice avoids excessive intake of fat-soluble vitamins.

Vitamin A, although essential, has been associated with congenital malformations when taken in high doses (>10,000 IU/d) during pregnancy. These malformations are similar to those produced by the *vitamin A* derivative isotretinoin (Accutane), which is a potent teratogen (Chap. 12, Retinoids). Beta-carotene, the precursor of *vitamin A* found in fruits and vegetables, has not been shown to produce *vitamin A* toxicity. Most prenatal vitamins contain *vitamin A* in doses considerably below the teratogenic threshold. Dietary intake of *vitamin A* in the United States appears to be adequate, and additional supplementation is not routinely recommended. In contrast, *vitamin A* deficiency is an endemic nutritional problem in the developing world (McCauley, 2015). *Vitamin A* deficiency, whether overt or subclinical, is associated with night blindness and with an increased risk of maternal anemia and spontaneous preterm birth (West, 2003).

Vitamin B₁₂ plasma levels drop in normal pregnancy, mostly as a result of reduced plasma levels of their carrier proteins—*transcobalamins*. *Vitamin B₁₂* occurs naturally only in foods of animal origin, and strict vegetarians may give birth to neonates whose *B₁₂* stores are low. Likewise, because breast milk of a vegetarian mother contains little *vitamin B₁₂*, the deficiency may become profound in the breastfed infant (Higginbottom, 1978). Excessive ingestion of *vitamin C* also can lead to a functional deficiency of *vitamin B₁₂*. Although its role is still controversial, *vitamin B₁₂* deficiency preconceptionally, similar to folate, may elevate the risk of neural-tube defects (Molloy, 2009).

Vitamin B₆, which is pyridoxine, does not require supplementation in most gravidas (Salam, 2015). For women at high risk for inadequate nutrition, a daily 2-mg supplement is recommended. As discussed in Caffeine, *vitamin B₆*, when combined with the antihistamine *doxylamine*, is helpful in many cases of nausea and vomiting of pregnancy.

Vitamin C allowances during pregnancy are 80 to 85 mg/d—approximately 20 percent more than when nonpregnant (see Table 9-5). A reasonable diet should readily provide this amount, and supplementation is not necessary (Rumbold, 2015). Maternal plasma levels decline during pregnancy, whereas cord-blood levels are higher, a phenomenon observed with most water-soluble vitamins.

Vitamin D is a fat-soluble vitamin. After being metabolized to its active form, it boosts the efficiency of intestinal calcium absorption and promotes bone mineralization and growth. Unlike most vitamins that are obtained exclusively from dietary intake, *vitamin D* is also synthesized endogenously with exposure to sunlight. *Vitamin D* deficiency is common during pregnancy. This is especially true in high-risk groups such as women with limited sun exposure, vegetarians, and ethnic minorities—particularly those with darker skin (Bodnar, 2007). Maternal deficiency can cause disordered skeletal homeostasis, congenital rickets, and fractures in the newborn (American College of Obstetricians and Gynecologists, 2017k). *Vitamin D* supplementation to women with asthma may decrease the likelihood of childhood asthma in their fetuses (Litonjua, 2016). The Food and Nutrition Board of the Institute of Medicine (2011) established that an adequate intake of *vitamin D* during pregnancy and lactation was 15 µg/d (600 IU/d). In women suspected of having *vitamin D* deficiency, serum levels of 25-hydroxyvitamin D can be obtained. Even then, the optimal levels in pregnancy have not been established (De-Regil, 2016).

Pragmatic Nutritional Surveillance

Although researchers continue to study the ideal nutritional regimen for the pregnant woman and her fetus, basic tenets for the clinician include:

1. Advise the pregnant woman to eat food types she wants in reasonable amounts and salted to taste.
2. Ensure that food is amply available for socioeconomically deprived women.
3. Monitor weight gain, with a goal of approximately 25 to 35 lb in women with a normal BMI.
4. Explore food intake by dietary recall periodically to discover the occasional nutritionally errant diet.

5. Give tablets of simple iron salts that provide at least 27 mg of elemental iron daily. Give folate supplementation before and in the early weeks of pregnancy. Provide iodine supplementation in areas of known dietary insufficiency.
6. Recheck the hematocrit or hemoglobin concentration at 28 to 32 weeks' gestation to detect significant anemia.

COMMON CONCERNS

Employment

More than half of the children in the United States are born to working mothers. Federal law prohibits employers from excluding women from job categories on the basis that they are or might become pregnant. The Family and Medical Leave Act of 1993 requires that covered employers must grant up to 12 work weeks of unpaid leave to an employee for the birth and care of a newborn child (Jackson, 2015). In the absence of complications, most women can continue to work until the onset of labor (American Academy of Pediatrics and the American College of Obstetricians and Gynecologists, 2017).

Some types of work, however, may increase pregnancy complication risks. Mozurkewich and colleagues (2000) reviewed 29 studies that involved more than 160,000 pregnancies. With physically demanding work, women had 20- to 60-percent higher rates of preterm birth, fetal-growth restriction, or gestational hypertension. In a prospective study of more than 900 healthy nulliparas, women who worked had a fivefold risk of preeclampsia (Higgins, 2002). Newman and coworkers (2001) reported outcomes in more than 2900 women with singleton pregnancies. Occupational fatigue—estimated by the number of hours standing, intensity of physical and mental demands, and environmental stressors—was associated with an increased risk of preterm premature membrane rupture. For women reporting the highest degrees of fatigue, the risk was 7.4 percent.

Thus, any occupation that subjects the gravida to severe physical strain should be avoided. Ideally, no work or play is continued to the extent that undue fatigue develops. Adequate periods of rest should be provided. It seems prudent to advise women with prior pregnancy complications that commonly recur to minimize physical work.

Exercise

In general, pregnant women do not need to limit exercise, provided they do not become excessively fatigued or risk injury (Davenport, 2016). Clapp and associates (2000) reported that both placental size and birthweight were significantly greater in women who exercised. Duncombe and coworkers (2006) reported similar findings in 148 women. In contrast, Magann and colleagues (2002) prospectively analyzed exercise behavior in 750 healthy women and found that working women who exercised had smaller infants and more dysfunctional labors.

The American College of Obstetricians and Gynecologists (2017g) advises a thorough clinical evaluation before recommending an exercise program. In the absence of contraindications listed in Table 9-6, pregnant women are encouraged to engage in regular, moderate-intensity physical activity for at least 150 minutes each week. Each activity should be reviewed individually for its potential risk. Examples of safe activities are walking, running, swimming, stationary cycling, and low-impact aerobics. However, they should refrain from activities with a high risk of falling or abdominal trauma. Similarly, scuba diving is avoided because the fetus is at increased risk for decompression sickness.

TABLE 9-6

Some Contraindications to Exercise During Pregnancy

Significant cardiovascular or pulmonary disease
Significant risk for preterm labor: cerclage, multifetal gestation, significant bleeding, threatened preterm labor, prematurely ruptured membranes
Obstetrical complications: preeclampsia, placenta previa, anemia, poorly controlled diabetes or epilepsy, morbid obesity, fetal-growth restriction

Summarized from American College of Obstetricians and Gynecologists, 2017g.

In the setting of certain pregnancy complications, it is wise to abstain from exercise and even limit physical activity. For example, some women with

pregnancy-associated hypertensive disorders, preterm labor, placenta previa, or severe cardiac or pulmonary disease may gain from being sedentary. Also, those with multiple or suspected growth-restricted fetuses may be served by greater rest.

Seafood Consumption

Fish are an excellent source of protein, are low in saturated fats, and contain omega-3 fatty acids. The Avon Longitudinal Study of Parents and Children reported beneficial effects on pregnancy outcomes in women who consumed 340 g or more of seafood weekly (Hibbeln, 2007). Because nearly all fish and shellfish contain trace amounts of mercury, pregnant and lactating women are advised to avoid specific types of fish with potentially high methylmercury levels. These include shark, swordfish, king mackerel, and tile fish. It is further recommended that pregnant women ingest 8 to 12 ounces of fish weekly, but no more than 6 ounces of albacore or “white” tuna (U.S. Environmental Protection Agency, 2014). If the mercury content of locally caught fish is unknown, then overall fish consumption should be limited to 6 ounces per week (American Academy of Pediatrics and the American College of Obstetricians and Gynecologists, 2017).

Lead Screening

Maternal lead exposure has been associated with several adverse maternal and fetal outcomes across a range of maternal blood lead levels (Taylor, 2015). These include gestational hypertension, miscarriage, low birthweight, and neurodevelopmental impairments in exposed pregnancies (American College of Obstetricians and Gynecologists, 2016c). The levels at which these risks rise remains unclear. However, recognizing that such exposure remains a significant health issue for reproductive-aged women, the CDC (2010a) has issued guidance for screening and managing exposed pregnant and lactating women. These guidelines, which have been endorsed by the American College of Obstetricians and Gynecologists (2016c), recommend blood lead testing only if a risk factor is identified. If the levels are >5 $\mu\text{g}/\text{dL}$, then counseling is completed, and the lead source is sought and removed. Subsequent blood levels are obtained. Blood lead levels >45 $\mu\text{g}/\text{dL}$ are consistent with lead poisoning, and women in this group may be candidates for chelation therapy. Affected pregnancies are best managed in consultation with lead poisoning treatment experts. National and state resources are available at the CDC website: www.cdc.gov/nceh/lead/.

Automobile and Air Travel

Pregnant women are encouraged to wear properly positioned three-point restraints as protection against automobile crash injury (Chap. 47, Other Blunt Trauma). The lap portion of the restraining belt is placed under the abdomen and across her upper thighs. The belt should be comfortably snug. The shoulder belt also is firmly positioned between the breasts. Airbags should not be disabled for the pregnant woman.

In general, air travel in a properly pressurized aircraft has no harmful effect on pregnancy (Aerospace Medical Association, 2003). Thus, in the absence of obstetrical or medical complications, the American Academy of Pediatrics and the American College of Obstetricians and Gynecologists (2016a, 2017) have concluded that pregnant women can safely fly up to 36 weeks' gestation. It is recommended that pregnant women observe the same precautions for air travel as the general population. Seatbelts are used while seated. Periodic lower extremity movement and at least hourly ambulation help lower the venous thromboembolism threat. Significant risks with travel, especially international travel, are infectious disease acquisition and development of complications remote from adequate health-care resources (Ryan, 2002).

Coitus

In healthy pregnant women, sexual intercourse usually is not harmful. Whenever miscarriage, placenta previa, or preterm labor threatens, however, coitus is avoided. Nearly 10,000 women enrolled in a prospective investigation by the Vaginal Infection and Prematurity Study Group were interviewed regarding sexual activity (Read, 1993). They reported a decreased frequency of coitus with advancing gestation. By 36 weeks, 72 percent had intercourse less than once weekly. The decline is attributed to lower desire and fear of harming the pregnancy (Bartellas, 2000; Staruch, 2016).

Intercourse specifically late in pregnancy is not harmful. Grudzinskas and coworkers (1979) noted no association between gestational age at delivery and coital frequency during the last 4 weeks of pregnancy. Sayle and colleagues (2001) reported no increased—and actually a decreased—risk of delivery within 2 weeks of intercourse. Tan and associates (2007) studied women scheduled for nonurgent labor induction and found that spontaneous labor ensued at equal rates in groups either participating in or abstaining from intercourse.

Oral-vaginal intercourse is occasionally hazardous. Aronson and Nelson (1967) described a fatal air embolism late in pregnancy as a result of air blown into the vagina during cunnilingus. Other near-fatal cases have been described (Bernhardt, 1988).

Dental Care

Examination of the teeth is included in the prenatal examination, and good dental hygiene is encouraged. Indeed, periodontal disease has been linked to preterm labor. Unfortunately, although its treatment improves dental health, it does not prevent preterm birth (Michalowicz, 2006). Dental caries are not aggravated by pregnancy. Importantly, pregnancy is not a contraindication to dental treatment including dental radiographs (Giglio, 2009).

Immunization

Current recommendations for immunization during pregnancy are summarized in Table 9-7. Well-publicized concerns regarding a causal link between childhood exposure to the thimerosal preservative in some vaccines and neuropsychological disorders have led to some parents to vaccine prohibition. Although controversy continues, these associations have proven groundless (Sugarman, 2007; Thompson, 2007; Tozzi, 2009). Thus, many vaccines may be used in pregnancy. The American College of Obstetricians and Gynecologists (2016b) stresses the importance of integrating an effective vaccine strategy into the care of both obstetrical and gynecological patients. The College further emphasizes that information on the safety of vaccines given during pregnancy is subject to change, and recommendations can be found on the CDC website at www.cdc.gov/vaccines.

TABLE 9-7

Recommendations for Immunization During Pregnancy

Immunobiological Agent	Indications for Immunization During Pregnancy	Dose Schedule	Comments
Live Attenuated Virus Vaccines			
Measles	Contraindicated—see immune globulins	Single dose SC, preferably as MMR ^a	Vaccinate susceptible women postpartum. Breastfeeding is not a contraindication
Mumps	Contraindicated	Single dose SC, preferably as MMR	Vaccinate susceptible women postpartum
Rubella	Contraindicated, but congenital rubella syndrome has never been described after vaccine	Single dose SC, preferably as MMR	Teratogenicity of vaccine is theoretical and not confirmed to date; vaccinate susceptible women postpartum
Poliomyelitis oral = live attenuated; injection = enhanced-potency inactivated virus	Not routinely recommended for women in the United States, except women at increased risk of exposure ^b	Primary: Two doses of enhanced-potency inactivated virus SC at 4- to 8-week intervals and a 3rd dose 6–12 months after 2nd dose Immediate protection: One dose oral polio vaccine (in outbreak setting)	Vaccine indicated for susceptible women traveling in endemic areas or in other high-risk situations
Yellow fever	Travel to high-risk areas	Single dose SC	Limited theoretical risk outweighed by risk of yellow fever
Varicella	Contraindicated, but no adverse outcomes reported in pregnancy	Two doses needed: 2nd dose given 4–8 weeks after 1st dose	Teratogenicity of vaccine is theoretical. Vaccination of susceptible women should be considered postpartum
Smallpox (vaccinia)	Contraindicated in pregnant women	One dose SC, multiple pricks	Only vaccine known to cause fetal harm

	and in their household contacts	with lancet	
Other			
Influenza	All pregnant women, regardless of trimester during flu season (October–May)	One dose IM every year	Inactivated virus vaccine
Rabies	Indications for prophylaxis not altered by pregnancy; each case considered individually	Public health authorities to be consulted for indications, dosage, and route of administration	Killed-virus vaccine
Human papillomavirus	Not recommended	Three-dose series IM at 0, 1, and 6 months	Polyvalent vaccines available containing inactivated virus. No teratogenicity has been observed
Hepatitis B	Preexposure and postexposure for women at risk of infection, e.g., chronic liver or kidney disease	Three-dose series IM at 0, 1, and 6 months	Used with hepatitis B immune globulin for some exposures. Exposed newborn needs birth-dose vaccination and immune globulin as soon as possible. All infants should receive birth dose of vaccine
Hepatitis A	Preexposure and postexposure if at risk (international travel); chronic liver disease	Two-dose schedule IM, 6 months apart	Inactivated virus
Inactivated Bacterial Vaccines			
Pneumococcus	Indications not altered by pregnancy. Recommended for women with asplenia; metabolic, renal, cardiac, or pulmonary diseases; immunosuppression; or smokers	In adults, one dose only; consider repeat dose in 6 years for high-risk women	Polyvalent polysaccharide vaccine; safety in the first trimester has not been evaluated
Meningococcus	Indications not altered by pregnancy; vaccination recommended in unusual outbreaks	One dose; tetravalent vaccine; two doses for asplenia	Antimicrobial prophylaxis if significant exposure
Typhoid	Not recommended routinely except for close, continued exposure or travel to endemic areas	Killed Primary: 2 injections IM 4 weeks apart Booster: One dose; schedule not yet determined	Killed, injectable vaccine or live attenuated oral vaccine. Oral vaccine preferred
Anthrax	Chapter 64 (Mycotic Infections)	Six-dose primary vaccination, then annual booster vaccination	Preparation from cell-free filtrate of <i>B anthracis</i> . No dead or live bacteria. Teratogenicity of vaccine theoretical
Toxoids			
Tetanus-diphtheria-acellular pertussis	Recommended in every pregnancy, preferably between 27 and 36 weeks	Primary: Two doses IM at 1–2 month interval with 3rd dose	Combined tetanus-diphtheria toxoids with acellular pertussis (Tdap) preferred. Updating immune status

(Tdap)	to maximize passive antibody transfer	6–12 months after the 2nd Booster: Single dose IM every 10 years, as a part of wound care if ≥ 5 years since last dose, or once per pregnancy	should be part of antepartum care
Specific Immune Globulins			
Hepatitis B	Postexposure prophylaxis	Depends on exposure (Chap. 55, Pregnancy and Hepatitis B)	Usually given with hepatitis B virus vaccine; exposed newborn needs immediate prophylaxis
Rabies	Postexposure prophylaxis	Half dose at injury site, half dose in deltoid	Used in conjunction with rabies killed-virus vaccine
Tetanus	Postexposure prophylaxis	One dose IM	Used in conjunction with tetanus toxoid
Varicella	Should be considered for exposed pregnant women to protect against maternal, not congenital, infection	One dose IM within 96 hours of exposure	Indicated also for newborns or women who developed varicella within 4 days before delivery or 2 days following delivery
Standard Immune Globulins			
Hepatitis A: Hepatitis A virus vaccine should be used with hepatitis A immune globulin	Postexposure prophylaxis and those at high risk	0.02 mL/kg IM in one dose	Immune globulin should be given as soon as possible and within 2 weeks of exposure; infants born to women who are incubating the virus or are acutely ill at delivery should receive one dose of 0.5 mL as soon as possible after birth

^aTwo doses necessary for students entering institutions of higher education, newly hired medical personnel, and travel abroad.

^bInactivated polio vaccine recommended for nonimmunized adults at increased risk.

ID = intradermally; IM = intramuscularly; MMR = measles, mumps, rubella; PO = orally; SC = subcutaneously.

From the [Centers for Disease Control and Prevention, 2011](#); [Kim, 2016](#).

The frequency of pertussis infection has substantially risen in the United States. Young infants are at increased risk for death from pertussis and are entirely dependent on passive immunization from maternal antibodies until the infant vaccine series is initiated at age 2 months. For this reason, a three-agent tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine is recommended and is safe for pregnant women ([Centers for Disease Control and Prevention, 2013b, 2016](#); [Morgan, 2015](#)). However, as demonstrated by [Healy and coworkers \(2013\)](#), maternal antipertussis antibodies are relatively short-lived, and Tdap administration before pregnancy—or even in the first half of the current pregnancy—is not likely to provide a high level of newborn antibody protection. Thus, to maximize passive antibody transfer to the fetus, a dose of Tdap is ideally given to gravidas between 27 and 36 weeks' gestation ([American College of Obstetricians and Gynecologists, 2017j](#); [Centers for Disease Control and Prevention, 2013b, 2016](#)).

All women who will be pregnant during influenza season should be offered vaccination, regardless of gestational age. Those with underlying medical conditions that increase the risk for influenza complications are provided the vaccine before flu season starts. In addition to maternal protection against infection, prenatal maternal vaccination in one study reduced the infant influenza incidence in the first 6 months of life by 63 percent ([Zaman, 2008](#)). Moreover, it reduced all febrile respiratory illnesses in these infants by a third.

Women who are susceptible to rubella during pregnancy should receive measles, mumps, rubella (MMR) vaccination postpartum. Although this vaccine is not recommended during pregnancy, congenital rubella syndrome has never resulted from its inadvertent use. Breastfeeding is compatible with MMR vaccination ([Centers for Disease Control and Prevention, 2011](#)).

Caffeine

Whether adverse pregnancy outcomes are related to caffeine consumption is somewhat controversial. As summarized from [Chapter 18 \(Paternal Factors\)](#), heavy intake of coffee each day—about five cups or 500 mg of caffeine—slightly raises the miscarriage risk. Studies of “moderate” intake—less than 200 mg daily—did not find a higher risk.

It is unclear if caffeine consumption is associated with preterm birth or impaired fetal growth. [Clausson and coworkers \(2002\)](#) found no association between moderate caffeine consumption of less than 500 mg/d and low birthweight, fetal-growth restriction, or preterm delivery. [Bech and associates \(2007\)](#) randomly assigned more than 1200 pregnant women who drank at least three cups of coffee per day to caffeinated versus decaffeinated coffee. They found no difference in birthweight or gestational age at delivery between groups. The [CARE Study Group \(2008\)](#), however, evaluated 2635 low-risk pregnancies and reported a 1.4-fold risk for fetal-growth restriction among those whose daily caffeine consumption was >200 mg/d compared with those who consumed <100 mg/d. The [American College of Obstetricians and Gynecologists \(2016d\)](#) concludes that moderate consumption of caffeine—less than 200 mg/d—does not appear to be associated with miscarriage or preterm birth, but that the relationship between caffeine consumption and fetal-growth restriction remains unsettled. The [American Dietetic Association \(2008\)](#) recommends that caffeine intake during pregnancy be limited to less than 300 mg/d, which approximates three 5-oz cups of percolated coffee.

Nausea and Heartburn

Nausea and vomiting are common complaints during the first half of pregnancy. These vary in severity and usually commence between the first and second missed menstrual period and continue until 14 to 16 weeks' gestation. Although nausea and vomiting tend to be worse in the morning—thus erroneously termed *morning sickness*—both symptoms frequently continue throughout the day. [Lacroix and coworkers \(2000\)](#) found that nausea and vomiting were reported by three fourths of pregnant women and lasted an average of 35 days. Half had relief by 14 weeks, and 90 percent by 22 weeks. In 80 percent of these women, nausea lasted all day.

Treatment of pregnancy-associated nausea and vomiting seldom provides complete relief, but symptoms can be minimized. Eating small meals at frequent intervals is valuable. One systematic literature search reported that the herbal remedy ginger was likely effective ([Borrelli, 2005](#)). Mild symptoms usually respond to vitamin B₆ given along with doxylamine, but some women require phenothiazine or H₁-receptor blocking antiemetics ([American College of Obstetricians and Gynecologists, 2015c](#)). In some with *hyperemesis gravidarum*, vomiting is so severe that dehydration, electrolyte and acid-base disturbances, and starvation ketosis become serious problems.

Heartburn is another common complaint of gravidas and is caused by gastric content reflux into the lower esophagus. The greater frequency of regurgitation during pregnancy most likely results from upward displacement and compression of the stomach by the uterus, combined with relaxation of the lower esophageal sphincter. Avoiding bending over or lying flat is preventive. In most pregnant women, symptoms are mild and relieved by a regimen of more frequent but smaller meals. Antacids may provide considerable relief ([Phupong, 2015](#)). Specifically, aluminum hydroxide, magnesium trisilicate, or magnesium hydroxide is given alone or in combination. Management of heartburn or nausea that does not respond to simple measures is discussed in [Chapter 54 \(Management\)](#).

Pica and Ptyalism

The craving of pregnant women for strange foods is termed pica. Worldwide, its prevalence is estimated to be 30 percent ([Fawcett, 2016](#)). At times, nonfoods such as ice—pagophagia, starch—amylophagia, or clay—geophagia may predominate. This desire is considered by some to be triggered by severe iron deficiency. Although such cravings usually abate after deficiency correction, not all pregnant women with pica are iron deficient. Indeed, if strange “foods” dominate the diet, iron deficiency will be aggravated or will develop eventually.

[Patel and coworkers \(2004\)](#) prospectively completed a dietary inventory on more than 3000 women during the second trimester. The prevalence of pica was 4 percent. The most common nonfood items ingested were starch in 64 percent, dirt in 14 percent, sourdough in 9 percent, and ice in 5 percent. The prevalence of anemia was 15 percent in women with pica compared with 6 percent in those without it. Interestingly, the rate of spontaneous preterm birth before 35 weeks was twice as high in women with pica.

Women during pregnancy are occasionally distressed by profuse salivation—*ptyalism*. Although usually unexplained, ptyalism sometimes appears to follow salivary gland stimulation by the ingestion of starch.

Headache or Backache

At least 5 percent of pregnancies are estimated to be complicated by new-onset or new-type headache (Spierings, 2016). Common headaches are virtually universal. Acetaminophen is suitable for most of these, and an in-depth discussion is found in Chapter 60 (Headache).

Low back pain to some extent is reported by nearly 70 percent of gravidas (Liddle, 2015; Wang, 2004). Minor degrees follow excessive strain or significant bending, lifting, or walking. It can be reduced by squatting rather than bending when reaching down, by using a back-support pillow when sitting, and by avoiding high-heeled shoes. Back pain complaints increase with progressing gestation and are more prevalent in obese women and those with a history of low back pain. In some cases, troublesome pain may persist for years after the pregnancy (Norén, 2002).

Severe back pain should not be attributed simply to pregnancy until a thorough orthopedic examination has been conducted. Severe pain has other uncommon causes that include pregnancy-associated osteoporosis, disc disease, vertebral osteoarthritis, or septic arthritis (Smith, 2008). More commonly, muscular spasm and tenderness are classified clinically as acute strain or fibrositis. Although evidence-based clinical research directing care in pregnancy is limited, low back pain usually responds well to analgesics, heat, and rest. Acetaminophen may be used chronically as needed. Nonsteroidal antiinflammatory drugs may also be beneficial but are used only in short courses to avoid fetal effects (Chap. 12, Angiotensin-Converting Enzyme Inhibitors and Angiotensin-Receptor Blocking Drugs). Muscle relaxants that include cyclobenzaprine or baclofen may be added when needed. Once acute pain is improved, stabilizing and strengthening exercises provided by physical therapy help improve spine and hip stability, which is essential for the increased load of pregnancy. For some, a support belt that stabilizes the sacroiliac joint may be helpful (Gutke, 2015).

Varicosities and Hemorrhoids

Venous leg varicosities have a congenital predisposition and accrue with advancing age. They can be aggravated by factors that raise lower extremity venous pressures, such as an enlarging uterus. Femoral venous pressures in the supine gravida rise from 8 mm Hg in early pregnancy to 24 mm Hg at term. Thus, leg varicosities typically worsen as pregnancy advances, especially with prolonged standing. Symptoms vary from cosmetic blemishes and mild discomfort at the end of the day to severe discomfort that requires prolonged rest with feet elevation. Treatment is generally limited to periodic rest with leg elevation, elastic stockings, or both. Surgical correction during pregnancy generally is not advised, although rarely the symptoms may be so severe that injection, ligation, or even stripping of the veins is necessary.

Vulvar varicosities frequently coexist with leg varicosities, but they may appear without other venous pathology. Uncommonly, they become massive and almost incapacitating. If these large varicosities rupture, blood loss can be severe. Treatment is with specially fitted pantyhose that will also minimize lower extremity varicosities. With particularly bothersome vulvar varicosities, a foam rubber pad suspended across the vulva by a belt can be used to exert pressure on the dilated veins.

Hemorrhoids are rectal vein varicosities and may first appear during pregnancy as pelvic venous pressures rise. Commonly, they are recurrences of previously encountered hemorrhoids. Up to 40 percent of pregnant women develop these (Poskus, 2014). Pain and swelling usually are relieved by topically applied anesthetics, warm soaks, and stool-softening agents. With thrombosis of an external hemorrhoid, pain can be considerable. This may be relieved by incision and removal of the clot following injection of a local anesthetic.

Sleeping and Fatigue

Beginning early in pregnancy, many women experience fatigue and need greater amounts of sleep. This likely is due to the soporific effect of progesterone but may be compounded in the first trimester by nausea and vomiting. In the latter stages, general discomforts, urinary frequency, and dyspnea can be additive. Sleep duration may be related to obesity and gestational weight gain (Facco, 2016; Lockhart, 2015). Moreover, sleep efficiency appears to progressively diminish as pregnancy advances. Wilson and associates (2011) performed overnight polysomnography and observed that women in the third trimester had poorer sleep efficiency, more awakenings, and less of both stage 4 (deep) and rapid-eye movement sleep. Women in the first trimester were also affected, but to a lesser extent. Daytime naps and mild sedatives at bedtime such as diphenhydramine (Benadryl) can be helpful.

Cord Blood Banking

Since the first successful cord blood transplantation in 1988, more than 25,000 umbilical cord blood transplantations have been performed to treat hemopoietic cancers and various genetic conditions (Butler, 2011). There are two types of cord blood banks. Public banks promote allogeneic donation, for use by a related or unrelated recipient, similar to blood product donation (Armson, 2015). Private banks were initially developed to store stem cells for future autologous use and charged fees for initial processing and annual storage. The American College of Obstetricians and Gynecologists (2015d) has concluded that if a woman requests information on umbilical cord banking, information regarding advantages and disadvantages of public versus private banking should be explained. Some states have passed laws that require physicians to inform patients about cord blood banking options. Importantly, few transplants have been performed by using cord blood stored in the absence of a known indication in the recipient (Screnci, 2016). The likelihood that cord blood would be used for the child or family member of the donor couple is considered remote, and it is recommended that directed donation be considered when an immediate family member carries the diagnosis of a specific condition known to be treatable by hemopoietic transplantation (Chap. 56, Anemias).

REFERENCES

- Aerospace Medical Association, Medical Guidelines Task Force: Medical guidelines for airline travel, 2nd ed. Aviat Space Environ Med 74:5, 2003
- Afshar Y, Wang ET, Mei J et al.: Childbirth education class and birth plans are associated with a vaginal delivery. Birth 44(1):29, 2017 [PubMed: 27859592]
- Ahmad F, Hogg-Johnson S, Stewart D, et al: Computer-assisted screening for intimate partner violence and control. Ann Intern Med 151(2):94, 2009
- American Academy of Pediatrics, American College of Obstetricians and Gynecologists: Guidelines for perinatal care, 8th ed. Elk Grove Village, AAP, 2017
- American College of Obstetricians and Gynecologists: Intimate partner violence. Committee Opinion No. 518, February 2012
- American College of Obstetricians and Gynecologists: Alcohol abuse and other substance use disorders: ethical issues in obstetric and gynecologic practice. Committee Opinion No. 633, June 2015a
- American College of Obstetricians and Gynecologists: Fetal growth restriction. Practice Bulletin No. 134, May 2013, Reaffirmed 2015b
- American College of Obstetricians and Gynecologists: Nausea and vomiting of pregnancy. Practice Bulletin No. 153, September 2015c
- American College of Obstetricians and Gynecologists: Umbilical cord blood banking. Committee Opinion No. 648, December 2015d
- American College of Obstetricians and Gynecologists: Air travel during pregnancy. Committee Opinion No. 443, October 2009, Reaffirmed 2016a
- American College of Obstetricians and Gynecologists: Integrating immunization into practice. Committee Opinion No. 661, April 2016b
- American College of Obstetricians and Gynecologists: Lead screening during pregnancy and lactation. Committee Opinion No. 533, August 2012, Reaffirmed 2016c
- American College of Obstetricians and Gynecologists: Moderate caffeine consumption during pregnancy. Committee Opinion No. 462, August 2010, Reaffirmed 2016d
- American College of Obstetricians and Gynecologists: Neural tube defects. Practice Bulletin No. 44, July 2003, Reaffirmed 2016e
- American College of Obstetricians and Gynecologists: Prenatal and perinatal human immunodeficiency virus testing: expanded recommendations. Committee Opinion No. 635, June 2015, Reaffirmed 2016f

American College of Obstetricians and Gynecologists: Prevention of early onset group B streptococcal disease in newborns. Committee Opinion No. 485, April 2011, Reaffirmed 2016g

American College of Obstetricians and Gynecologists: Ultrasound in pregnancy. Practice Bulletin No. 175, December 2016h

American College of Obstetricians and Gynecologists: Weight gain during pregnancy. Committee Opinion No. 548, January 2013, Reaffirmed 2016i

American College of Obstetricians and Gynecologists: Avoiding inappropriate clinical decisions based on false-positive human chorionic gonadotropin test results. Committee Opinion No. 278, November 2002, Reaffirmed 2017a

American College of Obstetricians and Gynecologists: Fetal alcohol spectrum disorders (FASD) prevention program. 2017b. Available at: <http://www.acog.org/alcohol>. Accessed October 23, 2017

American College of Obstetricians and Gynecologists: Gestational diabetes mellitus. Practice Bulletin No. 180, July 2017c

American College of Obstetricians and Gynecologists: Marijuana use during pregnancy and lactation. Committee Opinion No. 722, October 2017d

American College of Obstetricians and Gynecologists: Method for estimating the due date. Committee Opinion No. 700, May 2017e

American College of Obstetricians and Gynecologists: Opioid use and opioid use disorder in pregnancy. Committee Opinion No. 711, August 2017f

American College of Obstetricians and Gynecologists: Physical activity and exercise during pregnancy and the postpartum period. Committee Opinion No. 650, December 2015, Reaffirmed 2017g

American College of Obstetricians and Gynecologists: Carrier screening for genetic conditions. Committee Opinion No. 691, March 2017h

American College of Obstetricians and Gynecologists: Smoking cessation during pregnancy. Committee Opinion No. 721, October 2017i

American College of Obstetricians and Gynecologists: Update on immunization and pregnancy: tetanus, diphtheria, and pertussis vaccination. Committee Opinion No. 718, September 2017j

American College of Obstetricians and Gynecologists: Vitamin D: screening and supplementation during pregnancy. Committee Opinion No. 495, July 2011, Reaffirmed 2017k

American Dietetic Association: Position of the American Dietetic Association: nutrition and lifestyle for a healthy pregnancy outcome. J Am Diet Assoc 108:553, 2008 [PubMed: 18401922]

Armson BA, Allan DS, Casper RF, et al: Umbilical cord blood: counseling, collection, and banking. J Obstet Gynaecol Can 37:832, 2015 [PubMed: 26605456]

Aronson ME, Nelson PK: Fatal air embolism in pregnancy resulting from an unusual sex act. Obstet Gynecol 30:127, 1967 [PubMed: 6027480]

Ars CL, Nijs IM, Marroun HE, et al: Prenatal folate, homocysteine and vitamin B₁₂ levels and child brain volumes, cognitive development and psychological functioning: the Generation R Study. Br J Nutr 22:1, 2016

Barker DJ, Osmond C, Law CM: The intrauterine and early postnatal origins of cardiovascular disease and chronic bronchitis. J Epidemiol Community Health 43:237, 1989 [PubMed: 2607302]

Bartellas E, Crane JM, Daley M, et al: Sexuality and sexual activity in pregnancy. BJOG 107:964, 2000 [PubMed: 10955426]

Bech BH, Obel C, Henriksen TB, et al: Effect of reducing caffeine intake on birth weight and length of gestation: randomized controlled trial. BMJ

335:409, 2007 [PubMed: 17762003]

Berg CJ, Callaghan WM, Syverson C, et al: Pregnancy-related mortality in the United States, 1998 to 2005. *Obstet Gynecol* 116(6):1302, 2010 [PubMed: 21099595]

Berggren EK, Groh-Wargo S, Presley L, et al: Maternal fat, but not lean, mass is increased among overweight/obese women with excess gestational weight gain. *Am J Obstet Gynecol* 214(6):745.e1, 2016

Bergsjø P, Denman DW III, Hoffman HJ, et al: Duration of human singleton pregnancy. A population-based study. *Acta Obstet Gynecol Scand* 69:197, 1990 [PubMed: 2220340]

Berlin I, Grangé G, Jacob N, et al: Nicotine patches in pregnant smokers: randomized, placebo controlled, multicentre trial of efficacy. *BMJ* 348:g1622, 2014 [PubMed: 24627552]

Bernhardt TL, Goldmann RW, Thombs PA, et al: Hyperbaric oxygen treatment of cerebral air embolism from orogenital sex during pregnancy. *Crit Care Med* 16:729, 1988 [PubMed: 3371050]

Bleich AT, Sheffield JS, Wendel GD Jr, et al: Disseminated gonococcal infection in women. *Obstet Gynecol* 119(3):597, 2012 [PubMed: 22353959]

Bodnar LM, Simhan HN, Powers RW, et al: High prevalence of vitamin D insufficiency in black and white pregnant women residing in the northern United States and their neonates. *J Nutr* 137(2):447, 2007 [PubMed: 17237325]

Borrelli F, Capasso R, Aviello G, et al: Effectiveness and safety of ginger in the treatment of pregnancy-induced nausea and vomiting. *Obstet Gynecol* 105:849, 2005 [PubMed: 15802416]

Branson BM, Handsfield HH, Lampe MA, et al: Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. *MMWR* 55(RR-14):1, 2006 [PubMed: 16988643]

Braunstein GD: False-positive serum human chorionic gonadotropin results: causes, characteristics, and recognition. *Am J Obstet Gynecol* 187:217, 2002 [PubMed: 12114913]

Braunstein GD: The long gestation of the modern home pregnancy test. *Clin Chem* 60(1):18, 2014 [PubMed: 24025847]

Brown MA, Sinosich MJ, Saunders DM, et al: Potassium regulation and progesterone-aldosterone interrelationships in human pregnancy: a prospective study. *Am J Obstet Gynecol* 155:349, 1986 [PubMed: 3740152]

Butler MG, Menitove JE: Umbilical cord blood banking: an update. *J Assist Reprod Genet* 28:669, 2011 [PubMed: 21617932]

Cao XY, Jiang XM, Dou ZH, et al: Timing of vulnerability of the brain to iodine deficiency in endemic cretinism. *N Engl J Med* 331:1739, 1994 [PubMed: 7984194]

CARE Study Group: Maternal caffeine intake during pregnancy and risk of fetal growth restriction: a large prospective observational study. *BMJ* 337:a2332, 2008 [PubMed: 18981029]

Carter EB, Temming LA, Akin J et al.: Group prenatal care compared with traditional prenatal care: a systematic review and meta-analysis. *Obstet Gynecol* 128(3):551, 2016 [PubMed: 27500348]

Casey BM, Thom EA, Peaceman AM et al.: Treatment of subclinical hypothyroidism or hypothyroxinemia in pregnancy. *N Engl J Med* 376(9):815, 2017 [PubMed: 28249134]

Catalano PM: Increasing maternal obesity and weight gain during pregnancy: the obstetric problems of plentitude. *Obstet Gynecol* 110:743, 2007

[PubMed: 17906003]

Centers for Disease Control and Prevention: Entry into prenatal care—United States, 1989–1997. MMWR 49:393, 2000

Centers for Disease Control and Prevention: Spina bifida and anencephaly before and after folic acid mandate—United States, 1995–1996 and 1999–2000. MMWR 53(17):362, 2004 [PubMed: 15129193]

Centers for Disease Control and Prevention: Guidelines for the identification and management of lead exposure in pregnant and lactating women. November 2010a. Available at: <http://www.cdc.gov/nceh/lead/publications/leadandpregnancy2010.pdf>. Accessed September 19, 2016

Centers for Disease Control and Prevention: Prevention of perinatal group B streptococcal disease: revised guidelines from CDC, 2010. MMWR 59(10):1, 2010b

Centers for Disease Control and Prevention: General recommendations on immunization—recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 60(2):1, 2011

Centers for Disease Control and Prevention: PRAMS and smoking. 2013a. Available at: <http://www.cdc.gov/prams/TobaccoandPrams.htm>. Accessed September 18, 2016

Centers for Disease Control and Prevention: Updated recommendations for use of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine (Tdap) in pregnant women—Advisory Committee on Immunization Practices (ACIP), 2012. MMWR 62(7):131, 2013b

Centers for Disease Control and Prevention: Guidelines for vaccinating pregnant women. 2016. Available at: http://www.cdc.gov/vaccines/pubs/downloads/b_preg_guide.pdf. Accessed September 18, 2016

Chamberlain G, Broughton-Pipkin F (eds): Clinical Physiology in Obstetrics, 3rd ed. Oxford, Blackwell Science, 1998

Chen PH, Rovi S, Washington J, et al: Randomized comparison of 3 methods to screen for domestic violence in family practice. Ann Fam Med 5(5):430, 2007 [PubMed: 17893385]

Child Trends: Databank: late or no prenatal care. 2015. Available at: <http://www.childtrends.org/?indicators=late-or-no-prenatal-care>. Accessed September 19, 2016

Clapp JF III, Kim H, Burciu B, et al: Beginning regular exercise in early pregnancy: effect on fetoplacental growth. Am J Obstet Gynecol 183:1484, 2000 [PubMed: 11120515]

Clausson B, Granath F, Ekblom A, et al: Effect of caffeine exposure during pregnancy on birth weight and gestational age. Am J Epidemiol 155:429, 2002 [PubMed: 11867354]

Clement S, Candy B, Sikorski J, et al: Does reducing the frequency of routine antenatal visits have long term effects? Follow up of participants in a randomised controlled trial. BJOG 106:367, 1999

Coker AL, Garcia LS, Williams CM, et al: Universal psychosocial screening and adverse pregnancy outcomes in an academic obstetric clinic. Obstet Gynecol 119(6):1180, 2012 [PubMed: 22617583]

Cole LA: The utility of six over-the-counter (home) pregnancy tests. Clin Chem Lab Med 49(8): 1317, 2011 [PubMed: 21812725]

Coleman T, Chamberlain C, Davey MA, et al: Pharmacological interventions for promoting smoking cessation during pregnancy. Cochrane Database Syst Rev 12:CD010078, 2015

Cooper S, Taggar J, Lewis S, et al: Effect of nicotine patches in pregnancy on infant and maternal outcomes at 2 years: follow-up from the

randomized, double-blind, placebo-controlled SNAP trial. *Lancet Respir Med* 2(9):728, 2014 [PubMed: 25127405]

Cox Bauer CM, Bernhard KA, Greer DM, et al: Maternal and neonatal outcomes in obese women who lose weight during pregnancy. *J Perinatol* 36(4):278, 2016 [PubMed: 26741574]

Daru K, Cooper NA, Khan KS: Systematic review of randomized trials of the effect of iron supplementation on iron stores and oxygen carrying capacity in pregnancy. *Acta Obstet Gynecol Scand* 95(3):270, 2016 [PubMed: 26509354]

Davenport MH, Skow RJ, Steinback CD: Maternal responses to aerobic exercise in pregnancy. *Clin Obstet Gynecol* 59(3):541, 2016 [PubMed: 27042798]

De-Regil LM, Palacios C, Lombardo LK, et al: Vitamin D supplementation for women during pregnancy. *Cochrane Database Syst Rev* 1:CD008873, 2016

DeVader SR, Neeley HL, Myles TD, et al: Evaluation of gestational weight gain guidelines for women with normal prepregnancy body mass index. *Obstet Gynecol* 110:745, 2007 [PubMed: 17906004]

Donders GG, Halperin SA, Devligger R, et al: Maternal immunization with an investigational trivalent Group B streptococcal vaccine. *Obstet Gynecol* 127(2):213, 2016 [PubMed: 26942345]

Duncombe D, Skouteris H, Wertheim EH, et al: Vigorous exercise and birth outcomes in a sample of recreational exercisers: a prospective study across pregnancy. *Aust N Z J Obstet Gynaecol* 46:288, 2006 [PubMed: 16866788]

Duryea EL, McIntire DD, Leveno KJ: The rate of preterm birth in the United States is affected by the method of gestational age assignment. *Am J Obstet Gynecol* 213:331, e1, 2015

Ekstrand J, Boreus LO, de Chateau P: No evidence of transfer of fluoride from plasma to breast milk. *BMJ (Clin Res Ed)* 283:761, 1981

El-Mohandes A, Herman AA, Kl-Khorazaty MN, et al: Prenatal care reduces the impact of illicit drug use on perinatal outcomes. *J Perinatol* 23:354, 2003 [PubMed: 12847528]

Eriksen JLK, Pilliod RA, Caughey AB: Impact of late initiation of prenatal care on pregnancy outcomes among women who use drugs. Abstract No. 732. *Am J Obstet Gynecol* 214:S384, 2016

Facco F, Reid K, Grobman W, et al: Short and long sleep duration are associated with extremes of gestational weight gain. Abstract No. 33. *Am J Obstet Gynecol* 214:S24, 2016

Fawcett EJ, Fawcett JM, Mazmanian D: A meta-analysis of the worldwide prevalence of pica during pregnancy and the postpartum period. *Int J Gynaecol Obstet* 133(3):277, 2016 [PubMed: 26892693]

Fawzi WW, Msamanga GI, Urassa W, et al: Vitamins and perinatal outcomes among HIV-negative women in Tanzania. *N Engl J Med* 356:14, 2007

Fiore MC, Jaen CR, Baker TB, et al: Treating tobacco use and dependence: 2008 update. Clinical practice guideline. 2008. Available at: <http://www.ncbi.nlm.nih.gov/books/NBK63952/>. Accessed September 19, 2016

Fleming N, O'Driscoll T, Becker G, et al: Adolescent pregnancy guidelines. *J Obstet Gynaecol Can* 37(8):740, 2015 [PubMed: 26474231]

Foster M, Herulah UN, Prasad A, et al: Zinc status of vegetarians during pregnancy: a systematic review of observational studies and meta-analysis of zinc intake. *Nutrients* 7(6):4512, 2015 [PubMed: 26056918]

Giglio JA, Lanni SM, Laskin DM, et al: Oral health care for the pregnant patient. *J Can Dent Assoc* 75(1):43, 2009 [PubMed: 19239743]

Green PP, McKnight-Eily LR, Tan CH, et al: Vital signs: alcohol-exposed pregnancies—United States, 2011–2013. *MMWR* 65(4):91, 2016 [PubMed: 26845520]

Gregory KD, Johnson CT, Johnson TR, et al: The content of prenatal care. *Women's Health Issues* 16:198, 2006 [PubMed: 16920524]

Grenache DG: Variable accuracy of home pregnancy tests: truth in advertising? *Clin Chem Lab Med* 53(3):339, 2015 [PubMed: 25415638]

Grudzinskas JG, Watson C, Chard T: Does sexual intercourse cause fetal distress? *Lancet* 2:692, 1979 [PubMed: 90777]

Gutke A, Betten C, Degerskär K, et al: Treatments for pregnancy-related lumbopelvic pain: a systematic review of physiotherapy modalities. *Acta Obstet Gynecol Scand* 94(11):1156, 2015 [PubMed: 26018758]

Haragan AF, Hulsey TC, Hawk AF, et al: Diagnostic accuracy of fundal height and handheld ultrasound-measured abdominal circumference to screen for fetal growth abnormalities. *Am J Obstet Gynecol* 212(6):820.e1, 2015

Healy CM, Rench MA, Baker CJ: Importance of timing of maternal combined tetanus, diphtheria, and acellular pertussis (Tdap) immunization and protection of young infants. *Clin Infect Dis* 56(4):539, 2013 [PubMed: 23097585]

Herbert WNP, Bruninghaus HM, Barefoot AB, et al: Clinical aspects of fetal heart auscultation. *Obstet Gynecol* 69:574, 1987 [PubMed: 3547213]

Hibbeln JR, Davis JM, Steer C, et al: Maternal seafood consumption in pregnancy and neurodevelopmental outcomes in childhood (ALSPAC study): an observation cohort study. *Lancet* 369:578, 2007 [PubMed: 17307104]

Higginbottom MC, Sweetman L, Nyhan WL: A syndrome of methylmalonic aciduria, homocystinuria, megaloblastic anemia and neurologic abnormalities in a vitamin B12-deficient breast-fed infant of a strict vegetarian. *N Engl J Med* 299:317, 1978 [PubMed: 683264]

Higgins JR, Walshe JJ, Conroy RM, et al: The relation between maternal work, ambulatory blood pressure, and pregnancy hypertension. *J Epidemiol Community Health* 56:389, 2002 [PubMed: 11964438]

Hollier LM, Hill J, Sheffield JS, et al: State laws regarding prenatal syphilis screening in the United States. *Am J Obstet Gynecol* 189:1178, 2003 [PubMed: 14586375]

Horowitz HS, Heifetz SB: Effects of prenatal exposure to fluoridation on dental caries. *Public Health Rep* 82:297, 1967 [PubMed: 4381508]

Hyttén FE, Chamberlain G (eds): *Clinical Physiology in Obstetrics*, 2nd ed. Oxford, Blackwell, 1991

Hyttén FE, Leitch I: *The Physiology of Human Pregnancy*, 2nd ed. Oxford, Blackwell, 1971

Ickovics JR, Earnshaw V, Lewis JB, et al: Cluster randomized controlled trial of group prenatal care: perinatal outcomes among adolescents in New York City health centers. *Am J Public Health* 106(2):359, 2016 [PubMed: 26691105]

Institute of Medicine: *Dietary Reference Intakes: The Essential Guide to Nutrient Requirements*. Washington, The National Academies Press, 2006

Institute of Medicine: *DRI Dietary Reference Intakes for Calcium and Vitamin D*. Washington, The National Academies Press, 2011

Institute of Medicine and National Research Council: *Weight Gain During Pregnancy: Reexamining the Guidelines*. Washington, The National Academic Press, 2009

Jackson RA, Gardner S, Torres LN, et al: My obstetrician got me fired: how work notes can harm pregnant patients and what to do about it. *Obstet Gynecol* 126(2):250, 2015 [PubMed: 26241411]

Jebeile H, Mijatovic J, Louie JC, et al: A systematic review and meta-analysis of energy intake and weight gain in pregnancy. *Am J Obstet Gynecol*

214(4): 465, 2015 [PubMed: 26739796]

Jimenez JM, Tyson JE, Reisch JS: Clinical measures of gestational age in normal pregnancies. *Obstet Gynecol* 61:438, 1983 [PubMed: 6828273]

Johnson S, Cushion M, Bond S, et al: Comparison of analytical sensitivity and women's interpretation of home pregnancy tests. *Clin Chem Lab Med* 53(3):391, 2015 [PubMed: 25274958]

Kiel DW, Dodson EA, Artal R, et al: Gestational weight gain and pregnancy outcomes in obese women: how much is enough. *Obstet Gynecol* 110:752, 2007 [PubMed: 17906005]

Kim DK, Bridges CB, Harriman KH, et al: Advisory Committee on Immunization Practices recommended immunization schedule for adults aged 19 years or older—United States, 2016. *MMWR* 65(4):88, 2016 [PubMed: 26845417]

Kiss H, Widham A, Geusau A, et al: Universal antenatal screening for syphilis: is it still justified economically? A 10-year retrospective analysis. *Eur J Obstet Gynecol Reprod Biol* 112:24, 2004 [PubMed: 14687734]

Kyle UG, Pichard C: The Dutch Famine of 1944–1945: a pathophysiological model of long-term consequences of wasting disease. *Curr Opin Clin Nutr Metab Care* 9:388, 2006 [PubMed: 16778567]

Lacroix R, Eason E, Melzack R: Nausea and vomiting during pregnancy: a prospective study of its frequency, intensity, and patterns of change. *Am J Obstet Gynecol* 182:931, 2000 [PubMed: 10764476]

Leveno KJ, McIntire DD, Bloom SL, et al: Decreased preterm births in an inner-city public hospital. *Obstet Gynecol* 113(3):578, 2009 [PubMed: 19300320]

Liddle SD, Pennick V: Interventions for preventing and treating low-back and pelvic pain during pregnancy. *Cochrane Database Syst Rev* 9:CD001139, 2015

Litonjua AA, Carey VJ, Laranjo N, et al: Effect of prenatal supplementation with vitamin D on asthma or recurrent wheezing in offspring by age 3 years: the VDAART randomized clinical trial. *JAMA* 315(4):362, 2016 [PubMed: 26813209]

Lockhart EM, Ben Abdallah AM, Tuuli MG, et al: Obstructive sleep apnea in pregnancy: assessment of current screening tools. *Obstet Gynecol* 126(1):93, 2015 [PubMed: 26241261]

Loudon I: *Death in Childbirth*. New York, Oxford University Press, 1992

Luke B, Brown MB, Misiunas R, et al: Specialized prenatal care and maternal and infant outcomes in twin pregnancy. *Am J Obstet Gynecol* 934, 2003

Magann EF, Evans SF, Weitz B, et al: Antepartum, intrapartum, and neonatal significance of exercise on healthy low-risk pregnant working women. *Obstet Gynecol* 99:466, 2002 [PubMed: 11864675]

Maheshwari UR, King JC, Leybin L, et al: Fluoride balances during early and late pregnancy. *J Occup Med* 25:587, 1983 [PubMed: 6886867]

Man LX, Chang B: Maternal cigarette smoking during pregnancy increases the risk of having a child with a congenital digital anomaly. *Plast Reconstr Surg* 117:301, 2006 [PubMed: 16404282]

Margulies R, Miller L: Fruit size as a model for teaching first trimester uterine sizing in bimanual examination. *Obstet Gynecol* 98(2):341, 2001 [PubMed: 11506855]

Martin JA, Hamilton BE, Sutton PD, et al: Births: final data for 2006. *Natl Vital Stat Rep* 57(7):1, 2009

- McCauley ME, van den Broek N, Dou L, et al: Vitamin A supplementation during pregnancy for maternal and newborn outcomes. Cochrane Database Syst Rev 10:CD008666, 2015
- McDuffie RS Jr, Beck A, Bischoff K, et al: Effect of frequency of prenatal care visits on perinatal outcome among low-risk women. A randomized controlled trial. JAMA 275:847, 1996 [PubMed: 8596222]
- Metz TD, Stickrath EH: Marijuana use in pregnancy and lactation: a review of the evidence. Am J Obstet Gynecol 213(6):761, 2015 [PubMed: 25986032]
- Michalowicz BS, Hodges JS, DiAngelis AJ, et al: Treatment of periodontal disease and the risk of preterm birth. N Engl J Med 355:1885, 2006 [PubMed: 17079762]
- Molloy AM, Kirke PN, Troendle JF, et al: Maternal vitamin B₁₂ status and risk of neural tube defects in a population with high neural tube defect prevalence and no folic acid fortification. Pediatrics 123(3):917, 2009 [PubMed: 19255021]
- Montagnana M, Trenti T, Aloe R, et al: Human chorionic gonadotropin in pregnancy diagnostics. Clin Chim Acta 412(17-18):1515, 2011 [PubMed: 21635878]
- Morgan JL, Baggari SR, McIntire DD, et al: Pregnancy outcomes after antepartum tetanus, diphtheria, and acellular pertussis vaccine. Obstet Gynecol 125(6):1433, 2015 [PubMed: 26000515]
- Mozurkewich EL, Luke B, Avni M, et al: Working conditions and adverse pregnancy outcome: a meta-analysis. Obstet Gynecol 95:623, 2000 [PubMed: 10725502]
- Murray N, Homer CS, Davis GK, et al: The clinical utility of routine urinalysis in pregnancy: a prospective study. Med J Aust 177:477, 2002 [PubMed: 12405888]
- Newman RB, Goldenberg RL, Moawad AH, et al: Occupational fatigue and preterm premature rupture of membranes. Am J Obstet Gynecol 184:438, 2001 [PubMed: 11228500]
- Norén L, Östgaard S, Johansson G, et al: Lumbar back and posterior pelvic pain during pregnancy: a 3-year follow-up. Eur Spine J 11:267, 2002
- Nossier SA, Naeim NE, El-Sayed NA, et al: The effect of zinc supplementation on pregnancy outcomes: a double-blind, randomized controlled trial, Egypt. Br J Nutr 114(2):274, 2015 [PubMed: 26099195]
- Ota E, Mori R, Middleton P, et al: Zinc supplementation for improving pregnancy and infant outcome. Cochrane Database Syst Rev 2:CD000230, 2015
- Patel MV, Nuthalapaty FS, Ramsey PS, et al: Pica: a neglected risk factor for preterm birth. Obstet Gynecol 103:68S, 2004
- Patnode CD, Henderson JT, Thompson JH, et al: Behavioral counseling and pharmacotherapy interventions for tobacco cessation in adults, including pregnant women: a review of reviews for the U.S. Preventive Services Task Force. Ann Intern Med 163(8):608, 2015 [PubMed: 26389650]
- Partridge S, Balayla J, Holcroft CA, et al: Inadequate prenatal care utilization and risks of infant mortality and poor birth outcome: a retrospective analysis of 28,729,765 U.S. deliveries over 8 years. Am J Perinatol 29(10):787, 2012 [PubMed: 22836820]
- Phupong V, Hanprasertpong T: Interventions for heartburn in pregnancy. Cochrane Database Syst Rev 9:CD011379, 2015
- Pitkin RM: Calcium metabolism in pregnancy and the perinatal period: a review. Am J Obstet Gynecol 151:99, 1985 [PubMed: 3881031]
- Pollak KI, Oncken CA, Lipkus IM, et al: Nicotine replacement and behavioral therapy for smoking cessation in pregnancy. Am J Prev Med 33(4):297, 2007 [PubMed: 17888856]

Poskus T, Buzinskiene D, Drasutiene G, et al: Haemorrhoids and anal fissures during pregnancy and after childbirth: a prospective cohort study. *BJOG* 121(13):1666, 2014 [[PubMed: 24810254](#)]

Power ML, Wilson EK, Hogan SO, et al: Patterns of preconception, prenatal and postnatal care for diabetic women by obstetrician-gynecologists. *J Reprod Med* 58(1-2):7, 2013 [[PubMed: 23447912](#)]

Pritchard JA, Scott DE: Iron demands during pregnancy. In Hallberg L, Harwerth HG, Vannotti A (eds): *Iron Deficiency: Pathogenesis, Clinical Aspects, Therapy*. New York, Academic Press, 1970

Read JS, Klebanoff MA: Sexual intercourse during pregnancy and preterm delivery: effects of vaginal microorganisms. *Am J Obstet Gynecol* 168:514, 1993 [[PubMed: 8438920](#)]

Rink BD, Norton ME: Screening for fetal aneuploidy. *Semin Perinatol* 40(1): 35, 2016 [[PubMed: 26725144](#)]

Rumbold A, Ota E, Nagata C, et al: Vitamin C supplementation in pregnancy. *Cochrane Database Syst Rev* 9:CD004072, 2015

Ryan ET, Wilson ME, Kain KC: Illness after international travel. *N Engl J Med* 347:505, 2002 [[PubMed: 12181406](#)]

Sa Roriz Fonteles C, Zero DT, Moss ME, et al: Fluoride concentrations in enamel and dentin of primary teeth after pre- and postnatal fluoride exposure. *Caries Res* 39:505, 2005 [[PubMed: 16251796](#)]

Sagedal LR, Overby NC, Bere E, et al: Lifestyle intervention to limit gestational weight gain: the Norwegian Fit for Delivery randomized controlled trial. *BJOG* 124(1):97, 2017 [[PubMed: 26768233](#)]

Salam RA, Zuberi NF, Bhutta ZA: Pyridoxine (vitamin B₆) supplementation during pregnancy or labour for maternal and neonatal outcomes. *Cochrane Database Syst Rev* 6:CD000179, 2015

Sayle AE, Savitz DA, Thorp JM Jr, et al: Sexual activity during late pregnancy and risk of preterm delivery. *Obstet Gynecol* 97:283, 2001 [[PubMed: 11165596](#)]

Schauberger CW, Rooney BL, Brimer LM: Factors that influence weight loss in the puerperium. *Obstet Gynecol* 79:424, 1992 [[PubMed: 1738527](#)]

Schrag SJ: Maternal immunization to prevent neonatal group B streptococcal disease. *Obstet Gynecol* 127(2):199, 2016 [[PubMed: 26942342](#)]

Scott DE, Pritchard JA, Satin AS, et al: Iron deficiency during pregnancy. In Hallberg L, Harwerth HG, Vannotti A (eds): *Iron Deficiency: Pathogenesis, Clinical Aspects, Therapy*. New York, Academic Press, 1970

Scenci M, Murgi E, Valle V, et al: Sibling cord blood donor program for hematopoietic cell transplantation: the 20-year experience in the Rome Cord Blood Bank. *Blood Cells Mol Dis* 57:71, 2016 [[PubMed: 26852659](#)]

Sibai BM, Villar MA, Bray E: Magnesium supplementation during pregnancy: a double-blind randomized controlled clinical trial. *Am J Obstet Gynecol* 161:115, 1989 [[PubMed: 2665492](#)]

Siddique J, Lauderdale DS, VanderWeele TJ, et al: Trends in prenatal ultrasound use in the United States. *Med Care* 47:1129, 2009 [[PubMed: 19786915](#)]

Siu AL, U.S. Preventive Services Task Force: Behavioral and pharmacotherapy interventions for tobacco smoking cessation in adults, including pregnant women: U.S. Preventive Services Task Force Recommendation Statement. *Ann Intern Med* 163(8):622, 2015 [[PubMed: 26389730](#)]

Smith CA: Effects of maternal under nutrition upon the newborn infant in Holland (1944-1945). *Am J Obstet Gynecol* 30:229, 1947

Smith MW, Marcus PS, Wurtz LD: Orthopedic issues in pregnancy. *Obstet Gynecol Surv* 63:103, 2008 [PubMed: 18199383]

Spierings EL, Sabin TD: De novo headache during pregnancy and puerperium. *Neurologist* 21(1):1, 2016 [PubMed: 26703001]

Spindel ER, McEvoy CT: The role of nicotine in the effects of maternal smoking during pregnancy on lung development and childhood respiratory disease: implications for dangers of E-cigarettes. *Am J Respir Crit Care Med* 193(5):486, 2016 [PubMed: 26756937]

Staruch M, Kucharczyk A, Zawadzka K, et al: Sexual activity during pregnancy. *Neuro Endocrinol Lett* 37(1):53, 2016 [PubMed: 26994386]

Stein Z, Susser M, Saenger G, et al: Nutrition and mental performance. *Science* 178:708, 1972 [PubMed: 5082838]

Stephens TV, Payne M, Ball Ro, et al: Protein requirements of healthy pregnancy women during early and late gestation are higher than current recommendations. *J Nutr* 145(1):73, 2015 [PubMed: 25527661]

Stewart RD, Nelson DB, Adhikari EH, et al: The obstetrical and neonatal impact of maternal opioid detoxification in pregnancy. *Am J Obstet Gynecol* 209:267.e1, 2013

Sugarman SD: Cases in vaccine court—legal battles over vaccines and autism. *N Engl J Med* 257:1275, 2007

Tan PC, Yow CM, Omar SZ: Effect of coital activity on onset of labor in women scheduled for labor induction. *Obstet Gynecol* 110:820, 2007 [PubMed: 17906015]

Taylor CM, Golding J, Emond AM: Adverse effects of maternal lead levels on birth outcomes in the ALSPAC study: a prospective birth cohort study. *BJOG* 122(3):322, 2015 [PubMed: 24824048]

Thompson WW, Price C, Goodson B, et al: Early thimerosal exposure and neuropsychological outcomes at 7 to 10 years. *N Engl J Med* 257:1281, 2007

Till SR, Everetts D, Haas DM: Incentives for increasing prenatal care use by women in order to improve maternal and neonatal outcomes. *Cochrane Database Syst Rev* 12:CD009916, 2015

Tong VT, Dietz PM, Morrow B, et al: Trends in smoking before, during, and after pregnancy—pregnancy risk assessment monitoring system, United States, 40 sites, 2000–2010. *MMWR* 62(6):1, 2013 [PubMed: 24196750]

Tozzi AE, Bisiacchi P, Tarantino V, et al: Neuropsychological performance 10 years after immunization in infancy with thimerosal-containing vaccines. *Pediatrics* 123(2):475, 2009 [PubMed: 19171612]

U.S. Department of Health and Human Services: Reducing tobacco use: a report of the Surgeon General. Atlanta, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2000

U.S. Environmental Protection Agency: Fish: what pregnant women and parents need to know. 2014. Available at: <http://www.fda.gov/Food/FoodbornellnessContaminants/Metals/ucm393070.htm>. Accessed September 19, 2016

U.S. Preventive Services Task Force: Recommendation statement: clinical guidelines: folic acid for the prevention of neural tube defects. *Ann Intern Med* 150:626, 2009 [PubMed: 19414842]

Villar J, Báaqueel H, Piaggio G, et al: WHO antenatal care randomised trial for the evaluation of a new model of routine antenatal care. *Lancet* 357:1551, 2001 [PubMed: 11377642]

Vintzileos AM, Ananth CV, Smulian JC, et al: Prenatal care and black-white fetal death disparity in the United States: heterogeneity by high-risk conditions. *Obstet Gynecol* 99:483, 2002 [PubMed: 11864678]

Wang SM, Dezinno P, Maranets I, et al: Low back pain during pregnancy: prevalence, risk factors, and outcomes. *Obstet Gynecol* 104:65, 2004
[PubMed: 15229002]

Washington State Health Care Authority: Ultrasonography (ultrasound) in pregnancy: a health technology assessment. 2010. Available at:
http://www.hta.hca.wa.gov/documents/final_report_ultrasound.pdf. Accessed September 19, 2016

West KP: Vitamin A deficiency disorders in children and women. *Food Nutr Bull* 24:S78, 2003 [PubMed: 17016949]

Widen EM, Whyatt RM, Hoepner LA, et al: Excessive gestational weight gain is associated with long-term body fat and weight retention at 7 y postpartum in African American and Dominican mothers with underweight, normal, and overweight prepregnancy BMI. *Am J Clin Nutr* 102(6):1460, 2015 [PubMed: 26490495]

Wilcox AJ, Baird DD, Dunson D, et al: Natural limits of pregnancy testing in relation to the expected menstrual period. *JAMA* 286:1759, 2001 [PubMed: 11594902]

Wilson DL, Barnes M, Ellett L, et al: Decreased sleep efficiency, increased wake after sleep onset and increased cortical arousals in late pregnancy. *Aust N Z J Obstet Gynaecol* 51(1):38, 2011 [PubMed: 21299507]

Worthen N, Bustillo M: Effect of urinary bladder fullness on fundal height measurements. *Am J Obstet Gynecol* 138:759, 1980 [PubMed: 7446608]

Xu J, Kochanek KD, Murphy SL: Deaths: final data for 2007. *Nat Stat Vit Rep* 58(19):1, 2010

Zaman K, Roy E, Arifeen SE, et al: Effectiveness of maternal influenza immunization in mothers and infants. *N Engl J Med* 359(15):1555, 2008
[PubMed: 18799552]