key periods of organogenesis reduces other congenital anomalies, including sacral agenesis, caudal dysplasia, renal agenesis, and ventricular septal defect.

Once pregnancy is established, glucose control should be managed more aggressively than in the nonpregnant state. In addition to dietary changes, this enhanced management requires more frequent blood glucose monitoring and often involves additional injections of insulin or conversion to an insulin pump. Fasting blood glucose levels should be maintained at <5.8 mmol/L (<105 mg/dL), with avoidance of values >7.8 mmol/L (140 mg/dL). Commencing in the third trimester, regular surveillance of maternal glucose control as well as assessment of fetal growth (obstetric sonography) and fetoplacental oxygenation (fetal heart rate monitoring or biophysical profile) optimize pregnancy outcome. Pregnant diabetic patients without vascular disease are at greater risk for delivering a macrosomic fetus, and attention to fetal growth via clinical and ultrasound examination is important. Fetal macrosomia is associated with an increased risk of maternal and fetal birth trauma, including permanent newborn *Erb's palsy*. Pregnant women with diabetes have an increased risk of developing preeclampsia, and those with vascular disease are at greater risk for developing intrauterine growth restriction, which is associated with an increased risk of fetal and neonatal death. Excellent pregnancy outcomes in patients with diabetic nephropathy and proliferative retinopathy have been reported with aggressive glucose control and intensive maternal and fetal surveillance.

As pregnancy progresses, glycemic control may become more difficult to achieve due to an increase in insulin resistance. Because of delayed pulmonary maturation of the fetuses of diabetic mothers, early delivery should be avoided unless there is biochemical evidence of fetal lung maturity. In general, efforts to control glucose and avoid preterm delivery result in the best overall outcome for both mother and newborn. Preterm delivery is generally performed only for the usual obstetric indications (e.g., preeclampsia, fetal growth restriction, non-reassuring fetal testing) or for worsening maternal renal or active proliferative retinopathy.

GESTATIONAL DIABETES

Gestational diabetes occurs in approximately 4% of pregnancies. All pregnant women should be screened for gestational diabetes unless they are in a low-risk group. Women at low risk for gestational diabetes are those <25 years of age; those with a body mass index <25 kg/m^2, no maternal history of macrosomia or gestational diabetes, and no diabetes in a first-degree relative; and those who are not members of a high-risk ethnic group (African American, Hispanic, Native American). A typical two-step strategy for establishing the diagnosis of gestational diabetes involves administration of a 50-g oral glucose challenge with a single serum glucose measurement at 60 min. If the plasma glucose is <7.8 mmol/L (<130 mg/dL), the test is considered normal. Plasma glucose >7.8 mmol/L (>130 mg/dL) warrants administration of a 100-g oral glucose challenge with plasma glucose measurements obtained in the fasting state and at 1, 2, and 3 h. Normal plasma glucose concentrations at these time points are <5.8 mmol/L (<105 mg/dL), 10.5 mmol/L (190 mg/dL), 9.1 mmol/L (165 mg/dL), and 8.0 mmol/L (145 mg/dL), respectively. Some centers have adopted more sensitive criteria, using values of <5.3 mmol/L (<95 mg/dL), <10 mmol/L (<180 mg/dL), <8.6 mmol/L (<155 mg/dL), and <7.8 mmol/L (<140 mg/dL) as the upper norms for a 3-h glucose tolerance test. Two elevated glucose values indicate a positive test. Adverse pregnancy outcomes for mother and fetus appear to increase with glucose as a continuous variable; thus it is challenging to define the optimal threshold for establishing the diagnosis of gestational diabetes.

Pregnant women with gestational diabetes are at increased risk of stillbirth, preeclampsia, and delivery of infants who are large for their gestational age, with resulting birth lacerations, shoulder dystocia, and birth trauma including brachial plexus injury. These fetuses are at risk of hypoglycemia, hyperbilirubinemia, and polycythemia. Tight control of blood sugar during pregnancy and labor can reduce these risks.

TREATMENT GESTATIONAL DIABETES

Treatment of gestational diabetes with a two-step strategy—dietary intervention followed by insulin injections if diet alone does not adequately control blood sugar [fasting glucose <5.6 mmol/L (<100 mg/dL) and 2-h postprandial glucose <7.0 mmol/L (<126 mg/dL)]—is associated with a decreased risk of birth trauma for the fetus. Oral hypoglycemic agents such as glyburide and metformin have become more commonly utilized for managing gestational diabetes refractory to nutritional management, but many experts favor insulin therapy. For women with gestational diabetes, there is a 40% risk of being diagnosed with diabetes within the 10 years after the index pregnancy. In women with a history of gestational diabetes, exercise, weight loss, and treatment with metformin reduce the risk of developing diabetes. All women with a history of gestational diabetes should be counseled about prevention strategies and evaluated regularly for diabetes.

OBESITY

(See also Chap. 416) Pregnant women who are obese have an increased risk of stillbirth, congenital fetal malformations, gestational diabetes, preeclampsia, urinary tract infections, post-date delivery, and cesarean delivery. Women contemplating pregnancy should attempt to attain a healthy weight prior to conception. For morbidly obese women who have not been able to lose weight with lifestyle changes, bariatric surgery may result in weight loss and improve pregnancy outcomes. Following bariatric surgery, women should delay conception for 1 year to avoid pregnancy during an interval of rapid metabolic changes.

THYROID DISEASE

(See also Chap. 405) In pregnancy, the estrogen-induced increase in thyroxine-binding globulin increases circulating levels of total T_3 and total T_4. The normal range of circulating levels of free T_4, free T_3, and thyroid-stimulating hormone (TSH) remain unaltered by pregnancy.

The thyroid gland normally enlarges during pregnancy. Many physiologic adaptations to pregnancy may mimic subtle signs of *hyperthyroidism*. Maternal hyperthyroidism occurs at a rate of ~2 per 1000 pregnancies and is generally well tolerated by pregnant women. Clinical signs and symptoms should alert the physician to the occurrence of this condition. Hyperthyroidism in pregnancy is most commonly caused by Graves' disease, but autonomously functioning nodules and gestational trophoblastic disease should also be considered. Although pregnant women are able to tolerate mild hyperthyroidism without adverse sequelae, more severe hyperthyroidism can cause spontaneous abortion or premature labor, and thyroid storm is associated with a significant risk of maternal death.

Testing for *hypothyroidism* using TSH measurements before or early in pregnancy may be warranted in symptomatic women and in women with a personal or family history of thyroid disease. With use of this case-finding approach, about 30% of pregnant women with mild hypothyroidism remain undiagnosed, leading some to recommend universal screening. Children born to women with an elevated serum TSH (and a normal total thyroxine) during pregnancy may have impaired performance on neuropsychologic tests.

TREATMENT HYPERTHYROIDISM IN PREGNANCY

HYPERTHYROIDISM

Methimazole crosses the placenta to a greater degree than propylthiouracil and has been associated with fetal aplasia cutis. However, propylthiouracil can be associated with liver failure. Some experts recommend propylthiouracil in the first trimester and methimazole thereafter. Radioiodine should not be used during pregnancy, either for scanning or for treatment, because of effects on the fetal thyroid. In emergent circumstances, additional treatment with beta blockers may be necessary. Hyperthyroidism is most difficult to control in the first trimester of pregnancy and easiest to control in the third trimester.