small-for-gestational-age (SGA) infants suffer from *fetal growth restriction*. Fetal growth restriction (FGR) may result from fetal, maternal, or placental abnormalities, although in many cases the specific cause is unknown.

Fetal Abnormalities. Fetal influences are those that intrinsically reduce growth potential of the fetus despite an adequate supply of nutrients from the mother. Prominent among such fetal conditions are *chromosomal disorders, congenital anomalies, and congenital infections.* Chromosomal abnormalities may be detected in up to 17% of fetuses sampled for FGR and in up to 66% of fetuses with documented ultrasonographic malformations. Among the first group, the abnormalities include triploidy (7%), trisomy 18 (6%), trisomy 21 (1%), trisomy 13 (1%), and a variety of deletions and translocations (2%). *Fetal infection* should be considered in all infants with FGR. Those most commonly responsible for FGR are the TORCH group of infections (toxoplasmosis, rubella, cytomegalovirus, herpesvirus, and other viruses and bacteria, such as syphilis). Infants who are SGA because of fetal factors usually have symmetric growth restriction (also referred to as *proportionate FGR*), meaning that all organ systems are similarly affected.

Placental Abnormalities. During the third trimester of pregnancy, vigorous fetal growth places particularly heavy demands on the uteroplacental blood supply. Therefore, the adequacy of placental growth in the preceding midtrimester is extremely important, and *uteroplacental insufficiency is an important cause of growth restriction.* This insufficiency may result from *umbilical-placental vascular anomalies* (such as single umbilical artery, abnormal cord insertion, placental hemangioma), *placental abruption, placenta previa, placental thrombosis and infarction, placental infection*, or *multiple gestations* (Chapter 22). In some cases the placenta may be small without any detectable underlying cause. Placental causes of FGR tend to result in *asymmetric* (or disproportionate) growth retardation of the fetus with relative sparing of the brain. Physiologically, this general type of FGR is viewed as a down-regulation of growth in the latter half of gestation because of limited availability of nutrients or oxygen.

Maternal Abnormalities. By far the most common factors associated with SGA infants are maternal conditions that result in decreased placental blood flow. Vascular diseases, such as *preeclampsia (toxemia of pregnancy)* and *chronic hypertension*, are often the underlying cause. Another class of maternal diseases increasingly being recognized in the setting of FGR are *thrombophilias,* such as the acquired antiphospholipid antibody syndrome (Chapter 6). Inherited diseases of hypercoagulability are also associated with recurrent early pregnancy losses. The list of other maternal conditions associated with SGA infants is long, but some of the avoidable factors worth mentioning are maternal *narcotic abuse, alcohol intake,* and *heavy cigarette smoking. Drugs* causing FGR include both classic teratogens, such as chemotherapeutic agents, and some commonly administered therapeutic agents, such as phenytoin (Dilantin). *Maternal malnutrition* (in particular, prolonged hypoglycemia) may also affect fetal growth, but the association between SGA infants and the nutritional status of the mother is complex.

The SGA infant faces a difficult course, not only during the struggle for survival in the perinatal period, but also in childhood and adult life. Depending on the underlying cause of FGR and, to a lesser extent, the degree of prematurity, there is a significant risk of morbidity in the form of a major handicap, cerebral dysfunction, learning disability, or hearing and visual impairment.

Neonatal Respiratory Distress Syndrome

There are many causes of respiratory distress in the newborn. The most common cause is respiratory distress syndrome (RDS), also known as *hyaline membrane disease* because of the deposition of a layer of hyaline proteinaceous material in the peripheral airspaces of infants who succumb to this condition. Others include excessive sedation of the mother, fetal head injury during delivery, aspiration of blood or amniotic fluid, and intrauterine hypoxia brought about by coiling of the umbilical cord about the neck. An estimated 24,000 cases of RDS are reported annually in the United States. Thankfully, improvements in management of this condition have sharply decreased deaths due to respiratory insufficiency from as many as 5000 per year a decade earlier to less than 900 cases per year currently.

In untreated infants (not receiving surfactant), RDS generally presents in a stereotypical fashion, with characteristic clinical findings. The infant is almost always preterm but has weight appropriate for gestational age, and there are strong, but not invariable, associations with *male gender*, *maternal diabetes*, and delivery by *cesarean section.* Resuscitation may be necessary at birth, but usually within a few minutes rhythmic breathing and normal color are reestablished. Soon afterward, often within 30 minutes, breathing becomes more difficult, and within a few hours cyanosis becomes evident. Fine rales can now be heard over both lung fields. A chest x-ray film at this time usually reveals uniform minute reticulogranular densities, producing a so-called *ground-glass picture.* In the full-blown condition the respiratory distress persists, cyanosis increases, and even the administration of 80% oxygen by a variety of ventilatory methods fails to improve the situation. If therapy staves off death for the first 3 or 4 days, however, the infant has an excellent chance of recovery.

Pathogenesis. **Immaturity of the lungs is the most important substrate on which RDS develops.** It may be encountered in full-term infants but is much more frequent in those "born before their time into this breathing world." The incidence of RDS is inversely proportional to gestational age. It occurs in about 60% of infants born at less than 28 weeks of gestation, 30% of those born between 28 to 34 weeks' gestation, and less than 5% of those born after 34 weeks' gestation.

The fundamental defect in RDS is a deficiency of pulmonary surfactant. As described in Chapter 15, surfactant consists predominantly of dipalmitoyl phosphatidylcholine (lecithin), smaller amounts of phosphatidylglycerol, and two groups of surfactant-associated proteins. The first group is composed of hydrophilic glycoproteins SP-A and SP-D, which play a role in pulmonary host defense (innate immunity). The second group consists of hydrophobic surfactant proteins SP-B and SP-C, which, in concert with the