Epidemiologic and genetic studies have identified additional vulnerability factors for SIDS in the "triple-risk" model. Infants who are born before term or who are low birth weight are at increased risk, and risk increases with decreasing gestational age or birth weight. As stated, male sex is associated with a slightly greater incidence of SIDS. SIDS in a prior sibling is associated with a fivefold relative risk of recurrence, highlighting the importance of a genetic predisposition; *traumatic child abuse must be carefully excluded under these circumstances.* Most SIDS babies have an immediate prior history of a mild respiratory tract infection, but no single causative organism has been isolated. These infections may predispose an already vulnerable infant to even greater impairment of cardiorespiratory control and delayed arousal. In this context, *laryngeal chemoreceptors* have emerged as a putative "missing link" between upper respiratory tract infections, the prone position, and SIDS. When stimulated, these laryngeal chemoreceptors typically elicit an inhibitory cardiorespiratory reflex. Stimulation of the chemoreceptors is augmented by respiratory tract infections, which increase the volume of secretions, and by the prone position, which impairs swallowing and clearing of the airways even in healthy infants. In a previously vulnerable infant with impaired arousal, the resulting inhibitory cardiorespiratory reflex may prove fatal. Genetic vulnerability factors in the infant include polymorphisms of genes related to serotonergic signaling and autonomic innervation, pointing to the importance of these processes in the pathophysiology of SIDS.

In addition to infant vulnerability factors, several maternal risk factors have also been identified. *Maternal smoking during pregnancy* has consistently emerged as a risk factor in epidemiologic studies of SIDS, with children exposed to in utero nicotine having more than double the risk of SIDS as compared with children born to nonsmokers. Young maternal age, frequent childbirths, and inadequate prenatal care are all risk factors associated with increased incidence of SIDS in the offspring.

Among the potential "environmental stressors," prone or side sleeping positions, sleeping with parents in the first 3 months, sleeping on soft surfaces, and thermal stress are probably the most important modifiable risk factors for SIDS. The prone or side positions predispose an infant to one or more recognized noxious stimuli (hypoxia, hypercarbia, and thermal stress) during sleep. The side position was considered a reliable alternative to the prone sleeping position, but *the American Academy of Pediatrics now recognizes the supine sleeping position as the only safe position that reduces the risk of SIDS*. This "Back to Sleep" campaign has resulted in substantial reductions in SIDS-related deaths since its inception in 1994.

As has been stated, SIDS is far from the only cause of SUIDs. **In fact, SIDS is a diagnosis of exclusion, requiring careful examination of the death scene and a complete postmortem examination.** The latter can reveal an unsuspected cause of sudden death in as many as 20% or more of "SIDS" babies. Infections (e.g., viral myocarditis or bronchopneumonia) are the most common causes of sudden "unexpected" death, followed by unsuspected congenital anomalies. In part as a result of advancements in molecular diagnostics and knowledge of the human genome, several genetic causes of sudden "unexpected" infant death have emerged. For example, fatty acid oxidation disorders, characterized by defects in mitochondrial fatty acid oxidative enzymes, may be responsible for as many as 5% of SUIDs. Other newly emerging genetic causes of sudden death are listed in Table 10-6.

Tumors and Tumor-like Lesions of Infancy and Childhood

Only 2% of all malignant tumors occur in infancy and childhood; nonetheless, cancer (including leukemia) accounts for about 9% of deaths in the United States in children older than age 4 and up to age 14 years, and only accidents cause significantly more deaths. Benign tumors are even more common than cancers. Most benign tumors are of little concern, but on occasion they cause serious complications by virtue of their location or rapid increase in size.

It is sometimes difficult to separate, on morphologic grounds, true tumors or neoplasms from tumor-like lesions in the infant and child. In this context, two special categories of tumor-like lesions should be distinguished from true tumors.

- The term *heterotopia* (or *choristoma*) is applied to microscopically normal cells or tissues that are present in abnormal locations. Examples of heterotopias include a rest of pancreatic tissue found in the wall of the stomach or small intestine, or a small mass of adrenal cells found in the kidney, lungs, ovaries, or elsewhere. These heterotopic rests are usually of little significance, but they can be confused clinically with neoplasms. Rarely, they are sites of origin of true neoplasms, producing paradoxes such as an adrenal carcinoma arising in the ovary.
- The term *hamartoma* refers to an excessive, focal overgrowth of cells and tissues native to the organ in which it occurs. Although the cellular elements are mature and identical to those found in the remainder of the organ, they do not reproduce the normal architecture of the surrounding tissue. The line of demarcation between a hamartoma and a benign neoplasm is often unclear, since both lesions can be clonal. Hemangiomas, lymphangiomas, rhabdomyomas of the heart, adenomas of the liver, and developmental cysts within the kidneys, lungs, or pancreas are interpreted by some as hamartomas and by others as true neoplasms. Their unequivocally benign histology, however, does not preclude bothersome and rarely life-threatening clinical problems in some cases.

Benign Tumors and Tumor-Like Lesions

Virtually any tumor may be encountered in children, but within this wide array hemangiomas, lymphangiomas, fibrous lesions, and teratomas deserve special mention. You will notice that the most common neoplasms of childhood are so-called soft-tissue tumors of mesenchymal derivation. This contrasts with adults, in whom the most common tumors, benign or malignant, have an epithelial origin. Benign tumors of various tissues are described in