Table 10-6 Risk Factors and Postmortem Findings Associated with Sudden Infant Death Syndrome

Parental
Young maternal age (age younger than 20 years)
Maternal smoking during pregnancy
Drug abuse in *either* parent, specifically paternal marijuana and maternal opiate, cocaine use
Short intergestational intervals
Late or no prenatal care
Low socioeconomic group
African-American and American Indian ethnicity (? socioeconomic factors)
Infant
Brain stem abnormalities, associated with delayed development of arousal and cardiorespiratory control
Prematurity and/or low birth weight
Male sex
Product of a multiple birth
SIDS in a prior sibling
Antecedent respiratory infections
Germline polymorphisms in autonomic nervous system genes
Environment
Prone or side sleep position
Sleeping on a soft surface
Hyperthermia
Co-sleeping in first 3 months of life
Postmortem Abnormalities Detected in Cases of Sudden Unexpected Infant Death (SUID)*
Infections
Viral myocarditis
Bronchopneumonia
Unsuspected congenital anomaly
Congenital aortic stenosis
Anomalous origin of the left coronary artery from the pulmonary artery
Traumatic child abuse
Intentional suffocation (filicide)
Genetic and metabolic defects
Long QT syndrome (*SCN5A* and *KCNQ1* mutations)
Fatty acid oxidation disorders (*MCAD*, *LCHAD*, *SCHAD* mutations)
Histiocytoid cardiomyopathy (*MTCYB* mutations)
Abnormal inflammatory responsiveness (partial deletions in *C4a* and *C4b*)

*SIDS is not the only cause of SUIDs, but rather is a *diagnosis of exclusion*. Therefore, performance of an autopsy may often reveal findings that would explain the cause of an SUID. These cases should *not*, strictly speaking, be labeled as "SIDS." SCN5A, sodium channel, voltage-gated, type V, alpha polypeptide; KCNQ1, potassium voltage-gated channel, KQT-like subfamily, member 1; MCAD, medium-chain acyl coenzyme A dehydrogenase; LCHAD, long-chain 3-hydroxyacyl coenzyme A dehydrogenase; SCHAD, short-chain 3-hydroxyacyl coenzyme A dehydrogenase; MTCYB, mitochondrial cytochrome *b*; C4, complement component 4.

be described) and the geographic locale. Most infants who die of SIDS die at home, usually during the night after a period of sleep. For many years, prolonged apnea was considered to be a risk factor for SIDS. Infants who developed a so-called "*apparent life-threatening event*" (ALTE), characterized by some combination of apnea, marked change in color or muscle tone, choking or gagging, were considered at risk for subsequent SIDS. However, epidemiologic studies have demonstrated that these "life-threatening events" and SIDS have different risk factors and ages of onset, and are probably unrelated entities. Children experiencing ALTEs are often premature or have a mechanical basis for respiratory compromise. This distinction might explain why home apnea monitors, which have proliferated among American families for "SIDS prevention," have had minimal impact on reducing the risk of SIDS.

MORPHOLOGY

In infants who have died of suspected SIDS, a variety of findings have been reported at postmortem examination. They are usually subtle and of uncertain significance and are not present in all cases. Multiple petechiae are the most common finding (~80% of cases); these are usually present on the thymus, visceral and parietal pleura, and epicardium. Grossly, the lungs are usually congested, and vascular engorgement with or without pulmonary edema is demonstrable microscopically in the majority of cases. These changes possibly represent agonal events, because they are found with comparable frequencies in *explained* sudden deaths in infancy. Within the upper respiratory system (larynx and trachea), there may be some histologic evidence of recent infection (correlating with the clinical symptoms), although the changes are not sufficiently severe to account for death and should not detract from the diagnosis of SIDS. The CNS demonstrates astrogliosis of the brain stem and cerebellum. Sophisticated morphometric studies have revealed quantitative brain-stem abnormalities such as hypoplasia of the arcuate nucleus or a decrease in brain-stem neuronal populations in several cases; these observations are not uniform, however. Nonspecific findings include frequent persistence of hepatic extramedullary hematopoiesis and periadrenal brown fat; it is tempting to speculate that these latter findings relate to chronic hypoxemia, retardation of normal development, and chronic stress. Thus, autopsy usually fails to provide a clear cause of death, and this may well be related to the etiologic heterogeneity of SIDS. The importance of a postmortem examination rests in identifying other causes of SUID, such as unsuspected infection, congenital anomaly, or a genetic disorder (Table 10-6), the presence of any of which would *exclude* a diagnosis of SIDS; and in ruling out the unfortunate possibility of traumatic child abuse.

Pathogenesis. The circumstances surrounding SIDS have been explored in great detail, and it is generally accepted that it is a *multifactorial condition,* with a variable mixture of contributing factors. **A "triple-risk" model of SIDS has been proposed, which postulates the intersection of three overlapping factors: (1) a vulnerable infant, (2) a critical developmental period in homeostatic control, and (3) an exogenous stressor.** According to this model, several factors make the infant vulnerable to sudden death during the critical developmental period (i.e., the first 6 months of life). These vulnerability factors may relate to the parents or the infant, while the exogenous stressor(s) are environmental (Table 10-6).

While numerous factors have been proposed to account for a vulnerable infant, *the most compelling hypothesis is that SIDS reflects a delayed development of "arousal" and cardiorespiratory control.* The brain stem, and in particular the medulla oblongata, plays a critical role in the body's "arousal" response to noxious stimuli such as episodic hypercarbia, hypoxia, and thermal stress encountered during sleep. The serotonergic (5-HT) system of the medulla is implicated in these "arousal" responses, as well as regulation of other critical homeostatic functions such as respiratory drive, blood pressure, and upper airway reflexes. Abnormalities in serotonin-dependent signaling in the brain stem may be the underlying basis for SIDS in some infants.