

Recognition of the At-Risk Child

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From 1959 to 1966, Dr. Richard Naeye, a pathologist at Hershey Medical School, participated in the Collaborative Perinatal Project which studied 53,518 pregnancies. Of the infants subsequently born, 125 died of the Sudden Infant Death Syndrome (SIDS). Through the mass of information gleaned from looking at the pregnancies, labor, delivery, examination of the placenta and subsequent events in the infants' lives, Dr. Naeye was able to determine nine historical factors that increase an infant's risk of dying of SIDS. According to his statistical analyses, these are additive factors so that the presence of a number of them increase the risk in any one infant. The risk factors are 1) poor prenatal care, that is, few prenatal visits; 2) maternal smoking; 3) maternal anemia; 4) abnormal insertion of the umbilical cord, 5) lymphocytic infiltration of the decidua at the placental margin; 6) blood group B; 7) premature delivery; 8) abnormal neurological evaluation of the infant at the time of discharge from the hospital; 9) crowding in the home, that is, more than 2.0 people per room. In addition, there are two clinical factors that increase an infant's risk of dying of SIDS. These include a history of apnea and a family history of two siblings who have had apnea or died of SIDS.

The clinical problem of apnea is particularly important and can be put into two categories—*asleep* and *awake*. Within the *asleep* category are three types of infants at risk: 1)

those who are *asleep* and have an apneic episode that requires mouth-to-mouth resuscitation, vigorous stimulation or gentle stimulation to resolve the episode; 2) those who have color changes, either pallor or cyanosis; and 3) those who are noted to have bradycardia during sleep.

The *awake* category of infants having apneic episodes is also divided into three types: 1) those infants who first cry out and then become apneic, pallid or cyanotic, unresponsive and need resuscitation; 2) those who choke, cough or vomit, become apneic and need resuscitation; and 3) those who have apparent seizure-like episodes resulting in apnea and are resuscitated. All of these infants having apneic episodes, both *awake* and *asleep*, are at increased risk.

We know that in premature infants there are many causes of apnea and we are now learning that there are certain specific causes of apneic events in older children and that these, too, can be treated. The etiologies now known include sepsis, meningitis, seizure disorders, intracranial hemorrhage (more common in premature than full-term newborns), metabolic abnormalities, cardiac anomalies and arrhythmias, gastroesophageal reflux, pneumonia and congestive heart failure. The infant should be evaluated to determine if any of these abnormalities are present. After treatment, the infant should be tested for signs of impaired control of ventilation as should the infant in whom no abnormality was found.

We test by ascertaining if the infant is having hypoventilation or if he or she has an abnormal breathing pattern. Hypoventilation is tested by measuring minute ventilation on room air and response to breathing carbon dioxide during

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quiet sleep. We compared a group of "near miss" and control infants, and found that the "near miss" infants' response to CO₂ was significantly less than control infants' and that while breathing room air, the partial pressure of carbon dioxide in expired air was significantly increased. We concluded that the "near miss" infants had relative hypoventilation in quiet sleep and a depressed response to breathing 5% CO₂. We also found that while some "near miss" infants have poor control of ventilation, some do not, indicating that there are at least two different mechanisms that cause an infant to require resuscitation.

We evaluate an infant's breathing pattern by recording respirations and heart rate during sleep. We record the infants for 12 hours at night.

The "near miss" infant will frequently have abnormal breathing patterns, including prolonged sleep apnea, excessive short apnea, disorganized breathing and periodic breathing. Any of these can be accompanied by bradycardia. In a recent study, we have found that periodic breathing is a qualitative marker for respiratory instability.

We have also found these abnormal patterns in siblings of SIDS victims whom we have tested prior to any clinical apneic episode and therefore believe that these abnormalities are not the consequence of a resuscitative event but in fact may result in an episode of prolonged apnea that may require resuscitation to terminate.

The markers are intriguing and may help to explain some of the pathologic findings that have recently been described in the autopsies of SIDS victims. Some of the changes in the infants who died of SIDS resemble changes found in infants who were known to be hypoxic prior to death. These changes include hypertrophy of

the smooth muscle of the pulmonary vasculature, an increase in extramedullary hematopoiesis, an increase in the periadrenal brown fat, right ventricular hypertrophy (as yet unsubstantiated), and a depletion of the adrenal medulla. All of these indicate that the victim has had chronic hypoxia prior to death, although these are victims who have had no history of any cyanotic or apneic episodes. Therefore, the desaturation must occur while the infant is not being observed.

Recently, in separate studies, both Dr. Naeye and Dr. Takashima at Toronto Sick Children's Hospital have found a proliferation of glial cells in the medulla of SIDS victims. The proliferation, which is a response to hypoxia, was very prominent in the respiratory control centers in the medulla and in the nucleus ambiguus. These areas correspond to the watershed zones of the microvasculature. Dr. Takashima concluded that the change was the result of hypoxia. Since this occurs in the respiratory control centers, whatever initiates the first hypoxic event can subsequently result in poor control of ventilation which itself can lead to more hypoxia and thus set the SIDS victim in a vicious circle. Takashima also described periventricular and subcortical leukomalacia, a change known to be caused by hypoxia. Some victims therefore, without any history of a cyanotic episode, have pathologic evidence in brain, lung, liver, heart and adrenals of having experienced significant hypoxia while they were alive. Certainly, it is possible that the abnormalities in respiratory pattern that we have noted in siblings of SIDS victims and in "near miss" victims, could result in these abnormalities.

In summary, infants who have experienced an apneic episode which was terminated by resuscitation have signs of impaired control of ventilation.