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Brainstem abnormalities found in "SIDS" infants, in all kinds of sleep environments

Study reinforces that some babies have underlying vulnerability

BOSTON—Investigators at Boston Children's Hospital report that many infants dying suddenly and unexpectedly, in all kinds of sleep environments, have underlying brainstem abnormalities and are not all normal prior to death.

The researchers also point to the need to detect and treat this underlying vulnerability early, the focus of their current work. They report their findings in the December issue of *Pediatrics*.

The investigators, led by Hannah Kinney, MD, a neuropathologist at Boston Children's, have shown over the past two decades that infants who die suddenly, unexpectedly and without explanation—whose deaths are generally attributed to sudden infant death syndrome (SIDS)—have differences in brainstem chemistry that set them apart from infants dying of other causes.

These abnormalities impair brainstem circuits that help control breathing, heart rate, blood pressure and temperature control during sleep, and, the researchers believe, prevent sleeping babies from rousing when they rebreathe too much carbon dioxide (due to inadequate ventilation), breathe too little oxygen or become overheated (from overbundling).

At the same time, epidemiologic studies have shown that infants dying suddenly and unexpectedly are often found sleeping face down with their face in the pillow, or sleeping next to an adult in the bed—environments that have the potential to lead to smothering and death by asphyxia.

In the new study, Kinney and colleagues asked if all these infants are truly normal. They reexamined their data, reviewing the cases of 71 infants who died suddenly and unexpectedly, were autopsied at the San Diego County Medical Examiner's office from 1997 to 2008, and had brainstem samples available for analysis. The researchers grouped the infants according to sleep circumstances—those that were considered likely to generate asphyxia and those that were not—based upon death-scene investigation reports.

In the end, they compared 15 infants with SIDS whose deaths were deemed *not* to involve asphyxia (group A), 35 SIDS infants whose deaths were possibly asphyxia-related (group B) and 9 infants who clearly died from other causes (controls). They

excluded the other infants, who either had insufficient data or had evidence of other clear risk factors for death, such as exposure to drugs or extremes of temperature.

Brainstem neurochemical abnormalities—involving serotonin, serotonin receptors, GABA receptors and 14-3-3 (a protein that regulates serotonin)—were found in both group A and group B. Infants in these two groups—with and without environmental risk factors for asphyxia—had the same brainstem abnormalities, and both groups differed significantly from the controls.

"Even the infants dying in a potentially asphyxia-generating situation had an underlying brainstem abnormality that likely made them vulnerable to sudden death if there was any degree of asphyxia," Kinney says. "The abnormality prevents the brainstem from responding to the asphyxial challenge and waking."

The investigators believe these findings confirm that sudden unexplained death in infants is associated with underlying vulnerabilities, and that not all infants who die in compromised sleep environments are normal.

"Certainly, there are compromised sleeping environments that can cause any baby to die, such as entrapment in the crib, but if it's just sleeping face down, the baby who dies may have an underlying brainstem vulnerability," says Kinney. "We have to find ways to test for this underlying vulnerability in living babies and then to treat it. Our team is focused now upon developing such a test and treatment."

Kinney emphasized that the Back to Sleep campaign has saved thousands of infant lives, and has likely included vulnerable babies.

"Safe sleep practices absolutely remain important, so these infants are not put in a potentially asphyxiating situation that they cannot respond to," she says.

Funders of the study included the National Institutes of Health, the National Institute of Child Health and Development (# R01-HD20991), First Candle, the CJ Foundation for SIDS, the Jacob Neil Boger Foundation for SIDS, the Marley Jaye Cerella Foundation for SIDS, River's Gift and the Intellectual and Developmental Disabilities Research Center at Boston Children's Hospital (# P30-HD18655).

Bradley Randall, MD, of the University of South Dakota Sanford School of Medicine, was the study's first author. Co-authors were David Paterson, PhD, Kevin Broadbelt, PhD, Jhodie Duncan, PhD, and Othon Mena, MD, Boston Children's Hospital; Elisabeth Haas, MPH and Henry Krous, MD, University of California, San Diego; and Felicia Trachtenberg, PhD, New England Research Institutes (Watertown, MA).

Boston Children's Hospital is home to the world's largest research enterprise based at a pediatric medical center, where its discoveries have benefited both children and adults since 1869. More than 1,100 scientists, including seven members of the National Academy of Sciences, 14 members of the Institute of Medicine and 14 members of the Howard Hughes Medical Institute comprise Boston Children's research community. Founded as a 20-bed hospital for children, Boston

Children's today is a 395 bed comprehensive center for pediatric and adolescent health care. Boston Children's also is the primary pediatric teaching affiliate of Harvard Medical School. For more information about research and clinical innovation at Boston Children's, visit: ***http://vectorblog.org.***

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