PEDIATRICS

Multiple 'SIDS' Case Ruled Murder

OSWEGO, NEW YORK—A jury last week cut the ground out from under a landmark paper, published 22 years ago, that offered a medical explanation for multiple cases of sudden infant death syndrome (SIDS) in a single family in this rural part of New York state. The jury concluded that the deaths weren't SIDS at all: It convicted Waneta E. Hoyt, 48, of murdering her five babies between 1965 and 1971. The verdict, which may be appealed, would seem to discredit a paper that was once one of the most widely cited publications in SIDS research. Ironically, it was the paper itself that led directly to Hoyt's trial (*Science*, 8 April 1994, p. 197).

The paper, published in the October 1972 issue of *Pediatrics*, described the deaths of two of Hoyt's children, Molly and Noah. Three of Hoyt's other children had died earlier, apparently of SIDS. Written by Alfred Steinschneider, then an assistant professor of pediatrics at the Upstate Medical Center in Syracuse, New York, the paper reported that the two infants suffered bouts of sleep apnea, or loss of breath, when they were monitored in the hospital. Both children died soon after they were discharged, and Steinschneider suggested that apnea was to blame. The paper was widely interpreted as evidence that apnea-related SIDS runs in families.

A prosecutor who came across the paper in 1986 in connection with another case drew a different conclusion: He thought the deaths seemed like murder. After a lengthy investigation, Hoyt signed a confession, and charges were brought against her on 23 March last year. (Hoyt later recanted, saying that she had signed under duress.)

Steinschneider, now president of the American SIDS Institute in Atlanta, testified in Hoyt's defense at the trial. He said, "The nurses reported to me, and in the chart, that [Molly Hoyt] had a number of episodes where the [apnea] alarm would go off and they felt the need to stimulate the baby." Steinschneider's paper said the alarms were set to go off if breathing stopped for 15 seconds. A prosecution witness, John G. Brooks, professor and chair of pediatrics at the Dartmouth Medical School, testified that occasional apneic pauses of less than 20 seconds are not abnormal among babies.

In addition to raising doubts that Molly and Noah suffered life-threatening apneic episodes, the prosecution noted that one of Hoyt's other children died at the age of almost 28 months—well beyond the age when SIDS strikes. Witnesses said SIDS almost always occurs within the first 6 months of life, typically while a baby is unattended in a crib.

Although the verdict contradicts the basis of Steinschneider's 1972 paper, SIDS researchers disagree over the paper's legacy. Carl E. Hunt, professor of pediatrics at the Medical College of Ohio at Toledo, told *Science* that Steinschneider's early apnea work set the stage for current studies of complex cardiorespiratory events. "A number of studies since [1972] certainly do identify respiratory pattern abnormalities in subsequent siblings," Hunt said. Defense witness Dorothy H. Kelly, of the University of Texas and associate medical director of the Southwest SIDS Research Institute at Hermann Hospital in Houston, adds that a subtle chronic abnormality seems to run in some rare SIDS-prone families. But other researchers disagreed. "True SIDS is not, in my opinion or experience, a familial disorder," said J. Bruce Beckwith, professor of pediatrics at the Loma Linda University Medical Center.

–Ginger Pinholster

Ginger Pinholster is a free-lance writer in Wilmington, Delaware.

MEDICAL DEVICES

Companies Fear FDA Rule on Antibodies

Biomeda Corp. of Foster City, California, makes 400 antibody types that scientists use to track down proteins involved in processes as diverse as brain chemistry and tumor growth. But Biomeda's entire stock may soon be pulled from its U.S. catalog, held hostage in a dispute between manufacturers and the Food and Drug Administration (FDA) over new rules to regulate antibodies. "Our company will discontinue [selling] all our antibodies in the United States as soon as the regulation is enforced," asserts Biomeda President José Perdomo.

What prompts that threat is the expectation that FDA will soon adopt a recommendation from an advisory panel to classify antibodies used in immunohistochemistry (IHC) procedures as class 2 medical devices. That step would hold the antibodies to strict standards of sensitivity and specificity, at a cost that industry officials estimate would exceed $10,000 per antibody. Ironically, most IHC antibodies, of which about 2500 are now available, are currently in an even more restrictive category, class 3, which includes artificial hearts and other critical devices. FDA put them in that category—which it uses for many new devices—with a tacit understanding that the issue would be revisited when antibodies became more common in clinics.

That time arrived in 1991, when FDA cracked down on Centocor for marketing cancer antibodies to clinicians that the company had originally designated for research use only. Centocor stopped selling the antibodies, but "the FDA threatened to remove all unapproved monoclonal antibody reagents from the market," recalls Daniel Seckinger, president of the College of American Pathologists (CAP). Although CAP and several other societies believe the antibodies are "safe and effective," they petitioned FDA last spring to classify them as class 2 devices because clinical pathologists might misdiagnose a condition based on a poorly manufactured product or a faulty reading. "We've had experience with some that have not been perfectly manufactured," says David Corwin, associate director of Washington Pathology Consultants in Seattle.

Last October an FDA advisory panel agreed. A decision is pending, says FDA's Steven Gutman, acting director of the division of clinical laboratory devices, but antibody manufacturers will be monitored more closely. "The data we would require are data pathologists would like to see, whether or not a product is regulated," he says.

Manufacturers, however, claim a class 1 designation would be more appropriate. They say that the cost of meeting the requirements exceeds the sales of about half their IHC antibodies. "It would not be cost-effective to keep a great many of our products on the market," says Peter Takes, clinical trials coordinator at Sigma BioSciences in St. Louis.

Although the FDA rules would apply only to clinical use, scientists may see a decrease in the availability of some antibodies for research. "If some pathologist came up with wonderful data that X antibody is useful for diagnosing Y condition, then our antibody would be considered a diagnostic product," says James Stiehr, president of Affinity Bioreagents Inc. of Neshanic Station, New Jersey. Some industry officials say their companies will shift to overseas markets, making IHC antibodies harder to obtain, and more costly, for U.S. scientists.

Gutman is more optimistic. He says the agency is revising regulations to include a provision, similar to the Orphan Drug Act, to help keep low-volume devices on the market.

Nevertheless, industry is worried that FDA's decision could set a precedent for other biologics, including other types of antibodies, CD markers, and DNA probes. Predicts one industry official, "If FDA views [IHC antibodies] as a high-risk, class 2 device, anything that comes along after that will be viewed similarly."

–Richard Stone