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Update: Pulmonary Hemorrhage/Hemosiderosis Among Infants -- Cleveland, Ohio, 1993-1996

In November 1994, private physicians and public health officials in Cleveland, Ohio, and CDC reported a cluster of eight cases of acute pulmonary hemorrhage/ hemosiderosis that had occurred during January 1993-November 1994 among infants in one area of the city (1). Two additional cases were identified in December 1994. All 10 infants lived within seven contiguous postal tracts in eastern metropolitan Cleveland. Pulmonary hemorrhages recurred in five of the infants after they returned to their homes shortly after hospital discharge; one infant died as a result of pulmonary hemorrhage. This report summarizes the findings of the follow-up investigation, including a case-control study and an assessment by the county coroner of cases of infant death. These findings documented an association between acute pulmonary hemorrhage/hemosiderosis in this cluster of cases and mold growth in their water-damaged homes. Case-Control Study of Risk Factors for Pulmonary Hemorrhage

To determine risk factors for acute pulmonary hemorrhage among the infants in the cluster, the Rainbow Babies and Childrens Hospital (RBCH), the Cuyahoga County Board of Health, the Cleveland Department of Public Health, and CDC conducted a case-control study. A case was defined as an episode of acute, diffuse pulmonary hemorrhage of unknown etiology during the first year of life in a previously healthy infant that required hospitalization at RBCH during January 1993-December 1994. The study compared 10 case-infants with 30 age-matched control infants from the same area in Cleveland (2).

Of the 10 case-infants, nine were male; in comparison, of the 30 controls, 15 (50%) were male (p less than 0.05). Breastfeeding was reported for none of the case-infants but for 11 (37%) of the controls (odds ratio {OR}=0.2; 95% confidence interval {CI}=0-1.2). In addition, nine of 10 case-infants and 16 (53%) of 30 controls resided in households with smokers (OR=7.9; 95% CI=0.9-70.6). All 10 case-infants and seven (23%) of the 30 controls resided in homes where major water damage (as a result of chronic plumbing leaks or flooding) had occurred during the previous 6 months (OR=16.3; 95% CI=2.6-infinity). The latter finding prompted a visual inspection and quantitative air sampling for and microscopic identification of fungi in the study homes. The quantity of fungi, including the toxigenic fungus *Stachybotrys atra* (whose toxins have been implicated in hemorrhagic disorders in animals), was higher in the homes of case-infants than in those of controls (OR=1.6; 95% CI=1.0-30.8).

Active surveillance by the RBCH identified an additional 11 cases of acute pulmonary hemorrhage/hemosiderosis among infants in the Cleveland area during January 1995-December 1996. Of these 11 infants, two had died as a result of acute pulmonary hemorrhage. The demographic characteristics and clinical presentation of these 11 cases was consistent with the initial cluster of cases.

Based on the findings of the case-control study, health authorities in Cleveland recommended prompt clean-up and disposal of all moldy materials in the water-damaged homes and have designed a prevention program focusing on water-damaged homes. Coroner's Investigation of Infant Deaths

The three infant deaths resulting from pulmonary hemorrhage prompted the county coroner to re-examine all infant deaths in Cuyahoga County during January 1993-December 1995 to determine whether cases of pulmonary hemorrhage had been misclassified. Postmortem examinations were reviewed for all 172 infants who died in the county during that period, including 117 deaths attributed to SIDS; premature infants who died in a hospital were excluded. Pathologic lung specimens were sectioned, stained with Prussian blue, and screened for the presence of hemo-siderin.

Extensive hemosiderin-laden macrophages were present in lung tissue of nine (5%) infants -- a finding indicating major pulmonary hemorrhage preceding death. Of these nine deaths, two resulted from homicide, and one had a recent history of child abuse. No apparent etiologies for pulmonary hemorrhage/hemosiderosis were identified for the other six infants presumed to have died from SIDS, all of whom had lived in the same postal tracts as the initial cluster; three were male, and two were siblings. A review of the clinical circumstances for five infants indicated that some symptoms of pulmonary hemorrhage had been present before death: two infants had had episodes of epistaxis or mild hemoptysis within 7 days before death, and four had had additional symptoms (e.g., cough, pulmonary congestion, or black stools).

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Editorial Note

Editorial Note: The findings of the investigation described in this report suggest that, in Cleveland, the infants with pulmonary hemorrhage were more likely than controls to reside in homes that had been affected by major water damage during the previous 6 months. The water damage may have promoted the growth of fungi, including *S. atra*. Because *S. atra* requires water-saturated cellulose-based materials for growth in buildings, it is considered uncommon in homes. Although *S. atra* has been associated with gastrointestinal hemorrhaging in animals that had consumed moldy grain (3), the fungus previously has not been associated with disease in infants.

SIDS is diagnosed only after exclusion of other known causes of death. The review by the Cuyahoga County coroner indicated that some infant deaths initially attributed to SIDS actually resulted from pulmonary hemorrhage. Agonal alveolar hemorrhage may occur in approximately two thirds of infant autopsies (4); however, the presence of extensive hemosiderin-laden macrophages within the alveoli indicates major predeath pathologic processes, which precludes the diagnosis of SIDS. Macrophages require approximately 48 hours to convert the iron of the ingested erythrocytes into hemosiderin; therefore, the presence of hemosiderin-laden macrophages in alveoli indicates alveolar bleeding for at least 2 days preceding death (5). Causes of such bleeding and pulmonary hemosiderosis may include cardiac lesions associated with increased left atrial pressure, trauma, pneumonia, and perhaps suffocation.

The findings of this investigation -- including the association of environmental factors with pulmonary hemorrhage/hemosiderosis and the presence of extensive hemosiderin-laden macrophages in some infants with SIDS -- underscore the need for further investigation of these relations. In particular, further efforts are needed to clarify the association between pulmonary hemorrhage in infants and exposure to water-damaged building materials and to evaluate pathologic methods to identify and quantify pulmonary

hemorrhage and hemosiderosis.

References

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