Publication

A controlled study of the relationship between Bordetella pertussis infections and sudden unexpected deaths among German infants

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Objective. This was a prospective, controlled, multicenter study to investigate the relationship between Bordetella pertussis infections and sudden unexpected deaths among German infants. Design. Between 1995 and 1997, all infants who died at 7 to 365 days of age and for whom autopsies were performed in 1 of 8 participating institutes of legal medicine were enrolled. During a standardized autopsy, nasopharyngeal specimens (NPSs) and tracheal specimens were obtained for polymerase chain reaction (PCR) assays to detect B pertussis. The oligonucleotide primers PTp1 and PTp2, which specifically amplify a 191-base pair DNA fragment of the pertussis toxin operon of B pertussis, were used. Two control subjects (matched according to residence, age, gender, and nationality) were enrolled for each case subject, via a network of pediatricians in private practice, and NPSs were obtained from those infants. Parents of case subjects and control subjects were asked to provide specific information on respiratory illnesses of the child, contact with a known case of pertussis, or close contact with a person with a cough illness during the 4 weeks before death or enrollment, as well as the child‘s pertussis immunization status. The pathologists performing the autopsies were unaware of the PCR results. Results. Enrolled were 254 infants (66 deaths and 441 matched control subjects. Autopsies according to protocol were performed for 234 of the case subjects (92 diagnosis of sudden infant death syndrome (SIDS) was made for 76 the remaining subjects, causes of death were respiratory or other infections (14 aspiration (2 were positive for B pertussis for 12 case subjects (5.1 SIDS or respiratory infections) and 5.3 12 case subjects with positive PCR results, 10 (83 Questionnaires had been returned by the parents of 5 of the 12 infants. Three had experienced a respiratory illness (all with cough), beginning 7, 14, and 19 days before death. None had a known contact with a case of pertussis. Four of 15 control infants (27 positive PCR findings for B pertussis had a cough illness, indicating possible pertussis, and 2 of those 4 developed typical symptoms (whooping). Background information was received from 116 parents (46 of case subjects and from parents of all control subjects. Upper respiratory tract infections within 4 weeks before death were reported for 53 case subjects (33 age-adequate numbers of pertussis vaccine doses. Conclusions. The concept of infection as a factor in SIDS is supported by a number of observations, including the seasonal distribution of the occurrence of SIDS; the high incidence of concurrent upper respiratory tract infections among infants dying as a result of SIDS; the peak age at 3 to 4 months; nicotine use in a child‘s household, which predisposes children to respiratory infections such as otitis media; and the protective role of breastfeeding. A prominent role might be suspected for B pertussis, for several reasons.

1) B pertussis infections in infancy are frequently associated with apneic spells, which are occasionally life-threatening and, if leading to death, might be reported as SIDS. 2) Epidemiologic evidence from the United Kingdom, Sweden, and Norway indicates that SIDS is associated with B pertussis infection. 3) In a previously published study, we detected B pertussis DNA in the nasopharynx of 9 of 51 consecutive infants (18 sudden unexpected deaths. This is the first prospective, controlled study to investigate the possible etiologic role of B pertussis in SIDS. Clinically unrecognized B pertussis infections were relatively frequent (5.3 The rate of infection was similar or perhaps greater for control subjects, compared with case subjects (1.7 were compared. This may seem surprising but is supported by other studies, in which asymptomatic infections or mild respiratory illnesses were observed among infants exposed to B pertussis. Careful autopsies, including histologic evaluations of organ specimens and use of PCR to detect B pertussis in NPSs and tracheal specimens, represented a strength of this study. Our general findings were as expected. The majority of cases were classified as SIDS. The second largest group included infants for whom respiratory infections were found. The findings of various other diagnoses, which in several instances would have been undiscovered otherwise, emphasize the need for autopsies after unexpected infant deaths. What is the significance of the identified B pertussis infections in 12 cases? Several pieces of evidence support the plausibility of a cause-and-effect relationship. Eight of the 12 case subjects died before 6 months of age, the typical age for death attributable to pertussis. In autopsies, 9 of the subjects were found to have signs of respiratory infections; for 2 infants, the autopsies suggested that death was attributable to a respiratory infection. One additional infant (data not shown) had brain edema.

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