malformation syndrome remains unknown. The concomitant maternal viral infection and the use of a sulfonamide for urinary tract infection may have been factors, as reported by Niikawa et al.[1] Regardless of the etiology, this case represents the first report of Niikawa-Kuroki syndrome in a non-Japanese child.

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Commentary: Timely topics

THE JOURNAL has always attempted to publish promptly any article of unusual importance or current interest, such as the report of the "epidemic" of hypochloremic alkalosis in infants being fed a particular soy protein formula or the relationship between infant botulism and the ingestion of honey. The Editorial Board has suggested the desirability of extending that policy to include the reservation of a few pages of each issue for articles that are particularly timely or that contain information of potential immediate importance to the health of children. The Publisher has agreed to cooperate in making possible the publication of such papers in the earliest issue. Practical considerations dictate that such articles may have to appear at the end of the issue, and that they not be unusually long. The editors must, of course, make the final decision regarding which communications deserve this special consideration. Comments will be appreciated.

The following paper was selected for prompt publication.

J. M. G.

Diphtheria–tetanus toxoids–pertussis vaccination and sudden infant deaths in Tennessee

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ON MARCH 9, 1979, the Tennessee Department of Health reported to the Centers for Disease Control that four sudden and unexplained deaths had occurred since November, 1978, in infants who had been vaccinated during the 24-hour period prior to death. All four deaths were classified as sudden infant death syndrome, and all had received a first vaccination of diphtheria–tetanus toxoids–pertussis vaccine and oral polio vaccine. All of the DTP was from the same lot; the OPV came from three different lots. As a precautionary measure, further use of the suspect DTP lot in public clinics was halted. An investigation was carried out to determine if there was a meaningful association between DTP vaccine from the suspect lot and sudden infant deaths in Tennessee.

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Abbreviations used

CDC:	Centers for Disease Control
SIDS:	sudden infant death syndrome
DTP:	diphtheria–tetanus toxoids–pertussis vaccine
OPV:	oral polio vaccine
NIH:	National Institutes of Health

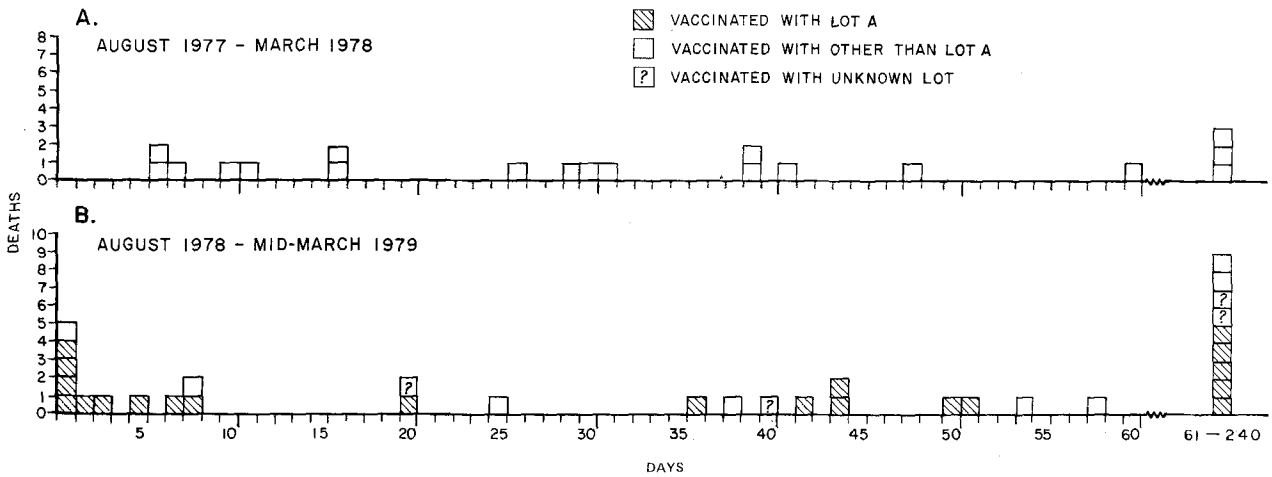

Figure. Sudden infant deaths, by number of days after infant's DTP vaccination, in Tennessee from August, 1977, to March, 1978, and from August, 1978, to March 15, 1979.

METHODS

The investigation compared the vaccination histories in cases of SIDS occurring in Tennessee *before* (August, 1977, through March, 1978, control period) and *during* (August, 1978, through March, 1979, study period) the time when the suspect DTP lot (lot A) was in widespread use. All infant deaths at less than one year of age in which SIDS was listed as the underlying cause were identified from all Tennessee death certificates, as were all infant deaths at less than one year classified as sudden unexplained death or death resulting from unknown causes (International Classification of Diseases 798.0). For the period December, 1978, through March, 1979, death certificates were not yet available on computerized tapes and a manual review of certificates was carried out. This was done at the state level for death certificates that had already been forwarded to the State Vital Records Office and at the county or local level for death certificates still being processed by local vital statistics registrars. Ascertainment was considered complete. Vaccination histories for each identified case of SIDS in each time period were determined by contacting parents or relatives and obtaining the name of the physician or clinic that had been seeing the infant. Parental records were accepted if the date of vaccination and the antigens received were specified. Health providers were contacted to verify vaccination histories and to obtain additional information on lot number and manufacturer. Additionally, a questionnaire was administered to each parent.

RESULTS

Death certificate searches revealed that 73 SIDS cases had occurred in the control period and that 83 cases were similarly diagnosed in the study period. Because infants less than 6 weeks of age at the time of death had not been eligible for vaccination, further analysis was restricted to the 45 SIDS infants 6 weeks of age or older from the control period and to 55 similar infants from the study period.

There were no significant differences in gender, race, frequency of autopsy, or mean age at death between these two groups.

In the control period, 19 of 45 (42%) infants had a history of DTP vaccination, compared to 33 of 55 (60%) infants in the study period ($P = 0.12$, Fisher exact test). Of the vaccinated infants in the study period, 79% had received only a first dose of DTP compared to 54% in the control period, but this difference was not statistically significant.

Eleven infants died within eight days of vaccination in the study period compared to three infant deaths within eight days of vaccination during the control period (Figure). Nine of the 11 infants of the study period had received lot A; of these, four infants had died within 24 hours of vaccination. The differences in the number of vaccinated infants who died within eight days or within 24 hours of vaccination with lot A in the study period and with any lot in the control period were not statistically significant at the 0.05 level ($P = 0.063$ and 0.066, respectively, Fisher exact test). Restricting the analysis to the study period and with the use of binomial distribution, the probability of having observed four or more deaths on any single one of the first eight days after use of lot A is 0.03.

Questionnaires were completed for 30 of the 45 cases in the control period (66.7%) and for 26 of the 55 (47%)

study period cases. Of these 26, the seven infants who died within eight days of vaccination with lot A were compared separately to the remaining 19 infants from the same study period and to the 30 infants from the control period.

Among infants who died within eight days after use of lot A, prematurity was less frequent, mean birth weight was greater, and mean hospital stay after birth was shorter than among the remaining SIDS infants in the study period or than among all the SIDS infants from the control period. However, when we restricted the analysis only to immunized SIDS infants, these differences disappeared.

DISCUSSION

A history of DTP vaccination was not significantly more common among the SIDS cases from the study period when lot A was in use than among those from the control period when lot A was not in use. The number of sudden unexplained infant deaths within the intervals of 24 hours or eight days after vaccination was not significantly greater in the study period, but the probability of observing these differences between the two time periods for each interval after vaccination was low ($P = 0.06$). However, the probability of observing four or more deaths on any single one of the first eight days after the use of lot A was 0.03. This evidence seems adequate to indicate an unusual temporal association between DTP vaccination with lot A and SIDS.

Whether or not this temporal association reflects a causal relationship remains undetermined; we found no evidence to support such a causal relationship. The overall incidence of SIDS in Tennessee did not increase during the time period when lot A was in use. Samples from lot A were tested at the Bureau of Biologics, Food and Drug Administration, and found acceptable with regard to potency and freedom from toxicity for all components.

Lot A consisted of 361,000 doses, distributed in 15 dose vials to 807 purchasers throughout the United States. The Tennessee Health Department received the largest single shipment (150,000 doses); only eight other health departments received at least 100 vials (> 1,500 doses). Lot A was the only lot in use in health department clinics in Tennessee for most of the study period. The question of whether or not lot A was causally associated with the deaths observed was examined in light of the more general question of whether or not any DTP vaccine can cause sudden infant deaths. There are limited discussions of this possibility in the medical literature and no evidence to support a causal relationship.[1-4] Anecdotal evidence from foreign countries where different DTP vaccination schedules were used beginning at later infant ages as compared to the United States experience does not suggest an association between DTP and SIDS because the age distribution curves of SIDS cases are similar, even though vaccination patterns are quite different.

Lot A was removed from circulation as a result of the cluster of deaths in Tennessee. No further clusters have been reported in any states subsequent to the use of other DTP lots. A panel of outside consultants convened at CDC to review the available evidence and concluded that a causal relationship between lot A and SIDS, although not totally excluded, had not been established.

More importantly, preliminary data from a National Institutes of Health–sponsored, multicenter, case control study on SIDS have failed to show any increased frequency of DTP vaccination among SIDS cases when compared to matched controls.[5] The findings of our study combined with the NIH results provide no support for reducing efforts to immunize infants with DTP.

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