PERTUSSIS VACCINE ENCEPHALOPATHY

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The possibility that severe neurologic disorders might follow the administration of pertussis vaccine has been widely recognized since the report of Byers and Moll in 1948.[1] During that year, a mouse toxicity test became a requirement for the licensure of pertussis vaccines in the United States.[2] It was hoped that vaccines passing this test would have significantly less toxicity in children and that, by their use, encephalopathy might be eliminated or at least its incidence reduced.[3] In 1953, the test for pertussis vaccine potency was revised,[4] and, in effect, a ceiling on maximum potency was imposed. It is possible that some batches of older vaccines may have exceeded by a considerable margin the required potency, and that this property may have been related to vaccine-induced encephalopathy.

Because of dating and distribution factors, it is unlikely that vaccines meeting the new standards for toxicity and potency were used exclusively in this country until 1955. Since then, there have been four reports of cases of pertussis vaccine encephalopathy in the United States.[5-8] The patients reported in these papers, however, may well have received vaccine standardized according to the older tests.

To determine if neurologic complications have occurred after the administration of vaccine meeting the new standards, a questionnaire was sent early in 1961 to 102 heads of pediatric departments and directors of children's hospitals in the United States. The questionnaire asked about the occurrence of pertussis vaccine encephalopathy during the years 1956 to 1960 inclusive.

Results of Questionnaire

Sixty-five reports were returned. Sixty-one informants stated that no instances of neurologic reactions had been observed in their hospitals. Fourteen reported that some type of reaction had been observed. One reply concerned a two-year-old boy who had a single febrile seizure a few hours after the administration of a booster dose of an undetermined type of DPT in 1956. Another reported three children with leg paralysis lasting not more than ten days; two of these children received their injections in the vastus lateralis muscle, and one received his in the gluteus muscle.

Twenty-one children from the remaining twelve institutions apparently had some type of encephalopathy. Eleven were boys and seven were

girls; in three instances, the sex was not stated. Two of the twenty-one had a history of convulsions before the vaccine reaction occurred. In Table 1 are recorded the ages of the children at the time of their reactions. The higher incidence in the younger age groups probably reflects only the frequency with which immunizations are given in those age groups. It can be seen in Table 2 that reactions were not confined to any one or two calendar years.

Most of the reactions occurred after the use of triple antigen, i.e., pertussis vaccine combined with diphtheria and tetanus toxoids (Table 3) This, too, probably reflects only the frequency of use of the various types of preparations and not a predilection of combined antigens to give rise to neurologic reactions. Of interest is the observation that three reactions have occurred following the use of quadruple antigen (DPT plus poliomyelitis vaccine). The manufacturers of the vaccines used were identified for only three patients--the product of a different firm was used in each of the three.

Reactions were recorded after each of the three injections which are recommended for primary immunization, as well as after booster injections (Table 4). It is remarkable that one child was reported to have had reactions after both his first and second injections and another child after both his second and third injections.

Sequelae

The sequelae of the reactions are summarized in Table 5. Eight children are mentally retarded. Although the questionnaire did not ask specifically, in three instances, it was noted that the retardation is severe. Twelve of the children have recurrent convulsions. Manifestations of cerebral palsy are present in four. No deaths were recorded, and three children recovered completely. The outcome in four is unknown.

Discussion

From the data in this report, no estimate of the incidence of neurologic reactions can be made. Two informants volunteered that in their institutions, the incidence of neurologic reactions in the past five years appeared to be about the same as it was ten or fifteen years ago. It is obvious that severe neurologic reactions have occurred in children after immunization with pertussis vaccines which have passed the toxicity and potency tests currently in use.

TABLE 1

Age at Time of Reaction

1-3 mo.	5
4-6 mo.	7
7-12 mo.	3
25-36 mo.	1
>36 mo.	2
Not Stated	3

TABLE 2

Year Reaction Occurred

1955	3
1956	4
1957	3
1958	1
1959	2
1960	5
1961	2
Not Stated	1

TABLE 3

Preparation Used

Alum-Precipitated DPT	12
Aluminum-Phosphate-Adsorbed DPT	1
DPT-Type Unknown	4
Pertussis Vaccine-Type Unknown	1
Quadruple Vaccine	3

TABLE 4

Injection with Which Reaction Occurred*

First Injection	8
Second Injection	7
Third Injection	3
Booster Injection	2
Not Stated	3

*One patient had reactions after both the first and second injections, and another patient had reactions after both the second and third injections.

TABLE 5

Sequelae+

M.R. and R.C.	5
M.R., R.C., and C.P.	1
M.R. and C.P.	1
M.R. Only	1
R.C. Only	4°
R.C. and C.P.	2
Complete Recovery	3
Not Stated	4

+M.R. - Mental Retardation
R.C. - Recurrent Convulsions
C.P. - Cerebral Palsy

°Two of these children had seizures before the reaction occurred.

References

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5. Cohen, M. J., et al.: Postimmunization Reactions, Harlem Hosp. Bull., 8:81-6, 1955.

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