

Infantile spasms and early immunization against whooping cough

Danish survey from 1970 to 1975

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SUMMARY 113 cases of infantile spasms were diagnosed in the period 1 April 1970 to 31 March 1975 after Denmark changed her immunization programme. Previously whooping cough vaccine was given as the triple combination at 5, 6, and 15 months of age. From 1 April 1970 it was given as a monovalent vaccine at 5 and 9 weeks of age and at 10 months of age. A comparison with previous material of 86 cases of infantile spasms from 1957 to 1967 showed no change in the age at onset. Though there may be an occasional connection between immunization and infantile spasms, the most important factor is a time-coincidence between any immunization given at a certain age with the neurological disorders which are natural for that age.

The problem of a possible connection between immunization and infantile spasms is still open to discussion. The immunization most suspected has been whooping cough vaccine given as triple vaccine or monovalent vaccine. Since Jeavons and Bower in 1964 suggested a possible connection, this has been discussed by several authors. Melchior (1971) felt that it was mainly a time-coincidence whereas Kulenkampff *et al.* (1974) suggested neurological complications of pertussis inoculation, including a few cases of infantile spasms. Melchior (1971) suggested that valuable information could be obtained if different vaccine programmes gave a different age distribution at onset of infantile spasms. The present report deals with the information obtained after April 1970 when Denmark changed her immunization programme. The first

injection of pertussis vaccine was now given at the age of 5 weeks, the second at the age of 9 weeks, and the last at the age of 10 months. Immunization against diphtheria-tetanus-polio was given at 5, 6, and 15 months of age.

Patients and methods

From 1 April 1970 to 31 March 1975, 113 infants with infantile spasms were admitted to the 20 paediatric departments in Denmark. There were 56 boys and 57 girls. The age of onset of the infantile spasms are given in Table 1 and in the Fig., together with previous data (Melchior, 1969). Only new patients admitted at the time when the new vaccination programme was introduced are included, and no patients from previous years, when the

Table 1 Age at the first infantile spasm in two Danish series

Age (m)	1957-1967		1970-1975	
	n	%	n	%
<2	5	6	13	12
2	5	6	12	11
3	9	10	14	12
4	17	20	8	7
5	17	20	26	23
6	13	15	12	11
7	4	5	9	8
8	5	6	8	7
9-11	8	9	6	5
12-17	3	3	5	4
Total	86	100	113	100

Received 6 May 1976

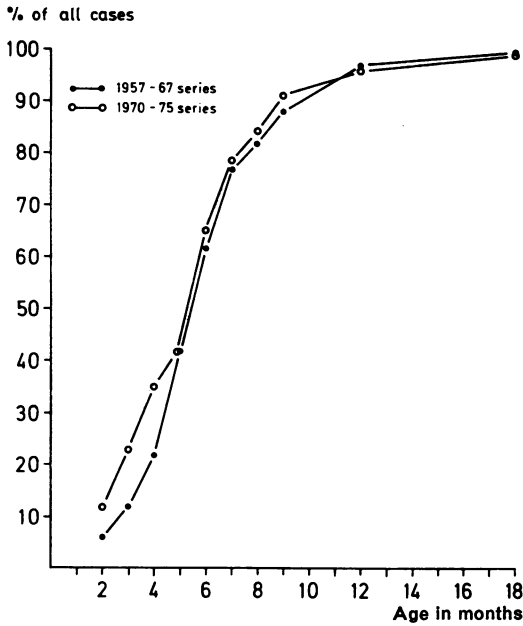


Fig. Comparison between age at onset of infantile spasms in two Danish series after different immunization programmes. The graphs show for each series the cumulative percentage of infants in the series who had started having infantile spasm at each age.

old vaccination programme was still being used. All hospital records were studied in order to find a possible aetiological factor for the infantile spasms. The group of *symptomatic* cases totalled 60 and the group of *cryptogenic* cases 40. 36 of the children were never vaccinated, and a further 61 were vaccinated but showed no time relation between vaccination and infantile spasms. Vaccination could be considered as a triggering mechanism in 3 cases. In 13 cases there was no obvious aetiology and, furthermore, some immunization had been given some time before the onset of infantile spasms. 6 children were immunized against whooping cough and 7 against diphtheria-tetanus-polio (Table 2).

The clinical data on the patients were obtained from the hospital records. All included convulsions typical of infantile spasms, and on electroencephalogram (EEG) 66 had typical hypsarrhythmia, 16 EEGs showed what could be considered as atypical hypsarrhythmia, 24 had severely abnormal EEGs of other kinds, and 7 had a normal EEG. The aetiology in the group of symptomatic cases included almost all the well-known factors such as prematurity, neonatal jaundice, perinatal asphyxia, cytomegalovirus infections, and severely retarded children due to chromosomal abnormalities, etc.

Discussion

The present series includes 113 children with infantile spasms. These were new cases admitted to all Danish paediatric departments from 1 April 1970 to 31 March 1975. This may be considered as an indicator of the total number of infantile spasms in Denmark, very few patients being treated outside the paediatric services owing to the medical tradition of the country.

Until now there has been no nationwide survey of infantile spasms in Denmark. However, a previous study covering the series of infantile spasms admitted to the Rigshospital in the years 1957 to 1967 was carried out, and it was suggested that this would include between one-third and one-half of the total number of patients in the country, thus suggesting a total between 16 and 24 cases annually (Melchior, 1969). This fits very well with 113 patients in the last 5 years and suggests no increase in the number of infantile spasms. A comparison of the age of onset of the infantile spasms shows no significant difference between the series of spasms before the new immunization programme and after (Wilcoxon's test and Spearman's rank analysis).

If we consider the whooping cough component as a separate aetiological factor, it is likely that there would be evidence of an earlier onset in the new series. This could be due either to an increasing number of early spasms occurring after early immunization or to a reduction of the number in the

Table 2 Aetiological classification of infantile spasms in relation to immunization

		Not vaccinated	Immunization without time relation to seizures	Immunization may be a trigger mechanism	Immunization and possible time relation to seizures			
					Pertussis		Di-Te-Pol	
				I	II	I	II	
Symptomatic	(n=60)	32	25	3				
Cryptogenic	(n=40)	4	36					
Immunization	(n=13)				1	5	3	4
Total	(n=113)	36	61	3	13			

Di-Te-Pol = diphtheria, tetanus, polio vaccine. I = first injection; II = second injection.

age group 6–8 months after removing the pertussis component from the previously used triple-vaccine. Even if we consider the monovalent pertussis vaccine as weaker than that previously used, and thus maybe less neurotoxic, the removal of pertussis immunization from the age group 6–8 months might have shown some reduction of the number of infantile spasms in that age group. For the purpose of the present study, in the 6 cases in which the history yielded no obvious explanation but immunization had been performed, the case records have been reviewed in detail. One child developed infantile spasms after the first immunization. There had been some bleeding during pregnancy and delivery had been induced. The child had had slight neonatal jaundice. The time interval between the immunization and infantile spasms was 17 days.

Five children developed infantile spasms after the second whooping cough immunization. One of these had a history of the cord around the neck; in another case the mother had epilepsy. One child had a family history of epilepsy and the birth-weight was 2500 g. The time interval in these cases was 7 days, 11 days, unknown, unknown, and 13 days.

These details in the case histories might place those children between the immunization group and the symptomatic group and they underline the recommendation by the Statens Serum Institut that special attention should be paid to children with a history of neonatal or prenatal problems before starting immunization. This recommendation is also the practical reason for the excess of nonvaccinated children in the group of symptomatic cases.

Of special interest is the occurrence of infantile spasms in 7 children, developing within 2 weeks of the diphtheria-tetanus-polio immunization. This seems to confirm the opinion that we are dealing mainly with a time-coincidence and suggests that whatever immunization we administer in the age groups between 1 and 2 months and 9 and 10 months, some children will develop neurological disorders which are typically associated with these age groups. Of course this does not solve the problem put forward by Kulenkampff *et al.* (1974) concerning more general neurological complications, but the actual problems presented in that study in addition to infantile spasms were convulsions occurring soon after immunization, mainly between 0 and 24 hours.

It is very difficult to evaluate the data in this report from the 36 case histories over a period of 11 years because these data give little indication of the extent of the damage which might have occurred had there been no vaccination. The recommendations from that paper are in very close agreement

with suggestions put forward some years ago by Statens Serum Institut in their instructions included with the whooping cough vaccine. They also agree with reports from other places concerning a possible coincidence or connection between whooping cough inoculation and neurological complications (Prensky, 1974).

We have no Danish reports on early convulsions in connection with whooping cough vaccination as in the British report (Kulenkampff *et al.*, 1974). Any such occurrence would probably be well known as almost every child who convulses for the first time, particularly after a medical procedure such as immunization, would be admitted to hospital and reported to the health department and to Statens Serum Institut. No such cases have been reported. Another problem which has been discussed previously is the occurrence of unexpected death in childhood where the time factor has been linked with immunization. This problem is still unsolved.

The present study once again implies that a causal connection between whooping cough immunization and infantile spasms is very unlikely except in a few cases and that time-coincidence is the most likely factor, but we still have no prospective studies concerning all immunized children, as suggested by Prensky (1974). Such a project is extremely difficult to carry out. At present we are looking into some of the problems in connection with whooping cough immunization, but this study is in its earliest stage. Further discussion on the connection between vaccination and brain damage, infantile spasms in particular, may seem superfluous. It is, however, of importance in maintaining the confidence of the general public in the vaccination programmes (*British Medical Journal*, 1975). A Danish survey (Holm *et al.*, 1974) showed only a slight decrease in the number of pertussis vaccinations, mainly with regard to the second and third doses. This could be due to the fact that doctors were keeping a closer watch for the occurrence of minor side effects than was the case at the time of the first vaccination. Mass vaccination is still very necessary for children, especially for infants under 12 months. This fact has again been shown during a recent epidemic of whooping cough in Denmark (Lautrop, 1976; Melchior and Jessen, 1976).

I thank the Danish Paediatric Departments for their co-operation in this survey.

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