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RESPONSES OF 6- AND 9-MONTHS-OLD INFANTS TO TWO AND THREE DOSES OF POLIOMYELITIS VACCINE

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The earliest time to start immunization against poliomyelitis is when satisfactory response will follow in all subjects. We have already shown that the response to active immunization in infants with high levels of maternally transmitted antibody is unsatisfactory (Perkins, Yetts, and Gaisford, 1958, 1959a). It was not possible to overcome the inhibitory effect of these antibodies in 1-week-old infants with current vaccines, even though the volume and number of the antigenic stimuli are increased, but we were able to show that in 16-weeks-old infants a more satisfactory basal immunity followed primary immunization with three doses of vaccine given at monthly intervals, though the maternal antibody still present in some of these infants inhibited their response to the most important component, type 1 (Perkins, Yetts, and Gaisford, 1959b). It seems clear, therefore, that satisfactory response will not be obtained in all infants until maternal antibody has fallen to non-inhibitory levels, and it is estimated that this will not be until after the age of 6 months.

An investigation was therefore made of the responses of 6- and 9-months-old infants both to two and to three doses of vaccine given as a primary course of immunization.

Procedures

Immunization of Infants.—Thirty-two infants were given intramuscularly three doses of vaccine, each of 1 ml., at intervals of four weeks. Post-immunization

blood samples were taken (a) four weeks after the second dose, which was at the time of the third dose, and (b) 14 to 21 days later. The infants were in two groups; 16 were 6 months old and 16 were 9 months old at the time of their first injection.

Vaccine.—Two batches of commercial vaccine were used and each group of infants was inoculated with a single batch. The 6-months-old infants were inoculated with vaccine A, prepared from Brunenders (type 1), MEF-1 (type 2), and Saukett (type 3), and that used for the 9-months-old infants—vaccine B—had the type 1 component prepared from the Mahoney strain. The antigenic activity in monkeys showed both vaccines to be satisfactory, with the type 1 potency of vaccine A being a little better than that of vaccine B.

Titration of Sera.—Sera were titrated by the method used in previous investigations (Biological Standards Control Laboratory, 1957; Perkins, Sousa, and Tobin, 1958). For each infant all serum samples were titrated in parallel in the same test in order that a valid comparison of antibody levels could be made. All titres are given as the dilution of serum in the serum-virus mixtures before the addition to cell cultures.

Antibody Levels Before Immunization

Table I gives the distribution of antibodies before immunization in all infants. Three infants had very high levels, two to type 1 and one to type 3. For this reason, and also because these infants gave exceptionally high antibody responses to the first two doses of vaccine, it was considered that they had been infected with poliomyelitis virus during the first few months of life. They were therefore eliminated from further analysis; this left 15 infants in the 6-months-old and 14 in the 9-months-old groups. As might be expected, there was a higher proportion of infants with maternal antibody in the 6-months-old group than in the 9-months-old group. However, maternal antibody had fallen to non-inhibitory levels (<64) to all types in all the 9-months-old infants and in all but two of the 6-months-old infants.

Response to Vaccine

The proportion of infants responding to two and three doses of vaccine and the geometric mean titre for each group are shown in Table II; the levels of responses are shown in the figure.

After two doses the responses to type 2 and 3 were good. There were only two infants, both in the 6-months-old group, who did not respond—one to type 2 and one to type 3—and both had inhibitory maternal antibody levels at the time of receiving the first dose of vaccine. The responses to type 1 were not so good; though they were better in 6-months-old than in 9-months-old infants. Three 6-months-old and six 9-months-old infants failed to respond and the 6-months-old responders gave slightly higher levels than those from the 9-months-old group.

Chart showing responses to poliomyelitis vaccine.

After three doses the responses were entirely satisfactory. All except the two infants who had inhibitory maternal antibody levels responded to all types, and the geometric mean titres for the groups increased by about tenfold. In comparing these results with those obtained in previous studies it is evident that better responses were obtained in these infants to the three-dose schedule than after injection of two doses of vaccine at any other age (Medical Research Council, 1957, 1958).

It is interesting to note that there was very little difference between the 6- and 9-months-old groups in

TABLE I.—Placentally Transmitted Maternal Antibody Levels to Poliomyelitis Virus Remaining in 6- and 9-months-old Infants

Age of Infants	No. of Subjects	Virus Type	No. of Sera with Antibody Level											
			< 8	8	16	32	64	128	256	512	1,024	2,048	4,096	8,192
6 months	16	1	11	1	0	1	2	0	0	0	0	1	0	0
		2	8	1	4	1	0	2	0	0	0	0	0	0
		3	11	1	1	1	1	2	0	0	0	0	0	0
9 "	16	1	13	1	1	0	0	0	0	0	0	0	1	0
		2	13	0	1	0	2	0	0	0	0	0	0	0
		3	13	1	1	0	0	0	0	0	0	0	0	1

TABLE II.—Proportion of 6- and 9-months-old Infants Responding to Two and Three Doses of Poliomyelitis Vaccine

Age of Infants	Vaccine	Proportion of Infants Responding (and Geometric Mean Titre)					
		Type 1 After		Type 2 After		Type 3 After	
		2 Doses	3 Doses	2 Doses	3 Doses	2 Doses	3 Doses
6 months	A	12/15 (39)	13/13 (870)	14/15 (140)	12/13 (1,080)	13/15 (122)	12/13 (1,140)
9 "	B	8/14 (8)	14/14 (71)	14/14 (100)	14/14 (1,378)	14/14 (134)	14/14 (1,520)
All infants		20/29 (18)	27/27 (237)	28/29 (119)	26/27 (1,226)	27/29 (128)	26/27 (1,322)

their responses to types 2 and 3, after either two or three doses of vaccine. The difference in the type 1 responses after two doses, however, was much accentuated by giving a third dose. Though all infants in both groups responded, the geometric mean titre for the 6-months-old group was more than twelve times that of the 9-months-old group. These results suggest that the antigenic activity of the type 1 component of vaccine A which was given to the 6-months-old infants was greater than that of vaccine B given to the 9-months-old infants.

Conclusions

Placentally transmitted maternal antibody had fallen to non-inhibitory levels in almost all 6-months-old infants and in all 9-months-old infants tested.

The responses of infants in these age groups to two doses of vaccine were good to the type 2 and 3 components, all infants responding, but those to type 1 were not quite so satisfactory because 3 out of 15 6-months-old and 6 out of 14 9-months-old infants failed to show a rise in antibody level. The responses after three doses, however, were much more satisfactory, all infants responding to type 1 giving higher antibody levels, and the responses to types 2 and 3 being very much higher than after two doses.

The 6-months-old infants responded better to type 1 than the 9-months-old infants, and this difference was most pronounced after the third dose. This was probably due to the difference in the antigenic activity of type 1 in the two vaccines used. Though a small difference was observed when measured in monkeys, it was not as marked as in the infants. It is important, therefore, that only vaccines highly potent in the type 1 component should be used for immunizing infants, and that three doses given at monthly intervals should constitute the primary course at this age.

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Since 1955 the medical and health services in Mauritius have been considerably expanded under a plan for capital expenditure. Part of the service was concerned with an island-wide campaign to eliminate malaria, which was previously regarded as a scourge of the colony. The effectiveness of the campaign can be gauged by a comparison of cases within a period of the last 12 years: in 1945 more than 3,000 cases of malaria were treated in hospitals, with a total of 148 deaths; in 1957 only four cases were treated in hospitals, with no deaths reported.

TESTS FOR PHENYLKETONURIA

RESULTS OF A ONE-YEAR PROGRAMME FOR ITS DETECTION IN INFANCY AND AMONG MENTAL DEFECTIVES

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The diagnosis of phenylketonuria is important for three different reasons: in young infants the detection of this metabolic error permits treatment with a low-phenylalanine diet in order to prevent or minimize mental deterioration; the ascertainment of all cases of phenylketonuria among mental defectives would permit an accurate estimate of the frequency in the population of the gene responsible; to the paediatrician the differentiation of phenylketonuria from other forms of mental deficiency is always important, not least because of the light it throws on the chances of later children in the family being affected. For these reasons any test which makes the diagnosis of phenylketonuria simpler or more reliable is to be welcomed.

Several workers have reported that phenylketonurics treated with a low-phenylalanine diet from the age of a few weeks developed normal intelligence, while in cases where treatment was delayed the I.Q. usually remained below the average, and in untreated phenylketonurics the modal I.Q. was 10 (Horner and Streamer, 1956, 1959; Armstrong, Low, and Bosma, 1957; Woolf, Griffiths, Moncrieff, Coates, and Dillistone, 1958; Hsia, Knox, Quinn, and Paine, 1958; Brimblecombe, Stoneman, and Maliphant, 1959; Armstrong, Centerwall, Horner, Low, and Weil, 1959). This emphasizes the importance of early detection if irreversible mental deterioration is to be avoided. Programmes aimed at detecting all cases in a community at a very early age have been suggested or initiated (Woolf, Griffiths, and Moncrieff, 1955; Centerwall, 1957a, 1957b; Hsia, 1957; Woolf *et al.*, 1958; Baird, 1958). We report here the findings of such a detection programme carried out in Cardiff over the period March 1, 1958, to March 1, 1959, and also a survey of four institutions for mental defectives. "Phenistix," a strip which is dipped into the urine like litmus paper, has been found to be a simple and satisfactory test for phenylketonuria.

Method

The mother of every child born in Cardiff was asked to bring a fresh specimen of her baby's urine to the infant-welfare clinic when the baby was 3 weeks old or as soon as possible after. A bottle containing a little chlorbutol as a preservative was provided by the health visitor. Ferric chloride solution (5%) was added drop by drop to the urine until a definite colour appeared.

Results

Though there were 4,530 live births in Cardiff during the year, only 1,192 specimens of urine were collected and tested. The mothers of the 73.7% of babies that were not tested generally complained that it was