RESPONSE OF 3-MONTHS-OLD INFANTS TO 3 DOSES OF TRIVALENT ORAL POLIOMYELITIS VACCINE

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The earliest age at which successful poliomyelitis immunization is likely to be achieved with oral vaccine has been the subject of a number of reports (Plotkin *et al.*, 1959; Pagano *et al.*, 1960; Lepow *et al.*, 1961). Most studies have been limited to giving type 1 virus or serial feeding of monovalent vaccine. Although in the first week infection has been achieved by feeding high doses of virus the antibody responses have been so unsatisfactory as to make this age impracticable for routine immunization. After the age of 2 months, however, the antibody responses are appreciably greater.

At the present time, in Britain three spaced doses of trivalent vaccine are used and have been found effective in infants 6–12 months of age (Public Health Laboratory Service, 1961). It is not known, however, whether such a schedule has a similar value in younger infants, and a study was therefore made to investigate this point.

Procedures

Immunization of Infants.—Thirty-three infants were given three doses of trivalent oral poliomyelitis vaccine at intervals of six weeks. At the time of giving the first dose of vaccine the infants were 3 months old. The vaccine was prepared from Sabin strains by the Wellcome Research Laboratories at Beckenham, and each dose, of 0.5 ml., contained $10^{6.0}$ TCD_{50} type 1, $10^{5.0}$ TCD_{50} type 2, and $10^{5.5}$ TCD_{50} type 3. Each dose was diluted with 1–2 teaspoonfuls of orange juice or blackcurrant juice and fed by spoon. Serum samples were taken on the day the first dose was given and four weeks after the third dose. Faecal samples were collected on the fourth and twelfth days after each dose. Paired sera were obtained from 30 infants and complete series of faecal samples from 32.

Isolation of Virus from Faeces.—A 10% suspension of faeces in Parker 199 medium containing antibiotics was centrifuged and the supernatant fluid inoculated into monkey-kidney-cell cultures. After incubation for one hour at 37° C. the fluid was changed and the cultures were incubated for seven days, observing cytopathic effects on days 4 and 7. Poliovirus isolations were typed with monospecific antisera.

Titration of Sera.—Poliomyelitis antibody titres to each of the three virus types were determined by the colour test. Serum samples from each subject were titrated in the same test together with the British standard poliomyelitis antisera (Perkins and Evans, 1959), which have now been adopted as International Standards (W.H.O., 1962). Comparisons of the titres of the infants' sera with those of the standards enable the antibody titres to be quoted in units, and these are shown in the Figure. Thus by this test a serum having a titre of 1:256 contains 10 International units/ml.

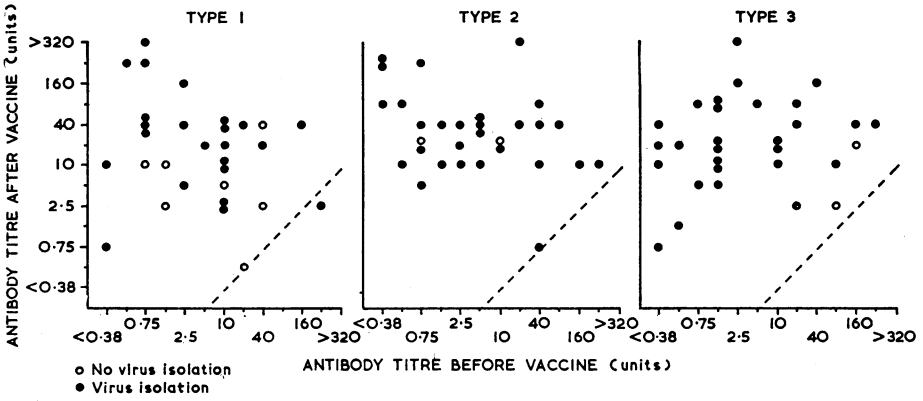
Responses of Infants to Vaccine

The results of virus isolation from the faeces after each dose are shown in the Table, from which it is clear that the infants were more readily infected with types 2 and 3 than with type 1. After all three doses had been given the majority (94%) had been infected by types 2 and 3 viruses, and 78% had been infected with type 1 virus. It is interesting to note that the type 3 virus persisted for the greatest time. The first dose of vaccine infected about the same number of infants with types 2 and 3 virus, and yet six weeks later when the second dose had been given only four continued to excrete type 2 virus whereas 16 continued to excrete type 3 virus and only five of these were new excreters.

Infection of 32 Infants by Three Doses of Trivalent Oral Poliomyelitis Vaccine

Virus Type	No. of Infants from whom Poliovirus was Isolated after			Total Isolations*	No. of Infants Infected by All 3 Types
	1st Dose	2nd Dose	3rd Dose		
1	6 (6)†	19 (15)	10 (4)	25 (78%)	23 (72%)
2	27 (27)	4 (2)	1 (1)	30 (94%)	
3	25 (25)	16 (5)	6 (0)	30 (94%)	

* Number of infants from whom poliovirus was isolated at any time during the course of immunization.
† Numbers in parentheses indicate number of infants infected for the first time.



Serological responses of 3-months-old infants to three doses of oral poliomyelitis vaccine.

The antibody responses are shown in the Figure, in which the interrupted line indicates the calculated titres of maternal antibody at the time of taking the second blood sample; a titre greater than fourfold above this line is taken as a serological response. Responses were shown by all infants except three to type 1, three to type 2, and one to type 3. Two of the infants failing to give a response to type 1 failed

to respond to type 2 also; the third infant not responding to type 1 had failed to become infected by this type, whereas he gave good responses to types 2 and 3, with which he had been infected. The third infant failing to respond to type 2 responded to types 1 and 3, and the single infant not responding to type 3, which had failed to infect, gave good responses to types 1 and 2, which had infected. In general, gut infection was associated with antibody response, but in some (notably in relation to type 1) a good response was obtained in infants from whom virus was not isolated. This discrepancy is most likely due to the small number of faecal samples taken and failure to isolate virus from short-lived infections.

Summary

Good antibody responses were obtained to all three virus types in 25 of 30 3-months-old infants who were given three doses of trivalent oral poliomyelitis vaccine at six-weeks intervals. The remaining five infants gave good antibody responses to one or two of the virus types.

The few infants who failed to respond were among those with the highest antibody titres before immunization. It is possible that, in these, maternal antibody had masked but not inhibited response; this question can be resolved only when the response to a booster dose given six to nine months later is known. If it proves to be satisfactory it will be possible to offer quadruple antigens in the form of either D.T.P. (diphtheria, tetanus, pertussis vaccine) + Salk vaccine or D.T.P. + oral trivalent Sabin vaccine, for routine immunization starting at 3 months of age.

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POLIOMYELITIS IN A NURSERY SCHOOL IN GLASGOW

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Very few cases of poliovirus infection were detected clinically or virologically in the West of Scotland for three years following the outbreak of 1958 (Bell and Grist, 1962). The finding of two cases of poliovirus type 1 infection in November, 1961, in the same nursery school was therefore remarkable.

This nursery school has accommodation for 40 children and at the time there were 37 children aged from 3 to 5 years on the roll. The staff consisted of one teacher, four nursery assistants, one student nursery assistant, two cleaners, and one dining-room attendant; their ages ranged from 17 to 45 years. In November, 1961, two pupils of this school were found to be suffering from poliomyelitis. There had been four cases of poliomyelitis (three of poliovirus type 1 and one of type 3) in Glasgow during the preceding two months.

Case 1.—J. H., a boy aged 4 years 3 months, was last at school on November 10. He became unwell later that day and was admitted to hospital on November 15. He had an aseptic meningitis and a temporary paralysis of the muscles supplied by the right facial nerve. There was no paralysis of the limbs. A specimen of faeces taken on November 16 was examined virologically with negative results, but poliovirus type 1 was cultured from a second specimen taken on December 1. He had received two doses of inactivated vaccine in May and June, 1961.

Case 2.—M.H., a girl aged 3 years 6 months, had a transient illness on Friday, November 10. On waking from her afternoon sleep that day she cried and refused her tea. In the children attending nursery schools such behaviour at that time of day is often the first sign of the onset of a febrile illness. She was sent home, but on Monday, November 13, she returned to school in her normal health. This transient illness, occurring on the same day as her school-mate (Case 1) sickened of poliomyelitis and 11 days before she herself sickened of poliomyelitis, may have been due to the early phase of viral invasion or merely coincidental. Conybeare (1946) described similar illnesses 12–13 days before onset of poliomyelitis. After this brief illness she remained well until November 21, but on waking from her afternoon sleep that day she was pale and trembling and obviously ill. She was sent home immediately and was admitted to hospital a few hours later. She had an aseptic meningitis but no paralysis. Poliovirus type 1 was cultured from a specimen of faeces taken on November 22. She had not been immunized against poliomyelitis.

The second patient had been admitted to hospital with a provisional diagnosis of cerebrospinal fever. On the afternoon of November 29 it was reported to the Health and Welfare Department that virological investigation had established the diagnosis of non-paralytic poliomyelitis. At the same time it was reported that the first patient, who had been admitted with a provisional diagnosis of tuberculous meningitis and who was a pupil of the same nursery school, might also be suffering from poliomyelitis though at that time the virological results were negative.

Preventive Measures

At this stage it became necessary to decide what administrative action should be taken to prevent the spread of infection. The school premises were inspected on November 30 and found to be in satisfactory condition. Since infection had already had time to spread throughout the school, immunization with inactivated vaccine (the only type then available) was not offered.