conducting tissue or to a transient disturbance in a healthy heart.

Many others have contributed to our experience of resuscitation and we are grateful to them and also to Dr. D. D. C. Howat for experiments in ventilation. We are grateful to the Medical Committee of St. George's Hospital and the Editor of the *Proceedings of the Royal Society of Medicine* for permission to reproduce the instructions for cardiac arrest.

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ADDENDUM.—Two further experiences, outside the consecutive series of cases described, serve to illustrate the importance of external massage. A woman aged 55 came to the casualty department complaining of chest pain and collapsed from ventricular fibrillation. External massage was required for 20 minutes before defibrillation was achieved, and she subsequently made a complete recovery and has returned home free of symptoms; the electrocardiogram showed changes of cardiac infarction limited to the diaphragmatic wall. In another woman, aged 61, with heart-block and ventricular fibrillation, external massage had to be continued for over an hour until procainamide restored normal rhythm. Tracheostomy was required owing to multiple rib fractures, but she made a complete recovery and is now living a fairly normal life with the aid of an artificial pacemaker.

VACCINATION IN INFANCY WITH ORAL POLIOMYELITIS VACCINE AND DIPHTHERIA, TETANUS, PERTUSSIS VACCINE

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Infant immunization against poliomyelitis, diphtheria, tetanus, and pertussis has been recommended by the Ministry of Health, using either inactivated poliovaccine (*Brit. med. J.*, 1961) or oral poliovaccine (M.O.H. Circular 3/62). Three doses of triple vaccine (diphtheria, tetanus, and pertussis) and three doses of poliovaccine are given at separate attendances, the complete schedule entailing six visits to a clinic. These visits could be reduced to three if oral poliovaccine were administered at the same time as triple vaccine. Reports from Hungary (Kelemen *et al.*, 1961) have already indicated that such a procedure is likely to be effective. However, so far there has been no information from British sources of the effectiveness of oral poliovaccine in infants under 6 months of age, either alone or in combination with triple vaccine. The effectiveness of inactivated poliovaccine in early infancy is materially reduced by interference by maternally transmitted antibodies, and the extent to which the oral vaccine can overcome such interference is important if the vaccine is to be employed in early infancy.

The studies described here form the first of a series to be carried out at University College Hospital and Guy's Hospital, London, and at the Swindon Public Health Department to determine the effectiveness in early infancy of oral poliovaccine and triple vaccine given simultaneously.

Procedure

The participants in this study were healthy infants attending for routine primary immunization at the infant welfare departments of University College Hospital (group 1) and Guy's Hospital (group 2). Pre-vaccination serum samples were obtained from all infants at their first attendance. One ml. of poliovaccine was administered orally from a syringe. The triple vaccine was given

subcutaneously. The infants returned on two occasions at intervals of six weeks for a further injection and oral feeding at each attendance. A post-vaccination serum sample was taken four weeks later. For all infants both pre- and post-vaccination samples were titrated for poliomyelitis-neutralizing antibodies and for all but two infants diphtheria and tetanus antitoxin was also titrated.

The infants in group 1 were given type 1 polio virus at the first visit, type 3 at the second, and type 2 at the third. In group 2 the three virus types were combined in a trivalent vaccine. In both hospitals the dose of each virus type was 10^6 TCD_{50}.

Both the oral poliovaccine and the triple vaccine were prepared at the Wellcome Research Laboratories. The oral poliovaccine contained the Sabin strains, the production and testing of which has already been described (Goffe *et al.*, 1961). The triple vaccine contained approximately 30 Lf of diphtheria toxoid, 6 Lf of tetanus toxoid, and 20×10^9 *Bordetella pertussis* organisms in a dose of 0.5 ml.

Results

Poliomyelitis Antibody

A total of 60 infants were vaccinated—33 in group 1 and 27 in group 2. The great majority in both groups were between 5 and 20 weeks old, but the infants in group 2 were on the whole younger than those in group 1 (Table I). Twenty-seven of the 33 mothers in group 1 and 17 of the 27 in group 2 had previously been immunized with inactivated poliovaccine.

TABLE I.—*Age Distribution of Infants in Both Groups*

Age in Weeks:	5–8	9–12	13–16	17–20	21–24	25–36	Total
Group 1 ..	0	1	20	7	3	2	33
„ 2 ..	6	20	1	0	0	0	27

Twenty-eight of the infants in group 1 and 24 in group 2 had pre-vaccination antibody to type 1. The corresponding figures were 28 and 25 for type 2, and 29 and 24 for type 3 (Figs. 1 and 2).

A comparison of pre- and post-vaccination median titres after sequential feeding (group 1) showed a satisfactory rise to all types: for type 1 from 40 to 609; for type 2 from 54 to 400; and type 3 from 85 to 497 (Table II). Twenty-four of 33 infants showed a rise in titre to type 1; all but one of the remainder had pre-vaccination levels of 64 or more, and in these the post-vaccination titres also showed a response allowing for the rate of disappearance of maternally conferred antibody (Perkins *et al.*, 1959). Individual responses were excellent to types 2 and 3.

After the trivalent poliovaccine (group 2) median titres showed a satisfactory rise after vaccination for type 2 from 69 to 696 and for type 3 from 68 to 411. A rise in titre occurred to type 2 in 23 and type 3 in 20 of 27 infants. All but one of the infants with pre-vaccination titres of less than 256 showed a rise of both type 2 and type 3; the post-vaccination titres of those with titres

TABLE II.—*Poliomyelitis Antibody Levels (Median Values) from Pre-vaccination and Post-vaccination Blood Samples*

Group	Blood Sample	Median Antibody Values		
		Type 1	Type 2	Type 3
1	Pre-vaccination	40	54	85
	Post-vaccination	609	400	497
2	Pre-vaccination	60	69	68
	Post-vaccination	103	696	411

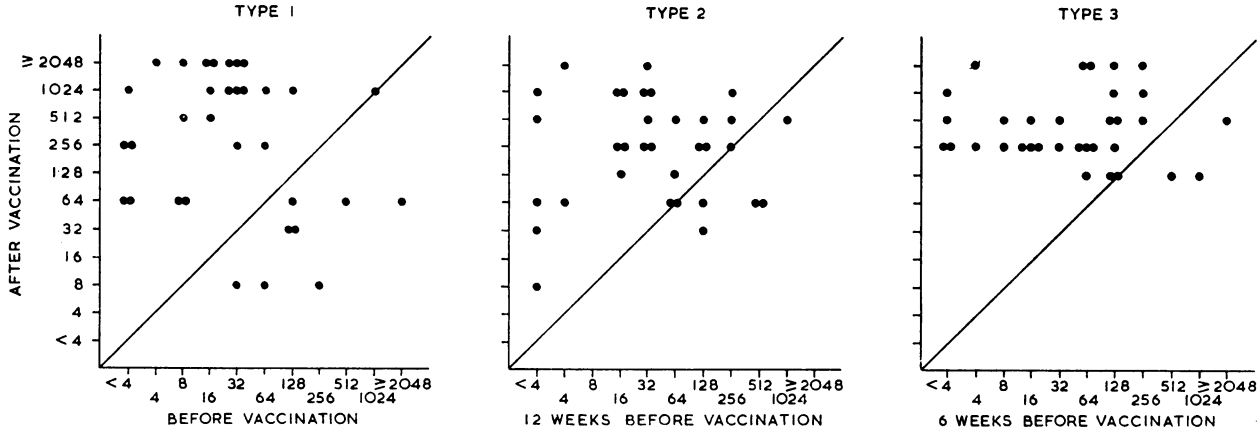

FIG. 1.—Individual poliomyelitis antibody titres before the first and after the third dose of oral vaccine. Group 1.

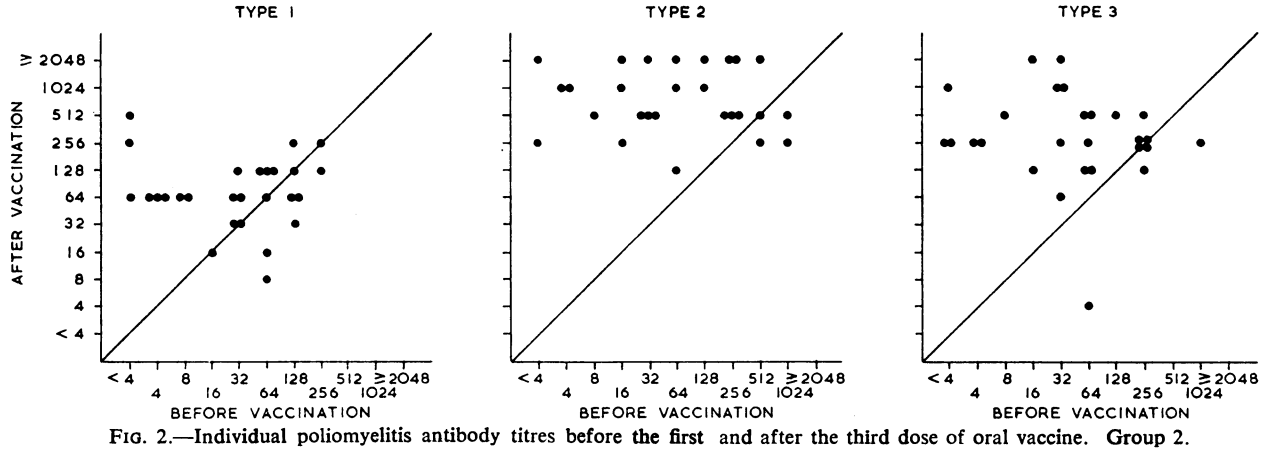

FIG. 2.—Individual poliomyelitis antibody titres before the first and after the third dose of oral vaccine. Group 2.

of 256 or more either rose or showed a response allowing for the decline of maternal antibody. The type 1 response was also satisfactory though not as good as that to types 2 and 3; the median titre rose after vaccination from 60 to 103 (Table II). Infants with pre-vaccination antibody titres of less than 16 to type 1 all showed a rise in titre after vaccination, whereas of those with pre-vaccination titres of 16 or more, 6 out of 19 showed a fall. However, all but one of these infants had higher post-vaccination titres than could be accounted for by maternal antibody alone, allowing for the decline in maternal antibody titres.

Diphtheria and Tetanus Antitoxin

All of the samples from infants in group 1 had satisfactory tetanus antitoxin titres after immunization, as did all but one for diphtheria antitoxin (Table III). In group 2, diphtheria and tetanus antitoxin titres were also satisfactory after vaccination; in three infants diphtheria antitoxin titres were lower than before vaccination but this signified an active response after correction for the expected rate of fall of the maternal

TABLE III.—*Diphtheria and Tetanus Titres of Infants after Three Injections of Triple Vaccine (Both Groups)*

Diphtheria			Tetanus		
Limits of Titres (Units/ml.)	No. of Infants		Limits of Titres (Units/ml.)	No. of Infants	
	Group 1	Group 2		Group 1	Group 2
<0·005	1	0	0·5–1	0	1
0·01–0·02	0	1			
0·02–0·05	0	0	1–2	1	1
0·05–0·1	0	3			
0·1–0·2	1	1	2–5	9	8
0·2–0·5	1	4			
0·5–1	8	10	5–10	15	11
1–2	14	6			
2–5	6	1	10–20	6	6
5–10	0	1			
Total infants	31*	27	Total infants	31*	27

* Antitoxin titres were not tested for 2 of the 33 infants in group 1.

antitoxin. Post-vaccination diphtheria antitoxin titres were lower in group 2 than in group 1, but titres of maternally conferred antitoxin of 0.005 units per ml. or more occurred more frequently in group 2 (13 out of 27) than in group 1 (5 out of 31). This finding was expected, since the infants in group 2 were, on the whole, younger than those in group 1.

Discussion

This investigation indicates that oral poliomyelitis vaccine (Sabin) in a dose of 10^6 for each virus type, given concurrently with triple vaccine (diphtheria, tetanus, and pertussis) is an adequate method of primary immunization in early infancy.

The effect of two poliomyelitis vaccination regimes was studied in two separate groups of infants. One group was given the vaccine sequentially, and in the other a trivalent vaccine was employed. All infants in both regimes had adequate tetanus antitoxin titres after vaccination, and all but one had satisfactory diphtheria antitoxin titres.

A feature of the current study was the age of the participants. Many of the infants were aged 3 months or less and the great majority were under 6 months. Most infants had high levels of maternal antibody before vaccination. Immunization of infants under 6 months of age against poliomyelitis with inactivated vaccine is adversely affected by the presence of maternal antibody (Perkins *et al.*, 1959; Brown and Kendrick, 1960; Hillary *et al.*, 1962; Butler *et al.*, 1962). In the current study a few infants with high pre-vaccination titres did not show a rise in titre after vaccination, but the extent of the post-vaccination decline in titre was less than would have been expected in the absence of effective vaccination. Moreover, with one exception, a decline was observed only in infants with pre-vaccination titres of 64 or greater. After three doses of the trivalent polio-vaccine (group 2), poliomyelitis antibody responses were extremely satisfactory to types 2 and 3, and the majority of type 1 antibody titres increased. The median post-vaccination titres to type 1 antibody were lower than to the other two types; nevertheless, more than three-quarters of these infants had antibody titres to type 1 of 64 or more after vaccination. After immunization with the poliovaccine given sequentially there was an excellent response to types 2 and 3 and also to type 1.

The infants given the poliovaccine sequentially were slightly older than those given the trivalent poliovaccine; caution must thus be exercised in comparing the relative adequacy of the two regimes. However, there was a higher median titre of type 1 antibody and a greater proportion showing a rise in titre in the infants given type 1 singly than in the infants given the trivalent poliovaccine (Figs. 1 and 2). It is possible, therefore, that the response to the type 1 component of the trivalent vaccine was reduced by the concurrent feeding of type 2 and type 3, which was not fully overcome by two further doses of trivalent vaccine. A relative increase in type 1 component, as in the vaccine currently issued by the Ministry of Health, might be expected to remedy this slight inequality. Since there is little to choose between giving single virus types of the polio-vaccine sequentially, or in three doses of all types combined, the latter method seems to be the more suitable in that the same preparation can be used for each vaccination session.

Summary

Oral poliomyelitis vaccine was given to two groups of infants at the same time as a triple vaccine (diphtheria, tetanus, and pertussis). More of the infants were under 6 months of age and many were 3 months or less. In one group of 33 infants the three poliovirus types were given sequentially. In the other group of 27 infants a trivalent poliovaccine was employed. Both regimes were satisfactory, but the latter is more practical for routine use. Both the immunization schedules studied require only three sessions for primary immunization instead of the larger number of visits which are required with the schedules currently recommended.

We thank the mothers of the infants who participated. We also thank Mr. Lavers and Mr. Michieli for the diagrams and Miss Robarts for the administrative and secretarial work involved. We also thank Dr. R. E. Bonham Carter, Sister Curtis, and the staff of the Child Welfare Department, University College Hospital; and Dr. R. C. MacKeith. Miss M. Theisen, and the staff of Solomon's Centre, Guy's Hospital.

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