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The response to oral poliovaccine in persons aged 16–18 years

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SUMMARY

Serum neutralizing antibodies to polioviruses were titrated in serum samples from 182 police cadets aged 16–18 years before and, in 168 of the cadets, 6 weeks after vaccination with a single dose of oral polio vaccine (OPV). Faecal excretion of poliovirus was also followed. Vaccination histories were obtained and confirmed whenever possible.

Pre-vaccination antibody could not be detected against type 1 in 9·3% cadets, against type 2 in 2·7% and against type 3 in 7·7%. Absence of antibody to at least one virus type was found in 14·3% of the cadets.

In 93 cadets in whom vaccination histories could be confirmed 40 had received only inactivated polio vaccine (IPV) previously; of these 23% lacked antibody to at least one virus type, and they had less intestinal immunity to a challenge dose of OPV than those previously given OPV. Only two of the cadets known to have had OPV were non-immune – both had received a single dose following full courses of IPV. However, cadets who had received OPV had their last dose of vaccine more recently (average 4·6 years) than those who had received only IPV (all 12 years or more).

The serum antibody response to a single booster dose of OPV, and the faecal excretion of each type of virus after vaccination, showed an inverse relation to the corresponding pre-vaccination antibody concentration. A single dose of OPV did not reliably boost the immunity of those who possessed adequate immunity, and a failure to respond was also observed in a proportion of the cadets with no detectable antibody, mostly in the case of type 3 antibody and particularly if antibody to types 1 or 2 virus was also absent. No evidence was obtained that intestinal immunity could be expected in the absence of detectable circulating antibody.

The reasons for the absence of a serological response to OPV in some subjects are discussed and consideration is given to the practical significance of the findings. It is suggested that reinforcement of polio immunity at school-leaving is important,

particularly at the present time when many of those aged 16–18 years will have been vaccinated only with IPV. A single dose of OPV is not ideal for this purpose, not only because a small proportion of persons are liable to be left unprotected, but also because failure to produce a reliable boost in persons with adequate immunity at the time of vaccination gives rise to the possibility that they may become susceptible later in adult life.

INTRODUCTION

Poliomyelitis has become rare in Britain since the introduction in 1956 of inactivated Salk vaccine and in 1961 of live attenuated Sabin vaccine. However, poliovirus strains with fully virulent characteristics are still isolated from specimens submitted to diagnostic laboratories (Miller, Reid & Diamond, 1970; P.H.L.S., 1973, 1974). Therefore, it would appear that this low incidence of the disease depends on maintaining an effective immunization programme.

Although it is reported that about 80 % of infants in Britain receive a primary course of three spaced doses of poliovaccine (D.H.S.S. 1972*a*), it cannot be inferred that a similar proportion of the population are immune, since the duration of the immunity produced by polio vaccine has not been precisely evaluated and all children may not respond to the three types of poliovirus. Serological surveys in a number of countries suggest that immunity is incomplete (Skelton, Schild and Stuart-Harris, 1966; Galbraith & Fernandes, 1969; McCollough, Glezen, Lamb & Chin, 1969; Reid, Yetts, Oddy & Benson, 1969; Murphy, *et al.* 1972; Rasmussen, Thomas, Mulrooney & Morrissey, 1973). Among 3 to 6-year-old children investigated in Scotland only 49 % had detectable serum antibody to the three types of poliovirus (Reid, Bell, Grist & Wilson, 1973), and Mortimer & Cunningham (1975) found that 12 % of 185 sera from children aged 5–14 years had no poliovirus antibody.

In the present investigation the immunity of a group who had recently left school has been examined, together with their response to a reinforcing dose of live polio vaccine. This age group was studied because a single dose of oral poliovaccine at 15–19 years of age is recommended in the immunization schedule (D.H.S.S., 1972*b*) and information is needed on the response to be expected in previously vaccinated persons in this age group. The study was made among volunteer police cadets aged 16–18 years, who came from many parts of the United Kingdom. The poliomyelitis vaccination history of the cadets was established whenever possible. The cadets' serological immunity to the three types of poliovirus was measured before and after a single dose of oral poliovaccine. Faecal samples were collected after vaccination and cultured for polioviruses to relate the findings to the presence or absence of intestinal immunity.

MATERIALS AND METHODS

The cadets were 16 to 18-year-old boys attending the Metropolitan Police Cadet Training School, Hendon, who agreed to participate after the proposed investigation had been fully explained to them. A vaccination history was provided by the

volunteers and confirmed by enquiries to Medical Officers of Health and, when necessary, general practitioners.

In January 1973 a blood sample (10 ml.) was collected by venepuncture from each volunteer who was then given a single dose of trivalent oral poliovaccine (Wellcome) containing $10^{6\cdot0}$ TCD 50 type 1, $10^{5\cdot0}$ type 2 and $10^{5\cdot5}$ type 3. Each cadet was also provided with three sterile screw-capped aluminium containers and spatulas and asked to collect faecal samples each week for 3 weeks, commencing 1 week after vaccination. A second blood sample was collected 6 weeks after vaccination.

The sera were separated, inactivated at 56° C. for 30 min and stored frozen at − 20° C. until the pre- and post-immunization samples were titrated in pairs for their content of neutralizing antibody to each type of poliovirus, using the galactose colour test (Perkins & Evans, 1959). The titrations were started at a final serum dilution of 1/8, and the results are given in terms of international units per ml. The lowest concentration of antibodies tested was 0·1 unit/ml. for type 1, and 0·03 unit/ml. for types 2 and 3 poliovirus.

Faceal samples were refrigerated at 0–4° C. and sent by post to the laboratory the following day. They reached the laboratory 48–72 hr. after collection. Faecal extracts were prepared and cultured in secondary monkey kidney cells (Mair & Tobin, 1960); when a delay in inoculating the tissue cultures could not be avoided faecal suspensions were stored at − 20° C. for up to 72 hr.

RESULTS

Serum neutralizing antibody before vaccination

One hundred and eighty two cadets provided an intial blood sample. Neutralizing antibody was not detected against type 1 in 17 cadets (9·3 %), against type 2 in 5 cadets (2·7 %), and against type 3 in 14 cadets (7·7 %). Twenty-six cadets (14·3 %) had no neutralizing antibody to at least one virus type (see Table 1).

Vaccination history. All the cadets except one claimed to have been vaccinated against poliomyelitis and the history was confirmed in the case of 93 of the 182 cadets from records held by the then medical officers of health and, in a few cases, family doctors. Cadets with a history of vaccination with oral polio vaccine (OPV) had received their last dose of vaccine more recently (average 4·6 years) than those who had received inactivated polio vaccine (IPV) (all 12 years or more), so that the findings do not provide a basis for comparing the duration or degree of immunity produced by the two types of vaccine. Of the 93 cadets only 26 (18 %) had received a reinforcing dose of poliovaccine before leaving school. Only 11 cadets had received OPV and no IPV and these have been grouped with the 42 who had had both OPV and IPV. The geometric mean concentration of antibody (GMC) to the three poliovirus types was lower in the cadets who had received IPV, and an absence of detectable serum antibody was commoner in this group, of whom 9 (23 %) had no detectable serum antibody to at least one poliovirus type (Table 2); each of these cadets had received 3 or more injections of IPV. The two cadets who had received OPV and who each lacked antibody to type 1 poliovirus

Table 1. *Cadets with no detectable serum poliovirus neutralizing antibody*

	Cadets with no antibody to poliovirus of:							
	Type 1 only	Type 2 only	Type 3 only	Type 1 and 2	Type 1 and 3	Type 2 and 3	Type 1 and 2 and 3	No. examined
No.	9	1	6	2	6	2	0	182
%	4·9	0·5	3·3	1·1	3·3	1·1	0	100

had both received only one dose of OPV after three and four injections of IPV respectively.

Virus excretion. In the 3 weeks after vaccination 135 cadets returned 3 samples of faeces, 20 returned 2 samples and 10 returned 1 sample. Isolation of a particular type of poliovirus from only the first specimen of faeces was recorded in 118 instances, in all but 4 of which the cadet had a 4-fold or greater rise in antibody to the corresponding virus. Consequently, the isolation of a poliovirus from any of the specimens of faeces was considered to be the result of multiplication of the virus in the intestine.

The excretion of each type of poliovirus after vaccination showed an inverse relation to the corresponding pre-vaccination antibody concentration – the greater the serum antibody concentration the smaller the proportion of cadets who excreted virus (Table 3). Glezen, McCollough, Lamb & Chin (1969) found such a relation only in respect of type 1 poliovirus in children who had received IPV previously. Of the 165 cadets who provided faecal samples, the vaccination history was confirmed in 81. Although the numbers are small the inverse relation between excretion and serum antibody appeared to hold both in the 36 of these 81 cadets who had received only IPV previously, and in the 45 with a history of vaccination with OPV; however, the proportion of excreters was greater among cadets with a history of vaccination with IPV (Table 4).

Antibody response

The antibody responses 6 weeks after vaccination were measured in the 168 cadets who provided two blood samples (Figs 1–3). The mean responses (Table 5) were similar to those observed by Reid *et al.* (1969) in 3 to 6-year-old children given one dose of OPV.

In cadets with pre-vaccination antibody the mean antibody response to each virus type was inversely related to the pre-vaccination concentration (Fig. 4). Similarly the proportion of non-responders (i.e. less than a 4-fold rise) was greater as the pre-vaccination antibody concentration increased (Table 5). However, failure to respond was observed at almost all concentrations of pre-vaccination antibody, and was commonest in the case of type 3 antibodies (Table 5).

Subjects with no pre-vaccination antibody. A serological response to a booster of poliovaccine is of particular importance in persons without antibody; not all such cadets responded. Of the 17 cadets in whom type 1 antibody was not detected,

Table 2. *Pre-vaccination serum antibody and vaccination history*

Vaccination history	No. of sera with type 1 antibody (units/ml.)						No. of sera	Geometric mean concentration		
	< 0·1	0·1	0·2–0·8	1·6–6·4	12·8–51·2	⩾ 102·4		Pre-vacc.	Post-vacc.	Ratio post/pre
IPV only	8*	3	8	5	13	3	40	2·5	36	14·4
OPV (with or without IPV)	2	0	8	7	31	5	53	14	55	3·9
	No. of sera with type 2 antibody (units/ml.)									
	< 0·125	0·125	0·25–1·0	2–8	16–64	⩾ 128				
IPV only	1†	3	13	18	5	0	40	2·2	67	30·5
OPV (with or without IPV)	0	1	13	16	21	2	53	7·7	33	4·3
	No. of sera with type 3 antibody (units/ml.)									
	< 0·031	0·031–0·125	0·025–1·0	2–8	16–64	⩾ 128				
IPV only	3‡	3	19	12	3	0	40	1·0	7·1	7
OPV (with or without IPV)	0	5	16	29	3	0	53	2·1	7·4	3·5

* Including two cadets without antibody to type 3 and 1 without antibody to type 2.
† This cadet also had no antibody to type 1.
‡ Including two cadets without antibody to type 1.

Table 3. *Prevaccination serum antibody and excretion of poliovirus*

Excretion of virus	Type 1 antibody (units/ml.)						
	< 0·1	0·1	0·2–0·8	1·6–6·4	12·8–51·2	102·4	Total
No. examined	16	5	34	29	66	15	165*
% +ve	94	100	65	31	17	7	38
	Type 2 antibody (units/ml.)						
	< 0·125	0·125	0·25–1·0	2–8	16–64	⩾ 128	Total
No. examined	5	9	51	59	36	5	165*
% +ve	100	89	61	47	25	0	49
	Type 3 antibody (units/ml.)						
	< 0·031	0·031–0·125	0·25–1·0	2–8	16–64	⩾ 128	Total
No. examined	12	19	73	55	6	0	165*
% +ve	75	74	41	25	17	0	41

* 165 of 182 cadets contributed both faecal and blood samples.

Table 4. *Vaccination history and virus excretion*

Vaccination history	No. tested	No. (%) excreters		
		Type 1	Type 2	Type 3
IPV only	36	18 (50)	25 (69)	18 (50)
OPV (with or without IPV)	45	9 (20)	11 (24)	16 (36)

Figures in parentheses indicate percentages.

one failed to respond and did not excrete type 1 virus; he responded to both type 2 and 3 virus. All 5 of those without antibody to type 2 responded. Of the 14 cadets without antibody to type 3, 12 provided second blood samples, and 6 of these (50%) failed to respond to type 3; from 2 of the 6 non-responders, type 3 virus was isolated from two faecal specimens. In 5 of the 6 non-responders to type 3 immunity was also lacking to one of the other two types of poliovirus, but they all responded to types 1 and 2 virus.

Vaccination history. The antibody response to the single dose of OPV was greater in the 40 cadets with a confirmed history of having had only IPV previously (Table 2); nevertheless 17 of the 40 failed to respond to one or other poliovirus and 3 of the 17 were left without detectable antibody to one virus type after vaccination.

The degree of intestinal immunity given by OPV is usually regarded as greater than that induced by IPV (Henry *et al.* 1966). Thus, in cadets with only a moderate amount of serological immunity (0·2–0·8 unit/ml for type 1 and 0·25–1·0 unit/ml for types 2 and 3), failure to excrete poliovirus and to demonstrate an antibody response to a single dose of OPV was observed in 14 of 20 instances (70%) in cadets with a confirmed history of receiving OPV, but only in 10 of 34 instances

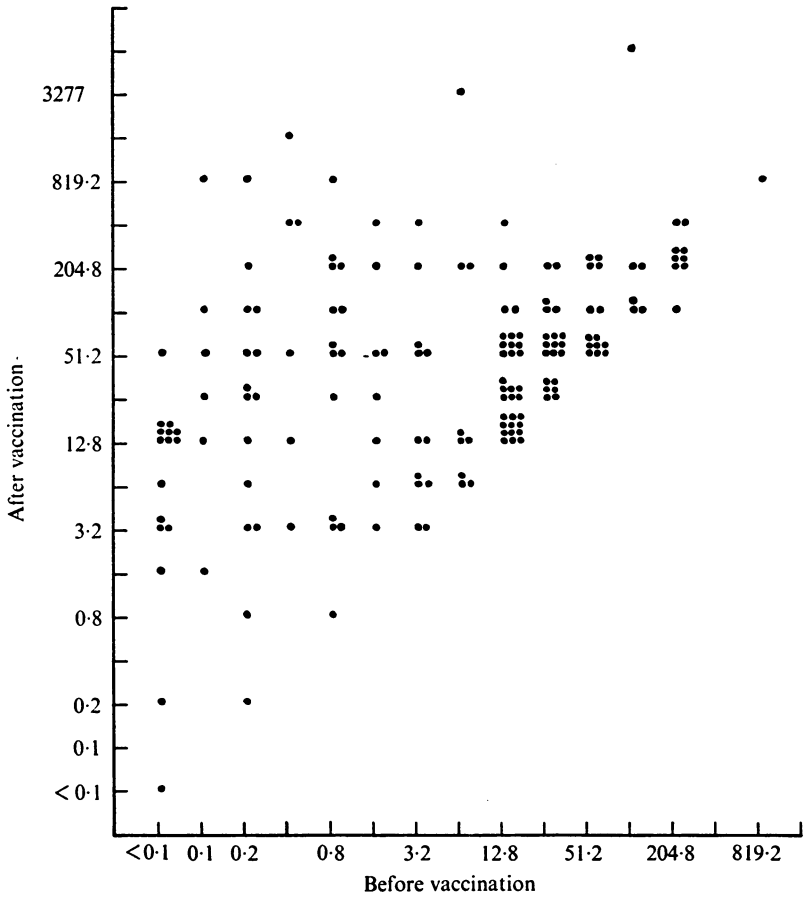

Fig. 1. Serum antibody concentration to type 1 poliovirus before and 6 weeks after vaccination with a single dose of OPV.

(29 %) in cadets who had previously been vaccinated only with IPV. However, in those with little or no detectable serum antibody no evidence was obtained that intestinal immunity was more likely to be present in cadets who had had OPV in the past. In cadets with low or absent serological immunity before vaccination (less than 0·2 unit/ml for type 1 and less than 0·25 unit/ml for types 2 and 3 poliovirus) there were no failures to excrete virus or to develop an antibody response in 5 instances in cadets with a past history of OPV vaccination; and 1 failure in 18 instances among cadets who had received IPV in the past.

Virus excretion. When cadets were grouped according to the degree of antibody response the proportion of individuals yielding each virus strain on faeces culture increased progressively with the height of the fold increase in antibody (Table 6).

DISCUSSION

The present findings in 16 to 18-year-old boys who had recently left school indicate that immunity to poliomyelitis in this age group is incomplete when

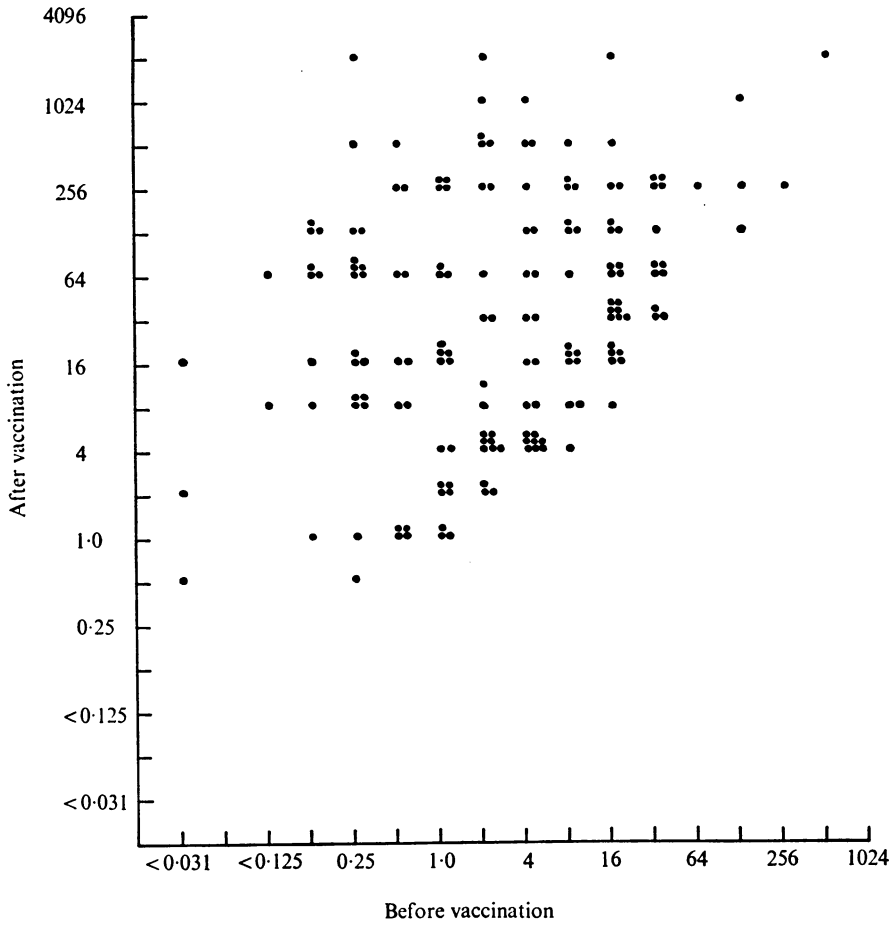

Fig. 2. Serum antibody concentration to type 2 poliovirus before and 6 weeks after vaccination with a single dose of OPV.

measured in terms of serum antibody and intestinal resistance to challenge with OPV. The cadets came from many parts of Britain, including Northern Ireland, but as future policemen they might not be entirely representative of all school-leavers; for instance, only 1 of the 182 cadets believed that he had never had polio vaccine. Among all school-leavers therefore a greater proportion may lack immunity to one or other type of poliovirus than the 14 % found in the present study (Mortimer & Cunningham, 1975). Absence of detectable serum neutralizing antibody was found mainly in cadets who had previously had only IPV, given 12 or more years previously; 23 % of 40 such cadets lacked antibody to one or other virus. Only 2 of 53 cadets with a confirmed history of OPV vaccination lacked detectable serum antibody, and both had only received one dose following a course of IPV. Those who had a history of vaccination with only IPV had less intestinal resistance to challenge with OPV than those previously vaccinated with OPV. Reinforcing vaccination against poliomyelitis must therefore be recommended before leaving school, particularly for those who have had IPV only. It

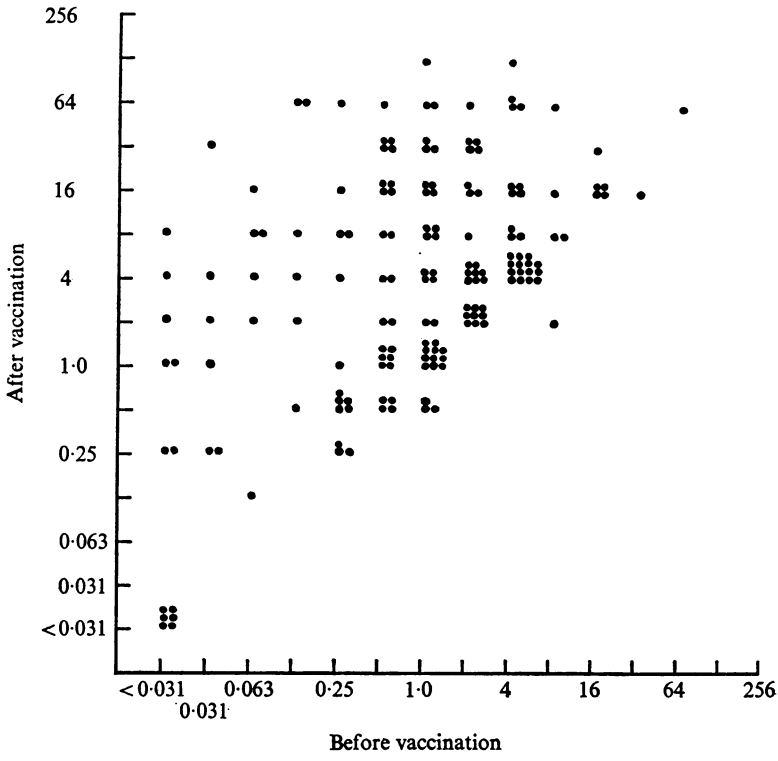

Fig. 3. Serum antibody concentration to type 3 poliovirus before and 6 weeks after vaccination with a single dose of OPV.

appears, however, that only a small proportion of children – about one-third – receive a dose of vaccine before they leave school. Since OPV was introduced as recently as 1962, there are many school leavers who have had only IPV, with perhaps a single reinforcing dose of OPV at school entry.

A single dose of OPV in many cadets failed to stimulate an antibody response to all three types of poliovirus, particularly in persons with pre-vaccination antibody, but also in a proportion of those without. Similar findings in 3 to 6-year-old children were reported by Reid *et al.* (1969), who found that a single dose of IPV was a more reliable booster. We did not test the effect of IPV, but there seems no reason to doubt that it would be equally effective at 16 years of age. However, the question should be considered – why does OPV not always boost immunity?

Presumably OPV may fail to boost immunity if the serum antibody has reached a ceiling; but this is unlikly when OPV is given to persons who have not been vaccinated for several years. Moreover, IPV acts satisfactorily in previously vaccinated children (Reid *et al.* 1969), which also suggests that antigenic competition between the antigens of the three poliovirus types is unlikely to be a factor. A serum antibody response to OPV depends on the multiplication of the vaccine viruses in the intestine (Beale, Davies & Thrower, 1965); in the present study excretion of virus was found to be related to the degree of antibody response, i.e.

Table 5. *Serum antibody response to a single dose of OPV*

	No. of sera with type 1 antibody (units/ml.)							
	< 0·1	0·1	0·2–0·8	1·6–6·4	12·8–51·2	⩾ 124	GMC	No. tested
Pre-vacc.	17	5	35	29	66	1	5·3	168*
Post-vacc.	1	0	4	23	87	53	51	168
Proportion with less than a 4-fold response	1/17	0/5	2/35	12/29	44/66	15/16		74/168
	No. of sera with type 2 antibody (units/ml.)							
	< 0·125	0·125	0·25–1·0	2–8	16–64	⩾ 128		
Pre-vacc.	5	9	52	60	37	5	3·5	168*
Post-vacc.	0	0	11	40	65	52	44	168
Proportion with less than a 4-fold response	0/5	0/9	12/52	28/60	20/37	3/5		63/168
	No. of sera with type 3 antibody (units/ml.)							
	< 0·031	0·031–0·125	0·25–1·0	2–8	16–64	⩾ 128		
Pre-vacc.	13	18	73	57	7	0	1·2	168*
Post-vacc.	6	1	41	70	48	2	5·5	168
Proportion with less than a 4-fold response	6/13	1/18	43/73	39/57	7/7	—		96/168

* 168 of 182 recruits who provided post-vaccination blood samples.

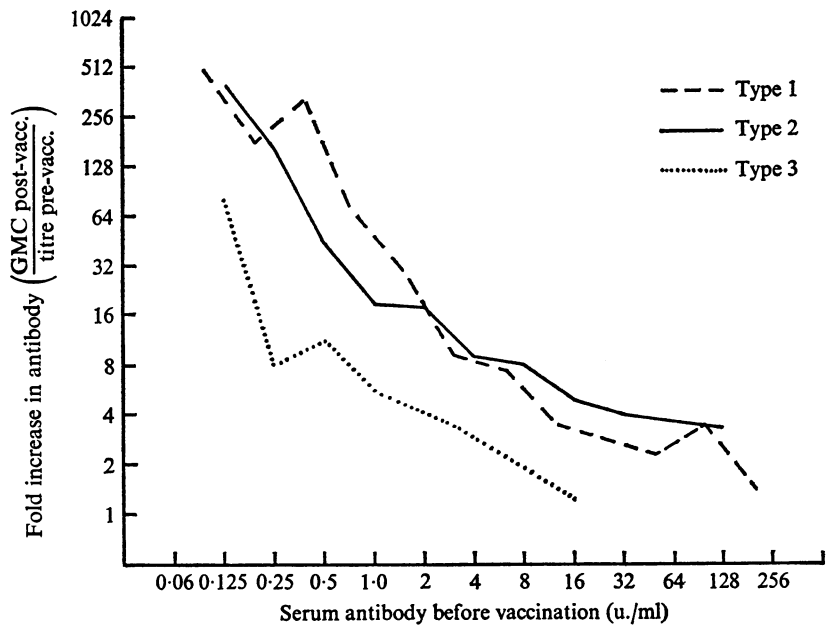

Fig. 4. The degree of antibody response according to the pre-vaccination serum antibody concentration.

Table 6. *Antibody response and virus excretion*

Virus type	Proportion of cadets excreting poliovirus according to the fold increase in antibody						
	< 4	4–8	16–32	64–128	256–512	⩾ 1024	Total
1	4/65 (6 %)	11/30 (37 %)	8/15 (53 %)	15/18 (83 %)	16/18 (89 %)	6/7 (86 %)	60/153 (39 %)
2	3/57 (5 %)	11/22 (50 %)	24/28 (86 %)	15/17 (88 %)	18/20 (90 %)	8/9 (89 %)	79/153 (52 %)
3	8/79 (10 %)	11/22 (50 %)	21/25 (84 %)	15/18 (83 %)	8/8 (100 %)	1/1 (– %)	64/153 (42 %)

the proportion of subjects excreting virus increased with the fold increase in antibody (Table 6). Moreover, an inverse relation was found between the excretion of each virus type in the faeces and the corresponding pre-vaccination serum antibody concentration (Table 3), and no evidence was obtained to suggest that intestinal immunity existed independently from circulating antibody in persons who had previously received OPV. Thus, although the immunity of the intestine may be mediated largely by secretory antibody (IgA) rather than circulating antibody (IgG), the observations suggest that serological and intestinal immunity are both expressions of the same immune response. A response to a reinforcing dose of OPV would therefore depend on the adequate multiplication of each virus in the intestine, which in turn reflects the degree of pre-vaccination serological immunity. In addition, multiplication of each virus in the intestine may be subject to interference from the other two viruses in triple OPV, and type 3 vaccine virus may particularly have been influenced in this way. Consequently, an absence of response in persons with little or no antibody is most likely in those who are non-immune to more than one virus and it does not seem probable that such persons would be protected by an independent intestinal immunity resulting from previous OPV vaccination.

Since a single dose of OPV is most likely to fail to boost immunity in those who already possess adequate immunity, and in the small proportion of people who lack antibody to two or more poliovirus types, the question should also be considered – is a single reinforcing dose of OPV sufficiently reliable for practical purposes? The most important group for consideration are those who are left without serum antibody to one or other poliovirus type after vaccination – i.e. from the results reported here, about 5 % of subjects. These persons are unlikely to be protected against natural infection by an independent intestinal immunity – thus, after receiving OPV, virus was excreted by 30 of 35 persons with no pre-vaccination antibody and in two of these who did not develop an antibody response there was good evidence of virus multiplication. This small proportion of susceptibles might well be acceptable in Britain since poliomyelitis is rare at present – perhaps because the present degree of immunity in the population gives a reasonably good herd immunity. However, the reinforcing dose of vaccine given before leaving school offers an opportunity to reach an entire age group at a time when successful

boosting of immunity should ideally ensure protection during adult life: the failure of a single dose of OPV to boost many of those with moderate antibody titres could lead to susceptibility later in adult life as their immunity wanes with the passage of time. These considerations suggest that a single dose of OPV is not entirely satisfactory as a booster at school leaving. The effectiveness of two or three doses of OPV should be explored, and administration of killed poliovaccine, combined with the tetanus toxoid already in use for this age group, might also be a practical alternative.

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