Short Paper

# Durability of immunity to diphtheria, tetanus and poliomyelitis after a three dose immunization schedule completed in the first eight months of life

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***Blood samples were obtained from school entrants whose primary immunization schedule had consisted of three doses of DT or DTP vaccine and three doses of OPV all given before the age of 8 months. The sera were separated and assayed for diphtheria antitoxin, tetanus antitoxin and antibodies to the three serotypes of poliovirus. The results of the assays showed that the abbreviated three dose schedule induced satisfactory immunity to all five infections until school entry and that a reinforcing dose at 18 months was unnecessary***

**Keywords:** Diphtheria; tetanus; poliomyelitis; immunization

## Introduction

Immunization in infancy is intended to provide immunity to diphtheria, tetanus, whooping-cough and poliomyelitis until reinforcing doses of vaccine are given at the time of school entry. The conventional schedule of immunization recommended in Britain[1] consists of first doses of adsorbed diphtheria–tetanus–pertussis (DTP) vaccine and oral poliovaccine (OPV) at 3 months of age followed by second doses at $4\frac{1}{2}$–5 months, and third doses at $8\frac{1}{2}$–11 months. An abbreviated schedule[1], which is intended to provide immunity to whooping-cough at an earlier age when whooping-cough is prevalent, consists of first doses at 3 months followed by second and third doses at 4 and 5 months. Unfortunately in some Health Districts the conventional schedule has been found difficult to implement because many parents fail to present their infants for the doses of vaccine scheduled for $8\frac{1}{2}$–11 months. Clinic attendance lists suggest that parental motivation to keep an appointment wanes when an infant reaches 7–8 months of age. A return to work by the mother, a further pregnancy, or pressing family activities such as escorting older children to and from school, may take precedence over a clinic appointment. The fear of an adverse reaction to immunization in a manifestly healthy toddler or a reluctance to see a toddler discomforted may influence some mothers.

In an attempt to ensure that every infant receives three doses of both DTP vaccine and OPV, the Central Manchester Health Authority has, since September 1977, offered only the abbreviated schedule of primary immunization. Parents reluctant to accept DTP vaccine for their infants have had the option of adsorbed DT vaccine. The consequences of the consistent use of this modified schedule together with the introduction in 1981 of a domiciliary service[2] have been that a higher proportion of infants has received three doses of the vaccines and economies have been made in the provision of immunization. On the other hand there has been some unease lest the abbreviated schedule has failed to provide immunity sufficient to provide protection until the reinforcing dose is given at the time of school entry.

## Methods

Approval was obtained from the local ethical committee for 100 children to be bled by venepuncture just before the administration of DT vaccine and OPV at the time of school entry. Ninetyfive children aged 4–5 years, resident in Manchester, and whose records showed them to have been immunized by the abbreviated schedule were selected for the study. As it is inevitable that in any immunization schedule some parents are a little slow to present their children for immunization, admission to the study was granted to any child who had received the third doses of the vaccines before the age of 8 months. Consent for a venepuncture was obtained from a parent

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0264-410X/89/040300-03 $03.00

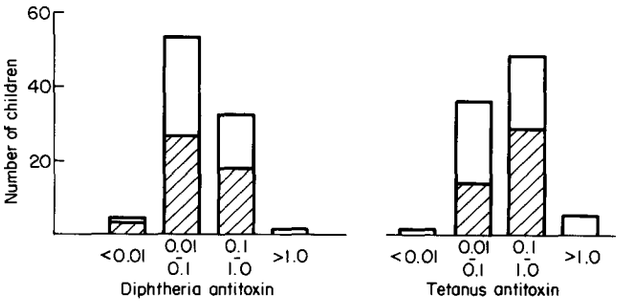


**Figure 1** Histograms showing the titres of diphtheria and tetanus antitoxins at the time of school entry in the sera of 92 children whose immunization with adsorbed DTP vaccine (shaded columns) and adsorbed DT vaccine (unshaded columns) and oral poliovaccine was completed by the age of 8 months

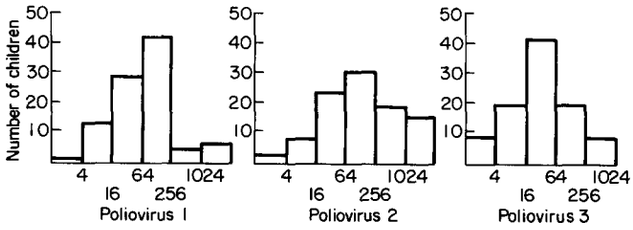


**Figure 2** Histograms showing the titres of antibodies to polioviruses of serotypes 1, 2 and 3 at the time of school entry in the sera of 92 children whose immunization with adsorbed DTP vaccine or adsorbed DT vaccine and oral poliovaccine was completed by the age of 8 months

of each child and a blood sample was taken at one of three community clinics just before the reinforcing doses of vaccine were given. The sera were separated and stored at −20°C until needed for assay.

Diphtheria antitoxin in the sera was estimated by neutralization tests in microtitre plates[3]. Hela cells, a dose of diphtheria toxin equal to two cytopathic doses and two-fold dilutions of serum were used throughout. The Third British Standard for Diphtheria Antitoxin was used as the reference preparation and the results were expressed in International Units (IU) of antitoxin per ml.

Tetanus antitoxin in the sera was estimated by an enzyme linked immunosorbent assay in microtitre plates[4]. A human immunoglobulin, the antitoxin content of which had been determined *in vivo* in terms of the International Standard for Tetanus Antitoxin, was used as the reference preparation and the results were expressed as IU antitoxin $ml^{-1}$.

In the absence of any certain knowledge of the antibodies that protect children against whooping-cough, no estimations of antibodies to *Bordetella pertussis* were made.

Antibodies to each of the three types of poliovirus were assayed by neutralization tests in microtitre plates[5]. The British reference preparations for each of the three antibodies were used as the reference materials and the results were expressed as the highest initial dilution of a serum that inhibited the cytopathic effect of the viruses.

## Results

The records showed that, of the 95 children in the study, 48 had been immunized with adsorbed DTP vaccine, 44 with adsorbed DT vaccine and three with a combination of the two vaccines. Of the 92 children who had received only DTP or DT vaccine, 58 had completed their courses of primary immunization by the age of 7 months and the remaining 34 had completed by the age of 8 months. The estimates of the diphtheria and tetanus antitoxin titres of the 92 children who had been immunized consistently with either DTP or DT vaccine are shown as histograms in *Figure 1*. $\chi^2$ tests showed that there were no significant ($p<0.05$) differences between the distributions of the estimates obtained from the sera of the children in the two groups. The estimates of the levels of antibody to each of the three serotypes of poliovirus are shown as histograms in *Figure 2*, no distinction being made in this Figure between the children immunized with the two types of bacterial vaccine (DTP and DT). The geometric means of the levels of antibody to poliovirus of serotypes 1, 2 and 3 were, respectively, 1/73, 1/106 and 1/28.

## Discussion

The titres of diphtheria antitoxin and of tetanus antitoxin that are conventionally regarded as sufficient to provide protection are, in both cases, 0.01 IU $ml^{-1}$. Thus the four children (4.3%) with diphtheria antitoxin titres of $<0.01$ IU $ml^{-1}$ and the one child with a tetanus antitoxin titre of $<0.01$ IU $ml^{-1}$ may be regarded as immunization failures. However the four children with low diphtheria antitoxin titres may be expected to benefit from the immunity of the herd and so be unlikely ever to be in contact with a case of diphtheria or a carrier. The child with a low titre of tetanus antitoxin (0.009 IU $ml^{-1}$) had clearly been primed and may be expected to respond rapidly to a dose of tetanus toxoid in the event of a tetanus prone wound.

The titres of antibody which provide protection from the three types of poliovirus are not known with exactitude but a titre of 1/4 is generally accepted as indicative of specific neutralizing antibody. No child had an antibody titre of $<1/4$ to poliovirus type 1 but two and eight children had antibody titres of $<1/4$ to poliovirus types 2 and 3 respectively, and so may have been inadequately immunized. This, however, may be an unduly pessimistic assessment as titres lower than 1/4 may be indicative of specific antibody and of immunological memory of poliovirus immunogens.

Although the results of this study record that among the 92 children vaccinated against five infections there were 15 instances (3.7%) in which immunity, as measured by serological assay, was less than that conventionally held to be protective, the overall immune response showed that a three dose immunization schedule implemented between the ages of $3\frac{1}{2}$ and 8 months induced satisfactory immunity that endured until reinforcing doses were due at the time of school entry. The epidemiological record of the Central Manchester Health Authority supports this view. Concern lest the abbreviated three dose schedule fails to provide adequate protection until school entry appears to be unfounded and thus the advantages of the abbreviated schedule in the form of greater parental compliance, earlier immunity to all five infections and also to whooping-cough, and a reduction in the costs of health care, may all be enjoyed.

## Acknowledgements

The authors are grateful to Dr Gill Roland, specialist in community medicine, and the community health doctors

in the Central Manchester Health Authority for taking the blood samples and the staff of the Manchester PHLS for separating the sera.

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