ERADICATION OF POLIOMYELITIS IN SINGAPORE

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SYNOPSIS

This paper reviews the measures taken for the control of poliomyelitis in Singapore that have resulted in its virtual eradication. It is estimated that the immunization programme will confer immunity on more than 90 per cent of the population up to the age of 25 years. The problem of waning immunity in adults no longer exposed to reinfection by poliovirus is discussed.

INTRODUCTION

Outstanding in the field of preventive medicine is the success that has been achieved in the control of poliomyelitis by the use of oral poliovaccine. In Singapore, the implementation of a programme of immunization against poliomyelitis has resulted in the rapid and dramatic decline in the incidence of paralytic poliomyelitis to its virtual eradication.

An account of the events leading to the introduction of immunization against poliomyelitis was given by Lee et. al. (1965). This paper recounts those events with further details and reports the results achieved over the past fifteen years.

POLIOMYELITIS ON THE INCREASE: THE 1958 OUTBREAK

In the immediate post-war years the epidemiological pattern of poliomyelitis in Singapore was that of an endemic disease periodically breaking out in epidemic form (Table 1). The number of cases given for the years 1946 to 1957 were based on clinical diagnosis as laboratory confirmation of poliomyelitis was not available until 1957.

Commencing August 1958, increasing numbers of poliomyelitis were reported and the disease assumed epidemic proportions, finally totalling 415 cases (Hale et. al., 1959). Day by day, cases were given prominence in the press and as the number of cases rose there was clamour for action from the public. Eleven weeks after the first case was reported, the

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TABLE 1 Notification of Poliomyelitis in Singapore 1946-1975

Year	1946	47	48	49	50	51	52	53	54	55	56	57	58	59	60
Cases	188	0	172	78	90	94	56	47	85	25	72	64	415	62	196
Year	1961	62	63	64	65	66	67	68	69	70	71	72	73	74	75
Cases	53	14	74	11	40	10	3	4	0	0	2	2	1	0	0

Ministry of Health decided to offer, on a voluntary basis, oral poliomyelitis vaccine to children between 3 months and 10 years of age. This decision was taken on the recommendation of the Advisory Committee[1].

Although the epidemic was due to the poliovirus type 1, it was decided to use a vaccine of the type 2 virus, for the following reasons:-

1. The vaccine type 2 virus would provide protection in the susceptible by interfering with the establishment of the epidemic type 1 virus.
2. At that time the live virus vaccine had yet to be used on a large scale and it was desirable to assess the safety of the vaccine under field conditions. The use of a virus type in the vaccine, different from that of the virus type causing the epidemic, would clearly distinguish virus induced cases from naturally infected cases.
3. The dissemination of large quantities of the live virus throughout the community could interfere with the natural transmission of the prevalent epidemic strain.

On the assurance that there would be adequate laboratory control of the campaign, Dr. A. Sabin made available his live vaccine for use in an attempt to modify the course of the outbreak. Vaccination centres, each in charge of a medical officer, were set up in various parts of the island and about 200,000 children received type 2 oral vaccine. No untoward effects followed the vaccination and no case of type 2 paralysis occurred in the vaccinees. An analysis of the data from this campaign showed that a substantial reduction in the risk of paralytic poliomyelitis was achieved as a result of the vaccination (Knowelden et. al., 1961).

In retrospect, it may be stated now that attempts to abort poliomyelitis epidemics by administration of live vaccine may safely use virus of the same type as the epidemic type. The safety of live vaccine having been well established, advantage should be taken of its greater efficienty as an interfering agent and as an immunizing antigen against the epidemic virus type.

1960 SEROLOGICAL AND FAECAL SURVEY

When the epidemic had subsided, the Government appointed a Committee[2] to study the problem of poliomyelitis and its prevention. In order to obtain a baseline for future comparative studies, a serological and a faecal survey was carried out in 1960 to assess the immune status of young children to poliomyelitis and to ascertain the prevalence of polioviruses in the community.

The serological survey revealed that by the age of three years the immunity level by natural infection exceeded 50 per cent for all three poliotypes, with susceptibility to infection, as to be expected, highest in the lowest age-groups. That poliomyelitis in Singapore was still of the infantile type was further borne out by an outbreak in 1960 which showed that 57 per cent of the cases were under 2 years and 88 per cent under 4 years of age. This survey also indicated that susceptibility to infection was highest against the poliovirus type 1.

The faecal survey showed an unexpectedly high rate (22.8 per cent) of naturally occurring enteroviruses. This could cause significant interference with vaccination by oral vaccine. Of the viruses isolated, 4.7 per cent proved to be polioviruses, mainly of types 1 and 3.

The findings of the survey were submitted in a Report to the Ministry of Health, Singapore (1961). The committee noted the occurrence in 1960 of 196 cases of paralytic poliomyelitis and concluded that further epidemics would be inevitable unless active preventive measures were adopted. It therefore recommended a programme of immunization with oral vaccine for all children from birth to school entry as the most effective way to control the disease in this country. This programme should be a voluntary one in the first instance backed by an extensive propaganda drive; however, if the acceptance rate proved unsatisfactory, the programme should be compulsory. The recommendation was approved by the government.

ORAL POLIOVACCINE

Oral poliovaccine consists of live virus which is able to confer protection against poliomyelitis. The strains of virus used in the vaccine were those selected by Dr. A. Sabin as combining maximum antigenicity with minimum virulence. Protection conferred by live vaccine is more effective than that conferred by inactivated vaccine. While inactivated vaccine stimulates antibody production and limits the spread of the poliovirus within the body of the vaccinee it does not interfere with spread of the virus in the community. Live vaccine, on the other hand, confers competitive 'block' and tissue resis-

tance in the intestinal cells of the vaccinee in addition to stimulating antibody formation. Used on a mass scale, live vaccine can limit the spread of poliovirus throughout the community and lead to the eradication of poliomyelitis. Two other important considerations are that live vaccine costs much less than inactivated vaccine and the mode of administration, by mouth, is readily acceptable and easily applicable on a mass scale.

COUNTERMEASURES: SURVEILLANCE

From 1959 onwards, all notified cases of poliomyelitis were investigated and laboratory confirmation attempted in each instance, thus giving a clearer epidemiological picture of poliomyelitis in Singapore. The age-specific incidence confirmed that children below the age of 5 years were most at risk, in particular those between six months and two years of age. Poliovirus type 1 was responsible for the majority of cases and for the epidemic waves, type 3 was of minor importance and type 2 relatively unimportant (Table 2). With the parameters of the disease in mind, a schedule of immunization with oral vaccine was evolved for the control of poliomyelitis.

PHASE I: 1962 IMMUNIZATION CAMPAIGN

The first phase of the poliomyelitis immunization programme began in March 1962. Children between the ages of 6 months and 5 years, appearing at the Maternal and Child Health Centres for their immunization against diphtheria, tetanus and pertussis (D.T.P.) were offered the poliovaccine on a voluntary basis. Vaccinees found oral vaccine most agreeable after having been injected with D.T.P. vaccine. Though it had been shown in the British Medical Research Council trials (P.H.L.S., 1961) that three doses of trivalent vaccine gave good results, it was decided to give initially two doses of trivalent vaccine three months apart. By November 1962, 205,000 children comprising about 60 per cent of the age-group concerned had been covered.

Evaluation of this regime in a group of children with no poliomyelitis antibodies prior to immuniza-

TABLE 2 Virus Isolations From Notified Cases of Poliomyelitis 1959-1975

YEAR / VIRUS ISOLATION	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	Total
Poliovirus type 1	19	111	11	4	39	5	21	—	—	3	—	—	—	2	—	—	—	215 (45.6%)
Poliovirus type 2	2	1	3	—	3	—	—	4	—	—	—	—	1	—	—	—	—	14 (3.0%)
Poliovirus type 3	11	15	8	2	1	1	—	—	—	1	—	—	—	—	1	—	—	40 (8.4%)
Other cytopathogenic agents	6	8	8	—	2	—	3	1	1	—	—	—	—	—	—	—	—	29 (6.1%)
Negative	22	59	20	5	24	4	16	5	2	—	—	—	1	—	—	—	—	158 (33.3%)
No faecal specimen	2	2	3	3	5	1	—	—	—	—	—	—	—	—	—	—	—	16 (3.4%)
TOTAL	62	196	53	14	74	11	40	10	3	4	0	0	2	2	1	0	0	472 (100.0%)

tion indicated that the conversion rate was 98.5 per cent for the type 2 poliovirus but only 50.0 per cent for the type 1 and 58.8 per cent for the type 3. Thus two doses of trivalent vaccine were inadequate, since protection against type 1 and type 3 poliomyelitis was considered of more importance epidemiologically than protection against type 2. Nevertheless it was gratifying to note that the incidence of poliomyelitis in that year dropped to a new low figure of 14, and it seemed reasonable to assume that this was to some extent the result of the vaccination campaign.

The children who received vaccine in this first phase were recalled for a third dose of trivalent vaccine but the response was poor and it was estimated that only about a third of them (32.6 per cent) eventually completed their primary course of three doses of poliovaccine.

PHASE II: IMPLEMENTATION OF REVISED PROGRAMME (1963)

The experience gained showed a need to revise the vaccination schedule. Since types 1 and 3 were responsible for the majority of cases it was considered desirable to immunize with these types as early as possible. Thus it was recommended that for primary immunization the first two doses should be of bivalent vaccine, consisting of the type 1 and type 3 viruses, followed by a third dose, of trivalent vaccine. This would increase the efficiency of immunization against types 1 and 3, since the type 2 virus in a trivalent mixture tends to interfere with immune response to the other types. In view of the high enterovirus carrier in the community, repeated administration of the vaccine was also advocated.

In March 1963, the second phase of the immunization programme was implemented with the amended schedule. Infants aged 3 to 4 months coming for their compulsory diphtheria immunization (D.T.P.) were offered at the same time a primary course of poliomyelitis immunization at monthly intervals. Under ideal conditions this regime may be expected to confer protection against all the three poliotypes. However, in view of possible interference by naturally occurring enteroviruses and other non-specific factors which may prevent the 'take' of the vaccine, a fourth dose consisting of trivalent vaccine was given a year later and another booster dose also of trivalent vaccine at the age of 4 years (Table 3).

As a supplementary measure, the programme

TABLE 3 Poliomyelitis Immunization Programme for 1964 — 1975 compared with 1976

AGE — GROUP		TYPES OF VACCINE GIVEN	
		1964 — 1975	1976
Infants (below 1 yr.)	3 months 4 months 5 months	1 + 3 1 + 3 1 + 2 + 3	1 + 3 1 + 3 1 + 2 + 3
Pre-school (2 — 5 yrs.)	18 months 4 years	1 + 2 + 3 1 + 2 + 3	1 + 2 + 3 1 + 2 + 3
Primary School Children	School entry 6 — 7 years	**Primary course** 1 + 3 1 + 3 OR **Booster dose** 1 + 3 1 + 2 + 3	**Primary course** 1 + 3 1 + 3 1 + 2 + 3 OR **Booster dose** 1 + 2 + 3
Primary School Leavers	11+ years	Nil	1 + 2 + 3
Secondary School Leavers	15+ years	Nil	1 + 2 + 3

was extended to primary school entrants in 1964. Those who had not had any poliovaccine previously were offered, with parental consent, a modified primary course of two doses of bivalent (types 1 and 3) vaccine a month apart. Those who had completed their primary and pre-school vaccinations were given a dose of bivalent (types 1 and 3) vaccine to boost immunity to these types and one month later a dose of trivalent vaccine.

When the programme was first introduced the number of vaccinations given, as may be expected, fell short of the number of live births to be covered. As the administration problems were ironed out and the procedures of immunization integrated with the general immunization programme for infants, the momentum increased and the coverage became more satisfactory (Table 4). The regulation that for

TABLE 4 Percentage Coverage of Primary Poliomyelitis Immunization in Cohorts 1964 — 1970

Age / Birth Cohort	Under 1	1 and over	2 and over	3 and over	4 and over	5 and over	6 and over
1964	39.98	63.46	77.19	83.86	88.84	91 31	93.81
1965	43.58	69.79	81.03	87.69	90.99	92.73	
1966	45 38	74.84	83 22	88 65	90.84		
1967	52 21	79.32	83.53	86.95			
1968	58.52	83.55	87.54				
1969	61.51	83.42					
1970	62.82						

admission to primary school a child must produce evidence of having completed the compulsory immunization against diphtheria served to ensure a good response to the poliomyelitis immunization that was offered concurrently.

For the years 1970 to 1975, the mean number of infants completing their primary poliomyelitis immunization course was 42,532, representing 93 per cent of the mean live births for the same period (Table 5). This high level of coverage was indeed

TABLE 5 Poliomyelitis Immunization of Singapore Children 1970 — 1975

YEAR	INFANTS AND PRE-SCHOOL CHILDREN			SCHOOL CHILDREN		
	No. of Live Births	No. given Primary Course (1)	No. given Booster Doses (2)	No. of School Entrants	No. given Primary Course (3)	No. given Booster Doses (4)
1970	45,934	44,285	67,742	55,625	—	81,539
1971	47,068	43,377	58,246	55,409	1855	80,784
1972	49,678	45,838	57,365	52,161	2348	89,709
1973	48,269	44,027	62,242	51,010	1522	83,982
1974	43,268	41,638	62,126	47,400	1567	78,688
1975	39,984	35,848	63,929	44,391	1659	69,949
MEAN	45,694	42,532	61,942	50,999	1491	80,775

Vaccine given (1) Two doses bivalent (types 1 + 3) and one dose trivalent
(2) Two doses trivalent
(3) Two doses bivalent
(4) One dose bivalent and one dose trivalent.

satisfactory. This conclusion was also borne out by the figures for the vaccinations at school entry for the years 1971-1975. Only between 3 to 4 per cent of school entrants required the primary course of poliomyelitis immunization which implied that the remaining 96 to 97 per cent had completed their primary immunization course.

The implementation of the immunization programme as the principal measure against poliomyelitis was accompanied by a marked decline in the incidence of paralytic poliomyelitis. From 1963 to 1968, the annual incidence of paralytic poliomyelitis was respectively 74, 11, 40, 10, 3 and 4 cases. In the subsequent years up to 1975, there were only 5 cases (Table 2). It is noteworthy that no child who had completed the primary immunization schedule contracted paralytic poliomyelitis during these years. This decline in poliomyelitis is also seen in the difference between 1067 notified cases for 1954 to 1964 and 62 cases for 1965 to 1975. Not a single case of the disease occurred in the years 1969, 1970, 1974 and 1975. Poliomyelitis can indeed be said to have been eradicated from this country.

PHASE III: EXTENSION OF IMMUNIZATION TO SCHOOL LEAVERS

The whole programme of immunization of children against various diseases was recently reviewed by an Expert Committee[3] which recommended in 1976 some amendments to the poliomyelitis immunization programme. The primary course for infants and the booster doses for pre-school children remained the same. However, for the primary school entrants, a three-dose regime consisting of two doses of bivalent and one of trivalent vaccine was given to those who missed immunization in their early years, whilst for the rest a single trivalent dose of vaccine was given as booster.

In order to enhance and maintain immunity, the programme was extended to primary school leavers (11+ years) with a single dose of trivalent vaccine and to secondary school leavers (15+ years) with a similar dose of vaccine.

By this amended programme, most children will have received between 5 and 8 doses of poliovaccine by adolescence which should provide adequate protection into adulthood.

DISCUSSION

The poliomyelitis immunization programme that has been in force for nearly fifteen years was aimed at preventing epidemics of poliomyelitis which cause much alarm and despondency. To protect each and every individual by immunization is of course impractical but it would appear that the immunization of a large segment of the population has brought down the circulation of poliovirus in the community to such a low level that the chances of any susceptible person being infected and developing paralytic poliomyelitis has been reduced to vanishing point.

The immunization programme was directed at children who were the largest group of susceptibles and most at risk. It has been shown that in poliomyelitis epidemics poliovirus is rapidly transmitted from infected young children to their families and playmates. The immunization of the very young not only protects them but removes from the environment a major source of poliovirus in epidemic times.

It will be noted from Table 3 that by the age of 15 a child may have received poliovaccine as often as eight times. The question may be asked if this is not too enthusiastic use of poliovaccine.

Immunization against poliomyelitis begins at a very young age when the immune response may

not be good for various reasons; however, immunization was considered desirable in view of the high attack rates in this age-group. Further immunization of the pre-school child to make up for possible ineffective earlier immunization was therefore a wise measure.

Immunization of children on entering school is justified on the score that some children do miss or fail to complete primary immunization. Booster doses given to those who had completed primary immunization ensures that any failure in vaccine "take" would be remedied.

The immunization of school leavers at the approximate age of 15 has as its aim the extension of protection against poliomyelitis from childhood into adult life. From a few studies that have been made on the persistence of antibodies after oral vaccination it seems that immunity is retained for up to ten years though antibody levels have possibly fallen (Sanders and Cramblett, 1974). Oral poliovaccine has not been in use long enough for us to know if immunity can be retained for as long as twenty years. We may be assured, however, that if the high coverage achieved by the immunization programme is maintained, including booster doses for school leavers, approximately 90 per cent of the population of Singapore will be immune to poliomyelitis till the age of 25 years and possibly beyond.

That immunity levels in the population will diminish with increasing age is a possibility that we shall have to investigate in due course. It has to be remembered that the high immunity levels found in adults prior to the widespread use of poliovaccine were due in part to the booster effect of repeated infection by poliovirus in epidemic seasons. The ecology of poliovirus has been profoundly disturbed by oral poliovaccine and adults are no longer being immunised by natural infection. Immunization of the young against poliomyelitis will, in the long term, result in reduced immunity in adults; the abolition of "infantile" poliomyelitis could mean the appearance of "adult" poliomyelitis. This can only be avoided if "herd immunity" is maintained at a high level so that virulent poliovirus introduced into the community will be unlikely to spread.

The danger, of course, is that with the passing of years the continued absence of poliomyelitis in this country that is hoped for will result in relaxation of control measures which include, apart from the immunization programme, continual study of the immunity status of our people to monitor its effectiveness. This must not be allowed to happen. Education of parents in the need of immunization against poliomyelitis must be kept up and health officers responsible for the immunization programme encouraged to achieve maximum targets.

Recent serological studies suggest that even in the United Kingdom and the United States where immunization with oral poliovaccine began about the same time as it did in Singapore, the immune status of the communities studied were unsatisfactory. Reid et. al. (1973) and Mortimer and Cunningham (1975) urged that more effort should be directed towards vaccinating U.K. children particularly at school entry. Oberhofer et. al. (1975) pointed out that the percentage of susceptibles in a certain community in Michigan increased with age. These authors stated that because of inadequate immunization of the young in that community, herd immunity was not good enough to protect adults from poliomyelitis. Reports such as these show that the battle against poliomyelitis is a continuing one.

A small study undertaken recently illustrates what can be done. The immune status of National Servicemen aged 18-21 years was evaluated. These subjects were "overaged" when the childhood immunization programme was introduced. It was found that a significant proportion was susceptible to one or more types of poliovirus infection (Lee et. al., 1977). It can be postulated that in course of time the number of susceptibles in the group studied will tend to increase due to waning immunity because reinforcement of immunity by natural infection now rarely occurs. What is the risk of contracting paralytic poliomyelitis in this group as the years go by? What is the risk in older age-groups? Should anything be done to reduce these risks? These are questions which surely need to be answered.

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FOOTNOTES

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