The early immunisation of infants in Malaysia

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Introduction

CHEN AND DUGDALE (to be published) in a survey of school children (ages six to seven years) in an urban area in Selangor, found that 11% of them had had no previous immunisation with smallpox, 26% had no B.C.G., 69% had no triple antigen (D.P.T.) or dual antigen (D.T.) (of those who had, only 18% had three or more doses) and 94% had no poliomyelitis immunisation (of those who had, only 3% had three or more does). This low rate of active artificial immunisation is one of the reasons why diseases like diphtheria, tetanus and poliomyelitis are still common in Malaysia.

There are many reasons for this low rate of immunisation, one of which is failure of parents to bring their children to clinics for immunisation. But even clinic patients have low rates of immunisation. Dugdale (1969) reported that only 68% of children who attended Municipal Infant Welfare clinics had smallpox vaccination and only 20% had three doses of triple antigen by the age of one year. He also pointed out that about 50% of the clinic patients stopped attending the clinics after the age of six months.

The rate of immunisation could be improved, using the existing services, by giving the maximal number of immunisations in the fewest number of visits, i.e., to combine antigens, and by giving immunisation as early as possible and completing the primary immunisation (other than reinforcing doses) before the child reaches the age of six months. With this in mind, the University Hospital, Malaysia, has adopted the following schedule of immunisation for infants born here since 1968:

At birth	— B.C.G. and smallpox
At 6 weeks	— 1st D.P.T. (triple antigen) and oral poliomyelitis (trivalent)
At 10 weeks	— 2nd D.P.T. and oral poliomyelitis
At 14 weeks	— 3rd D.P.T. and oral poliomyelitis
At 12 – 16 months	— reinforcing doses of D.T. (diphtheria and tetanus toxoid) and poliomyelitis.

This paper reports a study which tests the efficacy of immunising infants early, with regard to smallpox and diphtheria. Three groups of children, a study and two control groups, were used and were tested by means of primary smallpox vaccinations, re-vaccinations and Schick tests.

Methods

(a) Study population

Twenty-one children, who were immunised with

the above schedule, were studied. Schick tests and revaccinations were done at six months of age. Of the 21, 13 of them had a second Schick test between 12 and 19 months of age. These were done before they received reinforcing doses of D.T.

(b) Control populations

During the study, two groups of children were used as comparisons.

(i) The first group, Control I, consisted of 17 healthy children who had not received primary smallpox vaccinations. They were given primary smallpox vaccinations at the time that the study group received revaccinations (age about six months).

(ii) The second group, Control II, consisted of ten children whose ages ranged between four and 19 months. These were convalescent children, from the University Hospital, who had no history of clinical diphtheria or of previous artificial immunisation against diphtheria. They were given Schick tests.

(c) Tests

All Schick tests were done with diphtheria toxin in the left arm (test) and heat inactivated toxin in the right arm (control) and were read on the 4th or 5th day. The smallpox revaccinations were read on the 4th or 5th day and then again on the 7th, 8th or 9th day.

All tests were performed and read by one of the authors (M.M.C.)

Results

All the study children developed either an immune or a vaccinoid reaction to smallpox revaccination. The maximal area of papule or vesicle and surrounding erythema, at 4th or 5th day, was 10 mm., but the majority of them measured 4-5 mm. By the 7th, 8th or 9th day, reaction had diminished. All the Control I children developed primary reactions to smallpox vaccinations.

Everyone of the study children had a Schick negative reaction at six months and again between 12 and 19 months of age, while all the Control II children had Schick positive reactions.

Discussion

An important reason for the low rate of artificial active immunisation in Malaysia is the fact that immunisation is often scheduled to be completed late in infancy, whereas infants often cease to attend clinics by the age of six months. Another reason is the fact that antigens are usually given singly. An example of a schedule practised by some general practitioners, in Kuala Lumpur and Petaling Jaya, is as follows:-

At birth — B.C.G.
At 3 months — Smallpox
At 4 months — 1st D.P.T.
At 5 months — 2nd D.P.T.
At 6 months — 3rd D.P.T.
At 7 months — 1st poliomyelitis
At 8 months — 2nd poliomyelitis
At 9 months — 3rd poliomyelitis

The rate of immunisation can be raised by giving several antigens simultaneously and starting immunisation of children as early as possible and completing the primary immunisation before the age of six months. The aim is to provide maximal protection in the fewest possible visits. However, the following questions have to be answered before the above can be advocated.

Table I

Smallpox vaccination reactions of study children and of control children

Smallpox vaccination Reaction	Number of study children	Number of control children
Primary reaction	0	17
Immune or Vaccinoid reaction	21	0

Table II

Schick reactions of study children and of control children.

Schick Reaction	Number of study children		No. of control children between 4 & 19 months of age
	At 6/12 of age	Between 12 & 19 months of age	
Negative	21	13	0
Positive	0	0	10

(1) Is early immunisation effective?
(2) Do many complications arise as a result of early immunisation?
(3) Does simultaneous administration of several antigens lower immunity or result in adverse reactions?

(1) Is early immunisation effective?

There is a common belief that young infants are incapable of forming antibodies because of immunologic immaturity, and presence of passive immunity. However, studies have shown that even a newborn infant is capable of responding to an antigen by forming antibodies despite the presence of passively acquired antibodies to the same antigen.

Lin (1965) in Taiwan, giving B.C.G. and smallpox vaccination to newborn, found that the successful rate of takes was high and there was no evidence of increased risk of complications. This result is confirmed by Stanfield (1966) in East Africa and by the study, presented in this paper. Our percentage of takes in smallpox vaccinations among the newborn was 95% (545/574) as compared with 97% (65/67) among infants vaccinated for the first time after the age of two months.

Pearlman (1961) and Harris (1966), in their review of literature pointed out that infants, within the first month of life, were capable of producing protective levels of antibodies to diphtheria, pertussis and tetanus. They pointed out that Gaisford had shown that the majority of very young infants immunised with D.P.T. at 1, 5 and 9 weeks of life exhibited a satisfactory antibody level at 15 weeks.

A Schick negative reaction indicates that the individual has more than 1/250 units of diphtheria antitoxins per 1 cu. cm. of blood. A person whose Schick reaction is negative is protected from contracting clinical diphtheria (Hare 1956). The results of our study confirm that diphtheria toxoid, given early in infancy, produces a protective level of antibodies at six months.

Barret (1962) and Da Silva (1958) showed that very young infants were capable of producing antibodies to oral poliomyelitis vaccine, though the response was less compared with older infants (79% of infants fed poliomyelitis vaccine within 18 days of life produced antibodies as compared with 91% of infants fed the same vaccine between 4½ and 26 weeks of life).

(2) Do many complications arise as a result of early immunisation?

The high incidence of complications of primary smallpox vaccination, namely post-vaccinial encephalitis and generalised vaccinia, in infants under one year of age as reported by Wynne-Griffith has resulted in some countries recommending primary smallpox vaccination after the age of one year. However, Edsall (1961), in his review of literature, summarises that "the weight of experience indicates that the risk of post-vaccinal encephalitis can be minimised by universal vaccination beginning in infancy." In Taiwan, Lin (1965) found no evidence of increased risk of complications in infants receiving smallpox vaccination during the neonatal period. In Hongkong, where 80–95% of all newborn were immunised with B.C.G. and smallpox since 1952, Teng (1969 – personal communication) found no evidence of increased risk of complications. In the University Hospital, Malaysia, 75% of all newborn (about 4,500 babies) were given B.C.G. and smallpox vaccination at birth (sick and premature babies were not immunised till the time of discharge). Up to the time of writing, there have been no reports of serious complications in these newborn.

(3) Does simultaneous administration of several antigens lower immunity or result in adverse reactions?

Simultaneous administration of non-viral antigens have been practised for a long time without reduced immunological response or adverse reaction. However, it has been generally recommended (on theoretical grounds) that different live virus vaccines be given at least a month apart whenever possible. Field observations, however, indicate that, with simultaneous administration of certain live virus vaccines, there was no adverse reaction or lower immunity. In West Africa, millions of smallpox and measles vaccinations have been performed concurrently without significant problems. Smallpox vaccination has also proved to be compatible with simultaneous oral poliomyelitis vaccination. Smallpox vaccine has been given simultaneously, but at different sites, with diphtheria, pertussis, tetanus, typhoid, and inactivated poliomyelitis vaccines; the vaccines maintained their full efficacy and there was no intensification of reactions (W.H.O. 1968). Thus simultaneous administration of several antigens does not as a rule reduce immunity or result in adverse reaction.

Summary

Smallpox vaccination and B.C.G. were given to

Table III

Comparison of the suggested schedule of immunisation (for children first seen at birth) with two schedules presently used in West Malaysia

Vaccines	Time of Immunisation			Remarks on Proposed Schedule
	Ministry of Health	Some Private clinics in Selangor	Proposed schedule	
B.C.G.	At birth	At birth	At birth	On the left arm
Smallpox	5 months	3 months		On the right arm
1st D.P.T. (triple antigen)	2 months	4 months	6 weeks (at post-natal visit)	(1) Use alum absorbed type of D.P.T.
1st Oral poliomyelitis (trivalent)	—	7 months		(2) Check B.C.G. & smallpox scars if absent to repeat.
2nd D.P.T.	3 months	5 months	10 weeks	The interval between immunisation should be at least 4 weeks. But there is no upper limit between the interval, that is, there is no need to repeat an injection once it is given, no matter how long the interval has lapsed.
2nd Oral poliomyelitis	—	8 months		
3rd D.P.T.	4 months	6 months	14 weeks	
3rd Oral poliomyelitis	—	9 months		
Reinforcing dose of D.T. (diphtheria and tetanus toxoid)	1½ —,2 yrs. (D.P.T. is used here)	—	12 — 16 months of age (8 — 12 months after the third doses of D.P.T. & polio.)	May give measles vaccine if available.
Reinforcing dose of oral poliomyelitis (trivalent)	—	—		(School age) —
1st smallpox	6 — 7 years	—	booster (School age)	
1st D.T. (alum absorbed) booster	—	6 — 7 years (School age)		
Further smallpox booster	16 — 17 yrs. (Secondary school leaver)	—	Every ten years	
Further D.T. booster	—			
Tetanus toxoid	12 years (Primary school leavers) & again at 16 — 17 yrs. (Secon. Sch. leavers)			

about 4,500 neonates in the Obstetric Unit, University Hospital; 95% of the infants had a primary reaction to smallpox vaccinations and there were no serious complications. To test the efficiency of smallpox vaccinations in neonates, 21 had repeat vaccinations at the age of six months. All showed an immune or a vaccinoid reaction, but a group of controls, who had not had neonatal vaccination, had primary reactions. Vaccination of neonates, therefore, appears to be both safe and effective.

The group of 21 children also had triple antigen given at 6, 10 and 14 weeks of age. Later, Schick tests (21 at six months of age, 13 after one year) showed that all these children were immune to diphtheria. A control group showed no immunity.

In spite of theoretical objections, early vaccination and immunisation with triple antigen appears to be safe and effective. We suggest the following schedules of immunisation for communities, such as Malaysia, in which the majority of infants are delivered by qualified midwives but are rapidly lost to follow-up (tables III and IV).

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Table IV

Suggested schedule of immunisation for a child first seen between 6 weeks and 1 year of age

Time of immunisation	Vaccine	Remarks
X months	B.C.G. Smallpox D.P.T. (alum absorbed)	On the left arm On the right arm
X + 1 month	2nd D.P.T. (alum absorbed) 1st oral polio (trivalent)	Check B.C.G. and smallpox scar, if absent, to repeat.
X + 3 months	3rd D.P.T. (alum absorbed) 2nd oral polio (trivalent)	May give measles vaccine if available when child is 1 year old.
X + 11 to 15 months	Reinforcing doses of D.T. (alum absorbed) and polio (trivalent)	–
Thereafter	Booster doses of smallpox and D.T.	as in Table III (proposed schedule)

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