IMMUNIZATION OF THE RURAL BANTU AGAINST DIPHTHERIA IN THE*

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Barr *et al.*[1-3] have shown that, in man, maternally-transmitted antitoxin interferes with the production of active immunity against diphtheria if the serum of the baby contains more than 0·04 unit of antitoxin per ml. at the time of immunization. Mason *et al.*[4] extended this finding to guinea-pigs passively immunized with homologous antitoxic serum and then actively immunized with ADF (dissolved toxoid-antitoxin floccules adsorbed on aluminium phosphate).

The opportunity occurred of carrying out an experiment in very young Bantu babies in the Pietersburg District of the Northern Transvaal. Because inapparent infections are common in this area[5] there was a chance that an initial depression of active-immunity production caused by a high, passively produced, serum-antitoxin titre would be overcome in 2 years by these mild antigenic stimulations.

MATERIALS AND METHODS

Children and immunization. Blood samples were taken before immunization from 125 children between the ages of 60 and 129 days and serum-antitoxin values were obtained for 100 of them. Immediately after the bleeding, each child received, subcutaneously, 25 Lf (0·5 ml.) of alum-precipitated toxoid (APT) and again 6–8 weeks later. Further blood samples were taken 3, 6, 12 and 24 months after the 1st injection of APT.

Antitoxin assays. The same stable toxin, capable of detecting 0·001 unit of antitoxin, was used throughout the experiment, and titrations were carried out intracutaneously in the guinea-pig.

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RESULTS

In Table I, the ages of the children and their serum-antitoxin titres before immunization are recorded. Of the 100 children,

TABLE I. AGE AND SERUM-ANTITOXIN TITRES (UNIT PER ML.) OF CHILDREN BEFORE IMMUNIZATION

Age of children (days)	0·001 IV	0·002	0·004	0·01	0·02	0·04	0·1	0·2	0·5	0·75	*Total*
60– 69 ..	—	—	1	—	1	2	1	—	—	—	5
70– 79 ..	—	—	1	2	1	4	5	2	1	—	16
80– 89 ..	—	1	1	—	4	5	—	1	1	—	13
90– 99 ..	2	—	2	5	2	5	1	—	—	—	17
100–109 ..	2	—	1	5	3	—	2	1	—	1	15
110–119 ..	—	2	3	6	3	2	1	—	3	1	21
120–129 ..	—	2	3	5	2	1	—	—	—	—	13
Total ..	4	5	12	23	16	19	10	4	5	2	100

21 had circulating antitoxin titres of 0·1 unit per ml. or more. It may be of significance that all the 13 sera from the members of the oldest age-group had less than this amount and that only a single individual had one of 0·04 unit per ml.

On the assumption that 0·004 unit of antitoxin per ml. of serum will produce the Schick-negative state and that 0·04 per ml. will confer immunity, the results of the antitoxin assays carried out on sera taken 3, 6, 12 and 24 months after the start of immunization have been summarized and are presented in Table II. Because the number of children under test is small, and to simplify presentation, 2 groups only have been compared, viz. those initially with 0·04 unit per ml. or less (group A), and those initially with 0·1 unit per

ml. or more (group B). All the group-A children tested were Schick-negative and 98·7%, 97·4%, 86% and 79·7% respectively were protected 3, 6, 12 and 24 months after

TABLE II. IMMUNITY STATE OF BABIES OF GROUPS A AND B AFTER ACTIVE IMMUNIZATION, BASED ON SERUM-ANTITOXIN TITRES

Group	*Time (months)	No. tested	Schick-negative		Protected	
			No.	%	No.	%
A	3	78	78	100	77	98·7
	6	77	77	100	75	97·4
	12	57	57	100	49	86
	24	64	64	100	51	79·7
B	3	19	19	100	17	89·5
	6	20	20	100	13	65
	12	17	16	95·3	8	47
	24	13	10	77	4	30·7
A & B	3	97	97	100	94	97
	6	97	97	100	88	90·7
	12	74	73	98·6	57	77
	24	77	74	96	55	71·4

* Time=months after active immunization

immunization. These results are almost the same as those obtained in older children (1 to 2 years) of the same area immunized with the same batch of APT about 6 months previously. All these were Schick-negative, and 100%, 94%, 88·2% and 77·4% respectively were protected at the same time intervals.[5] Thus, it would appear that a passively produced titre of 0·04 unit per ml. or less does not interfere with the production of active immunity.

Although the number of children in group B is small, it is large enough to show that an initial high serum-antitoxin titre adversely affects the production of active immunity. The percentages Schick-negative after 3, 6, 12 and 24 months were, respectively, 100, 100, 95·3 and 77, and the percentages protected were 89·5, 65, 47 and 30·7. The results that concern protection are somewhat unexpected in view of the high incidence of inapparent infections in this area. An examination of all the results showed that 26 inapparent infections definitely occurred, serum-antitoxin titres rising 2 to 300 times without further artificial immunization. Of these increases in titre, 21 occurred in group A (28·7%) and 5 in group B (24%), the incidences indicating that both groups were subjected to about the same degree of antigenic stimulation of this nature. Thus it is obvious that the active basic immunity laid down originally was of a much poorer nature in group B than in group A. This is illustrated more forcibly in Table III, in which the actual serum-antitoxin titres obtained at the various time intervals are recorded. It will be seen that the percentage of higher titres is at all times greater in the babies of group A than in those of group B.

TABLE III. BABIES OF GROUPS A AND B AFTER ACTIVE IMMUNIZATION, SHOWING SERUM-ANTITOXIN TITRES (UNITS PER ML.)

Group	*Time (months)	≤·001	·002	·004	·01	·02	·04	·1	·2	≥·5	Total
A	3	—	—	—	1	—	—	5	3	69	78
	6	—	—	—	1	1	5	13	24	33	77
	12	—	—	1	3	4	8	17	7	17	57
	24	—	—	—	5	8	7	8	12	24	64
B	3	—	—	—	1	1	2	5	5	5	19
	6	—	—	—	1	6	1	5	5	2	20
	12	—	1	3	4	1	4	2	1	1	17
	24	1	2	1	2	3	1	1	—	2	13

* Time=months after active immunization

When the titres obtained in groups A and B are pooled (Table II) the results are satisfactory; 100%, 100%, 98·6% and 96% respectively are Schick-negative and 97%, 90·7%, 77·0% and 71·4% respectively are protected at the intervals noted.

DISCUSSION

The results confirm those of Barr *et al.*, who showed that circulating antitoxin titres of 0·1 unit or more per ml. of serum interfere with the production of active immunity and indicate that this depressing effect is not of a temporary nature but that it persists, in some instances, for at least 2 years. This result is somewhat surprising because the babies under test were living in the Northern Transvaal, where silent infections are common. Apparently, the passively transmitted antitoxin so interfered with active immunization that a number of children received a very poor basic immunization.

It would be advisable, as Barr and her colleagues suggest, to delay active immunization until the children are more than 4 months of age, by which time most circulating antitoxin titres would have fallen to 0·04 unit or less per ml. of serum. But in practice the ideal must often give way to the possible. Only 21% of the babies had 0·1 unit or more per ml. of serum and a not inconsiderable percentage of these did respond satisfactorily. Because in the Northern Transvaal distances are great, the assembling of children difficult, and special visits virtually impossible, the most practical procedure would probably be to immunize all the children, young babies included, who present themselves. The benefit to the majority would far outweigh the poor immunity conferred on the minority.

CONCLUSIONS

1. In Bantu babies of the Northern Transvaal active immunity against diphtheria is depressed when the circulating antitoxin titre is 0·1 unit or more per ml. of serum. This finding confirms that of Barr *et al.* in European children.

2. The sera of 21% of young babies contained 0·1 unit or more of antitoxin per ml.

3. Ideally, babies should not be immunized until they have reached the age of 4 months or more, by which time the circulating antitoxin titre of most children will have fallen to 0·04 unit or less per ml. of serum. But in the Northern Transvaal, where administrative and other difficulties are great, and because only 21% of the babies have high titres, and because some of these children respond satisfactorily, the practical approach is probably the active immunization of every child who presents himself.

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