Measles immunity in the first year after birth and the optimum age for vaccination in Kenyan children

Collaborative study by the Ministry of Health of Kenya and the World Health Organization*

There is still controversy about the optimum age for measles vaccination in developing countries, where the incidence of measles infection is higher in the first few months of life than it is in developed countries. This study was undertaken to collect reliable data in order to determine the optimum age for mass vaccination programmes. Haemagglutination inhibition (HI) antibodies were titrated periodically from birth to one year of age in children who were given the vaccine at different ages, between 5 and 9 months. It was found that 90% of children no longer have their maternal antibodies at 7–8 months of age, precisely at the period that the incidence of measles begins to rise sharply. Almost all children showed HI seroconversion when vaccinated at 7½ months (or later, but not before), even if a low level of maternal antibody still persisted when the vaccine was given. These data show that there is an advantage in carrying out measles vaccination at 7½ months of age in countries with conditions similar to that of Kenya. The duration of post-vaccinal immunity beyond one year of age has not been studied, but it can reasonably be expected that immunity after one vaccination can last for at least 3–5 years, thus exceeding the period when African children are most exposed to malnutrition.

In many African countries measles is one of the principal causes of morbidity and mortality among young children. In Kenya, where approximately 600 000 children are born each year, the reported yearly incidence of measles is 120 000, mostly in the first 2 years of life. From official notifications, Hayden (*1*) found that 2–3% of Kenyan children contract measles before they reach 6 months of age, 25–30% before the age of 12 months, and 55–60% before the age of 2 years. By the age of 4 years practically all children have experienced measles. Amongst the complications that contribute to the severity of this disease in Africa, Morley and many others quoted by Scrimshaw (*2*) believe that measles precipitates kwashiorkor in malnourished children. Hence the importance of vaccinating children as early as possible in countries where malnutrition still cannot be overcome. However, as reviewed by Duca (*3*), many difficulties are encountered when carrying out mass vaccination programmes against measles in tropical countries. For obvious logistic and financial reasons, it is particularly important to determine the earliest age at which measles vaccination can offer the maximum protection to children without necessitating a two-shot procedure.

Three factors have to be considered when determining the earliest possible age for vaccination against measles: the time of waning of antibodies of maternal origin, the rate of incidence of measles infection in the early months of life, and the efficiency of vaccination given before the age of 12 months. Considering data concerning these factors in temperate climates, Krugman (*4*) has been in favour of postponing vaccination until after 12 months of age. However, there are few serological data available in tropical areas to determine whether the same conclusion is applicable to these regions. In order to assess the three factors already mentioned, the Ministry of Health of Kenya, the World Health Organization, and the Nairobi City Council undertook a collaborative longitudinal study of 1087 children born in Nairobi. HI antibodies were titrated

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in blood samples collected at birth and at two-monthly intervals thereafter. One thousand children of normal weight at birth were divided into different groups which received measles vaccine at 5, 6, 7, 8, 9, and 12 months of age, and HI antibodies were titrated two months after vaccination. An additional group of 87 low birth weight children and premature children was also studied.

MATERIALS AND METHODS

Study population

All children of normal weight born at the Pumwani Maternity Hospital, Nairobi, between November 1974 and February 1975 were divided at random at birth into 5 groups of 200 children each. Out of each group of 200 children, 134 (two-thirds of the group) were to be vaccinated against measles at a given four-week period (FWP) [a] characterizing the group: 5, 6, 7, 8 or 9 FWPs. Sixty-six children (one-third of the group) were to be vaccinated at 12 FWPs to serve as a control. In the analysis of results all children vaccinated at 12 FWPs will be considered together. Medical surveillance was provided for all children in the study and in particular for those vaccinated later, i.e., at 12 FWPs. Seventy-six children with low weight at birth (less than 2500 grams) and 11 premature children born between the 28th and 37th week of gestation constituted an additional group. Twenty-nine of them (one-third) were to be vaccinated at 12 FWPs whereas 58 (two-thirds) were to be vaccinated at 7 FWPs.

Children were followed up until the 14th FWP by attending periodically at the child welfare clinic of the Pumwani Maternity Hospital for clinical examination, serial bleeding, and measles vaccination at the stated age. The timing of the visits was arranged in order to obtain blood specimens at intervals up to the age of 14 FWPs (as shown below).

Vaccination at : (FWPs)	*Visits and blood specimens taken at : (FWPs)*
5 (normal weight)	birth, 1, 3, 5, 7, 10, 12, 14
6 (normal weight)	2, 4, 6, 8, 10, 12, 14
7 (normal weight)	birth, 3, 5, 7, 9, 11, 12, 14
8 (normal weight)	4, 6, 8, 10, 11, 12, 14
9 (normal weight)	1, 2, 9, 11, 12, 14
7 (premature)	birth, 2, 4, 7, 9, 10, 12, 14

[a] Four-week periods after birth were used instead of months for computerization, but they are roughly equivalent. The approximate equivalents are as follows:

FWPs	= 5	6	7	8	9	10	11	12	13	14
Months	= 4.5	5.5	6.5	7.5	8.5	9	10	11	12	13

In addition, a blood specimen was taken from the cord of new-born babies in the two groups to be vaccinated at 5 FWPs and 7 FWPs, and also from their corresponding controls. One hundred and eighty-seven sera were also taken from mothers at the same time as the cord blood to compare the titre of their antibodies with that in the cord blood.

Blood was also taken from all children on the day of their vaccination. Children of the control groups (one-third of each group) were vaccinated at 12 FWPs but were also seen at the visits, when blood specimens were taken at the same time as the group to which they belonged. Those children vaccinated before 12 FWPs who had not seroconverted were re-vaccinated at the 12th FWP. In addition to measles vaccine, this pattern of visits meant that the children could be given BCG, oral poliomyelitis, DPT, and smallpox vaccines.

As expected, the attendance of children at the clinic decreased during the study period. The biggest decrease occurred during the first FWPs and the reason for this was that mothers from remote rural areas only came to Nairobi for delivery. Otherwise the population in Nairobi was easily followed up and defaulters were traced by nurses of the Ministry of Health and the Nairobi City Council. From a total of 1087 children included in the study at birth, 638 were lost before its completion. The quarterly attendance fell to 50, 45, 43, and 39%. Out of 8028 expected sera, 2893 were actually collected.

Results of clinical examinations and serological tests were recorded on individual cards and computerized in Nairobi. Inevitably, some doubtful data had to be eliminated during statistical analysis performed in Geneva, but most of the serological results were still acceptable for interpretation.

Serological tests

For HI tests, a quantity of 0.25 ml of blood (the equivalent of 0.125 ml of serum) was obtained by finger prick, collected in tubes containing 0.25 ml of phosphate buffered saline solution at pH 7.2, and centrifuged, thus making a serum dilution of 1 : 3. The HI test was carried out following the technique described by Lennette & Schmidt (*5*), with minor modifications. The antigen was locally prepared from the Edmonston strain in Vero cells and purified by the Tween–ether method according to Norrby (*6*). Sera were not routinely treated with kaolin or with African green monkey erythrocytes unless they gave equivocal results. Sera were serially diluted 1 : 2 in U-shaped plates by the microtitration method.

Antigen and sera were allowed to react at room temperature for 1 hour, after which 0.05 ml of 0.5% African green monkey erythrocytes in normal saline, pH 7.2, were added. Readings were taken after incubation at 37°C for 1 hour. The HI antibody titre was expressed as the reciprocal of the highest serum dilution with complete inhibition. Four haemagglutination units were used in each test. The results of the different runs were compared by repeating the titration of a standard positive serum.

A plaque reduction test was carried out on 107 blood specimens obtained from cord at delivery time to study neutralizing antibodies and compare them to the HI titres. A suspension of 120 000 Vero cells per millilitre was seeded in Linbro disposable trays. Twofold serum dilutions were made by the micromethod starting from 1 : 30 on a microtitration plate. A dilution of a locally isolated strain of measles virus (M32-4) giving about 20 plaques per cup was added to each serum dilution. The mixture was incubated for 15 min at 37°C and inoculated on to the cell monolayers. After 30 min of adsorption at 36°C, the cells were overlaid with carboxymethylcellulose Leibovitz medium. After incubation at 37°C for 7 days, the overlay was discarded and monolayers were stained with naphthalene black. The highest dilution that gave a 60% reduction of the number of plaques obtained in the virus titration controls was taken as the serum neutralizing titre.

Measles vaccine

One batch of live further attenuated Schwarz strain vaccine [a] in vials of 10 doses of 0.5 ml was used throughout this study. The vaccine was administered subcutaneously by syringe. One opened and partly-used vial and one complete control vial exposed to identical conditions were titrated in Vero cells after each vaccination session. Titration was carried out in cell cultures in tubes. The geometric mean titre (GMT) of 20 titrations was $10^{3.31}$ per 0.5 ml (range $10^{2.7}$–$30^{3.7}$) for the used vials and $10^{3.44}$ (range of $10^{2.5}$–$10^{4.0}$) for the control vials.

RESULTS

Comparison of HI titres and plaque reduction titres

One hundred and seven specimens of cord blood were titrated simultaneously by the HI and the plaque reduction (PR) methods and results are given in Table 1. The HI titres appear to be directly proportional to the PR titres.

[a] Lirugen Measles Virus Vaccine, Dow Pharmaceuticals, lot no. 185836B.

Table 1. Correlation between HI and PR titres in cord blood [a]

HI titres [b]	PR titres [b]									Total no. examined
	<30	30	60	120	240	480	960	1920	>1920	
< 3	0	0	0	0	0	0	0	0	0	0
3	0	**0**	**1**	0	0	0	0	0	0	1
6	0	**1**	**5**	**2**	**4**	0	0	0	0	12
12	0	0	**7**	**6**	**6**	**1**	0	**1**	0	21
24	0	0	**1**	**5**	**13**	**6**	0	**1**	0	26
48	0	0	0	0	**8**	**10**	**5**	0	0	23
96	0	0	1	0	3	**3**	**6**	**1**	0	14
192	0	0	0	0	**1**	0	**2**	**0**	**2**	5
> 192	0	0	0	0	0	2	**1**	**0**	**2**	5
Total no. examined	0	1	15	13	35	22	14	3	4	107

[a] The figures in bold type indicate the numbers of HI and PR titres that differ only by ± 1 dilution — a total of 91 samples (85 % of those tested).

[b] Reciprocals of serum dilution.

Table 2. Distribution of HI antibody titres according to age: children with normal weight at birth, no natural infection, detected clinically or serologically, and not vaccinated

Age (FWPs)	No. of samples examined	HI titres [a]										Geometric mean [b]	
		< 3	% of total < 3	3	6	12	24	48	96	192	384	Total	⩾ 3
Cord blood	382	0	0.0	5	36	70	94	80	63	19	15	32.4	32.4
1	201	1	0.5	8	28	50	50	41	13	6	4	21.4	21.7
2	146	5	3.4	8	21	42	35	20	10	5	0	16.7	18.5
3	171	22	12.9	25	36	42	29	10	6	1	0	8.2	11.2
4	133	35	26.3	19	38	24	13	2	2	0	0	4.7	8.2
5	141	76	53.9	20	28	10	5	2	0	0	0	2.4	6.4
6	127	93	73.2	19	9	4	2	0	0	0	0	1.5	4.8
7	111	89	80.2	10	7	4	1	0	0	0	0	1.4	5.3
8	82	72	87.8	5	3	1	1	0	0	0	0	1.2	5.2
9	88	83	94.3	4	0	1	0	0	0	0	0	1.1	4.0
10	57	54	94.7	3	0	0	0	0	0	0	0	1.1	3.0
11	45	43	95.6	1	1	0	0	0	0	0	0	1.1	4.2
12	65	65	100.0	0	0	0	0	0	0	0	0	0.0	0.0
13	15	15	100.0	0	0	0	0	0	0	0	0	0.0	0.0

[a] Reciprocal of dilution.
[b] Reciprocal of dilutions of titre for all examined and for positive (⩾ 3) only.

Waning of antibodies of maternal origin

A first analysis of the results of HI titration in specimens of cord blood and serial samples of blood of non-vaccinated children with normal weight at birth indicated a composite picture of two apparently distinct populations, one that had not had a natural measles infection and another that had. The evidence for natural infection was based on either a four-fold or higher rise in HI antibodies in serial serum samples or on unexplained high titres after the 7th FWP. After elimination of these cases with natural infection, the distribution of HI titres according to age is shown in Table 2. All 382 samples of cord blood were positive with a GMT of 1 : 32.4. The HI titres of 187 samples of cord blood were compared with the HI titres of blood from the respective mothers and 88.2% were found to be identical or within the range of plus or minus one dilution (Table 3).

The percentage of children with a HI titre inferior to 1 : 3 increased regularly with age (Table 2) and the GMT calculated either on positives only or on all children examined decreased progressively. HI antibodies were no longer detectable at 1 : 3 dilution in any of the children at 12 and 13 FWPs. The fact that between 5 and 6 FWPs the percentage of negatives increased sharply from 53.9% to 73.2% is worthy of note. Table 4 shows that the higher the titre of the cord blood, the longer children have antibodies detectable at 1 : 3 dilution.

Occurrence of measles infection

A clinical follow-up of children at 12 FWPs gave the opportunity to ask most mothers the precise date at which their children had measles. The date of occurrence of measles was known with sufficient accuracy in 43 cases and was uncertain in 30 cases, making a total of 73 clinically recognized cases (Table 5). For all these children a serological conversion confirmed the clinical diagnosis of measles. In addition, 16 children presented an HI seroconversion although their mothers had not reported the occurrence of any disease resembling measles. The probable date of occurrence of measles in such cases

Table 3. Correlation between HI titres in cord and mother's blood [a]

HI titres in cord blood	HI titres in mother's blood									Total no. examined
	<3	3	6	12	24	48	96	192	384	
< 3	0	0	0	0	0	0	0	0	0	0
3	0	**0**	**1**	0	0	0	0	0	0	1
6	0	**1**	**4**	**7**	0	0	0	0	0	12
12	0	1	**3**	**17**	**3**	3	1	0	0	28
24	0	0	0	**21**	**28**	**5**	1	0	0	55
48	0	0	1	1	**11**	**20**	**5**	2	1	41
96	0	0	0	3	2	**15**	**13**	**2**	1	36
192	0	0	0	1	1	0	**3**	**2**	**0**	7
384	0	0	0	1	0	0	2	**1**	**3**	7
Total no. examined	0	2	9	51	45	43	25	7	5	187

[a] The figures in bold type indicate the numbers of titres of cord blood and mother's blood that differ only by ± 1 dilution — a total of 165 samples (88.2 % of those tested).

was extrapolated from the dates of the two blood samples between which the seroconversion occurred. This was also applied to measles cases for which mothers could not indicate a precise date. Thus, the third column of Table 5 gives a more precise picture of the date of first detection of measles infection during the 12 FWPs of observation. It should be noted that there was a marked increase in the incidence of measles between the 7th and 8th FWP.

Table 4. Percentages of children with no detectable antibodies (HI titre <3) by age according to HI titre in cord blood

HI titres in cord blood	Age [a]		
	3	5	7
12	16.7	81.0	92.3
24	11.4	69.0	95.8
48	2.8	37.9	85.0
96	0.0	15.8	72.7

[a] Four-week periods after birth.

Table 5. Numbers of cases of measles infection by age at onset according to clinical and serological diagnosis

Age [a]	Clinical	Serological [b]
4	0	1
5	2	1
6	2	2
7	5	6
8	10	19
9	9	18
10	6	12
11	5	5
12	4	11
13	0	8
14	0	3
15	0	3
Unknown	30	0
Total no.	73	89

[a] Four-week periods after birth.

[b] Four-fold rise in HI titre (includes cases diagnosed clinically and those infections diagnosed serologically only). For those diagnosed serologically, the age indicates the age at which the rise in titre was first detected.

Results of primary vaccination at different ages

The HI testing of prevaccination sera showed that certain children had no detectable antibodies at 1 : 3 dilution when they were vaccinated, whereas others still had antibodies of maternal origin. In the first group it was possible to titrate HI antibodies 2 FWPs after vaccination only in a little less than 50% of vaccinated children. Table 6 gives the result of serological tests for these children according to the age at which they received the vaccine. Although variations may have been caused by a relatively small number of children in each group and by possible technical errors between titres of 1 : 3 and less than 1 : 3, a pattern of progressive increase in the percentage of positive results and increasing GMT is evident. The later the vaccination is given,

Table 6. Postvaccination HI titres according to age of vaccination: children with no prevaccination antibody detectable at 1 : 3

Age at vaccination [a]	No. examined	No. positive	% positive	Postvaccination HI titres									Geometric mean titre [b]	
				< 3	3	6	12	24	48	96	192	384	Total	⩾ 3
5	15	9	60.0	6	2	1	4	0	2	0	0	0	4.24	11.11
6	31	28	90.3	3	5	4	6	7	2	4	0	0	11.54	14.99
7	30	20	66.6	10	1	4	2	5	7	1	0	0	7.59	20.89
8	23	23	100.0	0	0	1	3	2	10	6	0	1	45.19	45.19
9	27	25	92.5	2	0	0	3	6	6	9	0	1	36.03	48.00
12	38	38	100.0	0	0	0	1	4	13	17	2	1	66.66	66.66

[a] Four-week periods after birth.
[b] Reciprocal of dilutions of titre for all examined and for positives only.

Table 7. Distribution of postvaccination HI titres according to age of vaccination: children with prevaccination HI antibodies >1 : 3

Pre-vaccination antibody titres	Age at vaccination [a]	Postvaccination HI titres [b]									Total no.	
		< 3	3	6	12	24	48	96	192	384	Positive	Examined
1 : 3	5	4	0	1	0	1	0	0	0	0	2	6
	6	1	2	0	0	0	1	0	0	0	3	4
	7	2	0	0	0	0	0	0	0	0	0	2
	8	0	0	0	0	1	1	1	0	0	3	3
	9	1	0	0	0	0	1	0	0	0	1	2
1 : 6	5	5	2	0	0	0	0	0	0	0	2	7
	6	2	0	0	0	0	0	0	0	0	0	2
	7	2	0	0	0	0	0	0	0	0	0	2
	8	1	0	0	0	0	1	0	0	0	1	2
1 : 12	5	0	0	0	1	0	0	0	0	0	1	1
	7	1	0	0	0	0	0	0	0	0	0	1

[a] Four-week periods after birth.
[b] The numbers of children with postvaccination HI titres showing a four-fold rise or more are underlined.

Table 8. Decrease in maternal antibodies with age: low birth weight and premature children [a]

Age [b]	No. examined	HI titres [c]									Geometric mean [d]	
		< 3	3	6	12	24	48	96	192	384	Total	⩾ 3
Cord blood	81	0	3	8	17	17	13	20	1	2	43.3	43.3
2	34	0	3	10	3	10	8	0	0	0	14.7	14.7
4	28	5	5	6	7	4	1	0	0	0	6.5	8.8
7	29	19	6	3	1	0	0	0	0	0	1.6	4.2
9	9	9	0	0	0	0	0	0	0	0	0.0	0.0
10	10	10	0	0	0	0	0	0	0	0	0.0	0.0
12	9	9	0	0	0	0	0	0	0	0	0.0	0.0

[a] Children with no natural infection, detected clinically or serologically, and not vaccinated.
[b] Four-week periods after birth.
[c] Reciprocal of dilution.
[d] Reciprocal of dilutions of titre for all examined and for positives only.

the better the immunological response. There is an evident difference between results at 7 FWPs and earlier and those at 8 FWPs and later. Results at 8 and 9 FWPs were not statistically different from those at the 12th FWP, when the vaccine gave 100% seroconversion and a GMT of 1 : 66.

In the second group (Table 7), children still had maternal antibodies detectable at 1:3–1:12 when they received the vaccine. Among 17 children with a 1:3 titre of maternal antibodies when they received the vaccine, 6 showed seroconversion to titres between 1 : 24 and 1 : 96. It should be noted that 4 of the 6 children who showed seroconversion were vaccinated at 8 or 9 FWPs. In contrast, there was only one case of seroconversion in a child who had a titre of 1 : 6 and none in those who had a titre of 1 : 12.

Children who belonged to the groups vaccinated between 5 and 9 FWPs and who did not seroconvert were vaccinated again at the 12th FWP: 20 of these children were examined 2 FWPs later in order to carry out tests for antibodies. None of them, however, had HI antibodies detectable at 1 : 3 when they were vaccinated and all of them showed seroconversion.

Premature and low birth weight children

All 81 samples of cord blood examined in this group had HI antibodies. Table 8 shows the rate of disappearance of maternal antibodies in this category of children. Two-thirds of the premature and low birth weight children were vaccinated at 7 FWPs. Only 7 children could be examined at 2 FWPs after vaccination for titration of their HI antibodies. Out of 5 who had no detectable antibodies in their prevaccination sample, 2 showed seroconversion to 1 : 24 and 1 to 1 : 96, and 2 did not show any rise in titre. One child who had a titre of 1 : 12 showed seroconversion to 1 : 48 and another with a titre of 1 : 6 in the prevaccination sample did not show a significant rise (four-fold) 2 FWPs after vaccination.

DISCUSSION

Different results may be obtained according to the type of antigen used for the detection of HI antibodies. Techniques using the Tween–ether purified antigen recommended by Norrby (*6*), and used in the present study, are 5–10 times more sensitive than those using the classical antigen. The discrepancies between various studies may also be explained by the first dilution at which sera are tested. By starting with dilutions of 1 : 2, Bass (*7*) showed that two-thirds of sera that would have been stated as negative if tested at 1 : 10 were in fact positive. In the present study, dilutions of sera for HI tests were started at 1 : 3. As shown in Table 1, the results of HI and PR tests are proportional. From the fact that PR test dilutions were 10 times higher than those of HI tests it can be said that the PR test is about 10 times more sensitive than the HI test. However, as no samples of HI negative cord blood were tested in

this experiment, it is not known whether some HI negative sera might have been found positive by PR tests.

From results of studies carried out with the classical antigen, it was generally thought that waning of measles antibodies of maternal origin was complete by 6 months of age. However, with the Tween-ether antigen, Stanfield (*8*) found that 35% of children in Uganda still had detectable antibodies at 6 months of age. Krugman (*9*), studying a group of American children, found that maternal antibodies were still detectable in 20% of them at 9 months of age, in 12% at 10 months of age, in 8% at 11 months of age, and were no longer detectable in any at 12 months of age.

At first sight, it appeared that a considerable proportion (22%) of children still had maternal antibodies at 12 FWPs. However, the GMT of positive sera showed an increase after the 7th FWP and it was evident that there were two different populations in this group of non-vaccinated children, i.e., those that had had a natural measles infection and those that had not. When children for whom serial sampling showed seroconversion or an isolated positive result that was not confirmed by a second test were discarded, the percentages of children with blood still positive at 8 FWPs and onwards were considerably lower than before. The cause of this error could only be detected by analysing sequential results and this leaves doubt as to the accuracy of studies based on a single serum specimen taken between 9 and 13 FWPs. We therefore consider it of particular interest when deciding upon the age for vaccination to note that 88% of children have no antibodies detectable at 1 : 3 at 8 FWPs and that half of the remaining 12% who have antibodies have titres below 1 : 6.

The fact that HI antibodies were present in all tests carried out on the 382 specimens of cord blood reported in Table 2, on the 81 reported in Table 8, and on the 187 samples of mothers' blood reported in Table 3 indicates clearly that measles virus is widespread in African populations. The antibody titre in samples of cord blood was rather high, with a GMT of 1 : 32 as shown in Table 2 and 1 : 43 in Table 8. Table 4 shows that the duration of protection is proportional to the antibody titre at birth.

There is little agreement among authors about the age at which measles becomes a danger in infancy. In Kenya, Hayden (*1*) found 2–3% of cases under 6 months of age and 25–30% under the age of 12 months. O'Donovan (*10*) stated that over half the total number of cases in Kenya occur under 24 months of age and mentioned a few cases in children less than 4 months old. Grigsby (*11*) found that a third of the cases in Nigeria occur in the first year and that cases as early as 4 months of age are not unusual. Guyer (*12*) found that in Cameroon 24% of children had measles between 6 and 11 months of age. This is much earlier than in temperate climates. However, Wilkins (*13*) found 44% of cases in children up to 12 months of age in Los Angeles County, USA, during the 1970 epidemic.

The present study was carried out to try to obtain more precise data on the frequency of measles infection between the ages of 6 and 12 months in Kenya. Table 5 shows clearly that this frequency increases rapidly after 7 FWPs of age. It should be noted that the total number of 89 cases included only those that were well-documented, and that the population under observation during the study period was less than the 1000 children selected at the beginning of the study. The apparent decrease in the number of measles cases after 9 FWPs is due to the fact that the non-vaccinated population diminished progressively in the study group because of vaccinations and defaulters. It should also be noted that all diseases described as measles by the mothers were confirmed serologically. On the other hand, 16 out of 89 measles infections (17.9%) remained unnoticed at the time of occurrence, either because of their mildness or because mothers were unable to recall them. Statistics based only on clinical or historical data are therefore somewhat doubtful. It can, however, be concluded from our data that the 8th FWP was marked by a definite increase in the attack rate of measles in the population under study.

There is also some disagreement on the results of measles vaccination in children vaccinated before they have reached their first birthday. Linnemann (*14* and *15*), and other authors, stated that over 40% of measles vaccination failures in the USA occurred in children who were vaccinated at less than 1 year of age. Krugman (*4*) found a seroconversion rate of 86% (HI antibodies) in American children vaccinated at 9–11 months of age compared with 95% after 12 months. Vaccination before 1 year of age is now not recommended in many countries. However, this may not be applicable to tropical countries with a high prevalence of measles before 1 year of age. With live Edmonston B vaccine, Meyer (*16*) in Upper Volta obtained rates of 50, 76, and 90% of seroconversion in children vaccinated at 5, 6, and 7 months, respectively. With the live further attenu-

ated vaccine, Borgoño (*17*), in Chile, obtained 94–99% of seroconversions in infants 8 months old. In Nairobi, Hayden (*1*) found 92% of seroconversions in children vaccinated between 6 and 9 months, as well as in those over 1 year of age. The present study confirmed that 100% seroconversion with a GMT of 1 : 66 can be obtained in vaccination after 12 FWPs (11 months of age). Table 6 shows also that similar results, with 92–100% seroconversions and 1 : 48 GMT, can be achieved when vaccination starts at 8 FWPs (7.5 months of age). Maternal antibodies must be at a titre of 1 : 6 to hamper the take of the vaccine (Table 7). Table 2 shows that only 4 children had maternal antibodies at titres of 1 : 6, 2 at 1 : 12, and 1 at 1 : 24 out of a total of 352 children examined in the group 8–13 FWPs of age. This would represent only 1.7% of non-receptive children in this age group. This percentage has to be balanced with other factors in favour of vaccinating the age group, such as the risk of natural infection and the logistic constraints.

Low birth weight children and premature children were studied separately to see whether different results would be obtained. Unfortunately their number was too low to establish statistically significant results. The impression gained from the present study is that there is no marked difference between the two groups concerning the waning of maternal antibodies (Table 8) and the results of vaccination at 7 FWPs. Wilkins (*13*) even found that better serological responses to vaccination were seen more frequently among low birth weight infants than their term counterparts when vaccinated at 11 months of age.

The present study thus demonstrates that children may be included in measles vaccination programmes as early as from 8 FWPs (7.5 months) after birth. In addition to possible logistic advantages, the inclusion of this age group in vaccination campaigns will protect a significant number of children who may be exposed as early as at 7.5 months of age to measles infection and its severe complications in countries where conditions are similar to those in Kenya. The long-term persistence of protection after " early " vaccination was not determined in this study. However, protection should last for at least 2–3 years (if not longer) without a second vaccination, thus protecting a high proportion of children when they are most exposed to the aggravating factor of malnutrition during this period.

RÉSUMÉ

IMMUNITÉ ANTIROUGEOLEUSE AU COURS DE LA PREMIÈRE ANNÉE DE LA VIE ET AGE OPTIMAL POUR LA VACCINATION CHEZ LES ENFANTS KÉNYENS

On a effectué une étude prospective sur 1087 enfants kényens nés à Nairobi; ces enfants ont été soumis à des examens sérologiques et cliniques entre la naissance et l'âge de 12 mois (13 périodes de 4 semaines ou P4S) en vue de suivre la disparition des anticorps antirougeoleux d'origine maternelle, de déterminer le moment de la survenue de l'infection morbilleuse naturelle et les résultats de la vaccination antirougeoleuse avant l'âge de 12 mois. Les épreuves d'inhibition de l'hémagglutination (HI) ont été effectuées avec un antigène au Tween-éther, à des dilutions commençant à 1: 3, sur le sang du cordon et sur des séries d'échantillons de sang prélevés à certains intervalles. Il a été ainsi confirmé que les anticorps maternels peuvent persister au-delà de l'âge de 6 mois: à 8 P4S, 90% des enfants ne présentaient plus d'anticorps décelables à la dilution de 1: 3 et entre 8 et 12 P4S, il n'y avait plus que 1,7% de sujets présentant des anticorps HI à 1: 6, dilution susceptible de compromettre l'efficacité du vaccin. Un groupe de 87 enfants prématurés ou ayant un poids faible à la naissance n'ont pas semblé se distinguer des nourrissons ayant un poids normal. On a enregistré 89 cas d'infection morbilleuse chez les enfants suivis pendant toute la période d'observation de 12 P4S, soit un peu moins de 50% du total du groupe enregistré au début de l'étude. Parmi ces cas, 16 (17,9%) n'ont été découverts qu'à l'occasion des épreuves sérologiques en série et auraient été méconnus si les observations avaient été fondées sur la seule clinique. Il y avait également une augmentation marquée du nombre d'infections morbilleuses à la 8e P4S. Le pourcentage de séro-conversions après vaccination à 12 P4S (11 mois) a atteint 100%, alors que la vaccination des enfants à 5 P4S n'a donné que 60% de séro-conversions même lorsque les nourrissons n'avaient plus d'anticorps maternels décelables à la dilution de 1: 3. La vaccination à 8 P4S (7,5 mois) ou après permettait d'obtenir 92% de séro-conversions. D'après ces données, les enfants peuvent être inclus dans les programmes de vaccination antirougeoleuse dès qu'ils atteignent l'âge de 7,5 mois s'ils sont exposés à un risque élevé d'infection comme dans les conditions de cette étude. Ces enfants seront ainsi protégés pendant la période où ils doivent faire face à la malnutrition qui est un facteur aggravant de la rougeole.

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Annex 1

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