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AGE OF MEASLES IMMUNIZATION IN TROPICS (*)

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ABSTRACT

Maternal immunity to measles was studied in a group of 500 newborn children and another group of 500 children aged one to 12 months, before vaccination.

The geometric mean titer of detectable hemagglutination-inhibition antibody was 16 for newborn children. This titer was absent in most children aged 3 to 5 months. Our previous studies indicate that from 1970 to 1972, children from the lower socio-economic classes aged 5 to 9 months were the main target of measles complications and deaths. Based on the present data, we suggest that children in developing countries should be vaccinated as young as 6 months and should be revaccinated 3 to 4 months later to assure full protection.

Following the large-scale production of live attenuated measles vaccine in Iran in 1970 and the annual mass immunization in rural regions of the country, the number of reported cases in these regions decreased from 63,751 in that year to 13,873 in 1975 (12). The mortality due to measles complications, exceeding 10,000 in 1964, was only about 200 in 1977. Large epidemics are no longer observed and even limited outbreaks are rare. The situation in large cities, among children from the lower socio-economic classes is still not satisfactory. While immunization against measles in public clinics is performed around the first, birthday, many children aged 5 to 9 months die from measles complications. It was necessary to evaluate the existing measles maternal antibody in a large number of children at birth and its decrease during the following months in order to prevent the high attack rates by early vaccinations.

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MATERIALS AND METHODS

Sources of specimens

Finger blood of 500 day-old children in FARAH Maternity and Child Care Center was absorbed onto squares of filter-paper discs of Whatman filter paper used for chromatography. Details are given in a previous report (7). Finger blood of 500 children aged 1 to 12 months was also taken in the same way from unvaccinated children who were brought to public immunization clinics in Tehran city. In preliminary experiments, it was found that to cover the surface, each filter paper measuring 3 cm by 3 cm, absorbed 0.16 ml of blood.

Serology

The blood was eluted from each square in 0.8 ml of saline the evening before the tests were to be run. Elution was carried out in test tubes, the squares being soaked overnight at 4°C. It was accepted arbitrarily that each blood sample would contain 50% cells and 50% serum; hence the initial dilution was 1:10. To remove the non specific inhibitors, diluted sample was equally mixed with 25% kaolin in PBS, pH 7.2, shaken for 20 min at room temperature and centifuged at 2000 rpm/min for 15 min. The clear supernatant was used as 1:20 treated serum.

Serologic method

Hemagglutinin (HA) was produced in our laboratory according to the Norrby technique (13). Measles antibody was measured by the hemagglutination inhibition (HI) test using 4 units of HA antigen. Positive and negatiue sera were included in each test.

RESULTS

Discs related to 115 day-old children and 113 infants at various ages were discarded because they were not fully covered with blood. HI titre of 385 newly-born children were from 1:20 to 1:640. Fifty children (13%) had no detectable antibody at birth. HI titre of 385 older children, aged one to twelve months, are reported in Table I.

The half life of immunoglobulins passively transferred by maternal antibody being short, most children 3 to 4 months old, have lost their circulating antibody. Only 7% of infants still had detectable antibody after 6 months of age. This low percentage remain immune sometimes until after their first birthday (Fig. 1).

Table I. Age distribution of maternal antibody

Age in Months	Total no Tested	Measles G M T∎												Seronegative
		<20	20	30	40	60	80	120	160	240	320	480	640	(<20)%
1Dayold	385	50	65	82	45	23	29	9	13	6	4	2	2	13
1	8	4	1		2				1					50
2	15	11			1		3							73
3	22	14	1	3	2	1		1						64
4	53	35	9	7	1	1								66
5	44	39	1	3		1								88
6	41	38	1	1	1									93
7	49	42	3	2		2								86
8	38	37	1											97
9	42	40	2											95
10	42	38	2	2										90
11	13	12		1										92
12	20	18	1	1										90

∎ Geometric Mean Hemagglutination-Inhibition Titre

Veinous sera of a small number of children less than 6 months old with undetectable HI antibody were retested. It was found that while some children have a titre of 1:4 or 1:2, others are free from circulating antibody and are then prone to the infection. This is in accordance with the findings of Stokes and his colleagues (1960) and Reilly et al. (1969) who had shown that most infants did not have any antibodies after six months of age. This susceptibility to measles in the tropics will not last for long time. According to Griffith (1975) in temperate countries, infants remain measles-suceptible for 2 to 4 years before they contract the disease, so nearly all are vaccine-susceptible for 2 to 4 years and are responsive to measles vaccine between the ages of 12 months and 3 years. In the tropics, however, children are infected by measles much earlier in life, in some cases between the ages of 5 to 9 months.

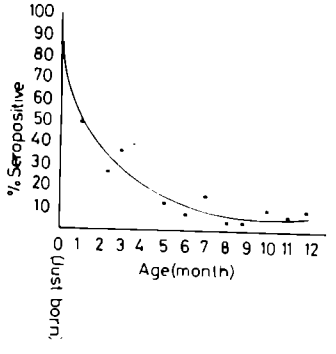

Fig. 1. Decrease of measles maternal antibody in unvaccinated children.

DISCUSSION

The American Public Health Service Advisory Committee on immunization practice has recommended (15) that "measles vaccine should be administered when children are at least 12 months old". However, in the face of epidemic exposure, it may be desirable to vaccinate infants as young as 6 months recognizing that the proportion of seroconversions declines progressively with diminished age. Infants vaccinated under these conditions should be revaccinated after reaching 1 year of age. Therefore, measles vaccination in Western countries is routinely performed after the first birthday.

In Iran, since 1970, in four field trials, children of 9 to 12 months from the central part of the country were immunized. 5 to 8% of these children had detectable measles antibody and did not respond to vaccination (8,9,10). In another field trial made in the Caspian Sea area, the average of seropositive children before vaccination was 20% (11,12). The programme of mass vaccination after the first birthday in rural areas of the country was started in 1970 and has continued each year. As a result large outbreaks are no longer observed and mortality in remote regions has sharply declined. In large cities of the country, however, in the lower economic classes, mortality due to measles complications before the first birthday is prevalent. In a previous report (6), it was noted that, in the workers' area of Tehran, a significant number of deaths due to measles occur in infants under 12 months of age. Referring to the data presented in this report, at the age of six months, maternal antibody is no longer detectable in the majority of children. As stated before, some of these children still had a trace of maternal antibody which probably, in combination with cell-mediated immunity, protected them against measles infection. These children do not respond to vaccination but are susceptible to the disease at the age of 9 to 12 months. On the other hand, some children, from 4 to 6 months old, are free from measles maternal antibodies and are victims of the disease long before their first birthday. Burrows and Cruickshank (1976) have found that 65 per cent of African children at the age of four months still have residual antibody but that this proportion drops sharply to less than 20 per cent between six and nine months. According to these authors, there is a considerable danger period between six and nine months during which a significant proportion of children are susceptible to infection but cannot be protected by vaccination. In recent years, the value of early vaccination has become controversial. While Perkins (1975) favours vaccination at about six months of age when the children are contacted on few occasions, Beale (1974) and Griffith (1975) attribute programme failures, to some extent, to early vaccinations.

In the light of our studies and the views expressed above, we support the idea of immunization against measles twice in the tropics. First, inoculation

should be done when the child is 6 months old, and the second dose should be injected 3 to 4 months later. In all cases, a live attenuated vaccine should be utilized in a suitable way.

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