

Prevalence of measles antibody in children of different ages in Shiraz, Islamic Republic of Iran

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معدل انتشار أضداد الحصبة لدى الأطفال من مختلف الأعمار في Shiraz، جمهورية إيران الإسلامية
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الخلاصة: دفعنا إلى إجراء هذا البحث حصول فاشية من الحصبة ناجمة عن فشل ثانوي في اللقاح، وذلك للتعرف على معدل انتشار أضداد الحصبة لدى الأطفال. فقمنا بدراسة 608 من الأطفال في سبع مجموعات عمرية مختلفة هي 6 أشهر، و9 أشهر، و14 شهراً، و18 شهراً، و6 سنوات، و10 سنوات، و15 سنة. ولم يكن الأطفال في سن 6 أشهر و9 أشهر قد تلقوا أي تطعيم ضد الحصبة، أما بقية المجموعات فقد تلقت جرعتين من اللقاح في عمر 9 أشهر و15 شهراً. في حين تلقى أفراد مجموعة 15 عاماً جرعة إضافية. وقد لوحظ أن أضداد الحصبة العابرة للمشيمة قد نقصت من 10.0% في عمر ستة أشهر إلى صفر بالمائة في عمر تسعة أشهر. وأصبحت أضداد الحصبة إيجابية في 52.9% في عمر 14 شهراً، و89.4% في عمر 18 شهراً، ثم 60.8% في عمر 6 سنوات، و45.0% في عمر 10 سنوات، لتعود فتصبح 96.8% في عمر 15 عاماً. وهكذا فلنكني تزداد مستويات أضداد الحصبة يُوصى بإعطاء جرعة تعزيزية من التطعيم، إما مع الجرعة المعززة لللقاح الثلاثي (الحنك والشاهوق والكزاز) أو قبل دخول المرحلة الثانوية.

ABSTRACT An outbreak of measles due to secondary vaccine failure prompted this investigation into the prevalence of measles antibody in children. We studied 608 children in 7 different age groups: 6, 9, 14 and 18 months and 6, 10 and 15 years. Children in the 2 youngest groups received no vaccination; the rest were vaccinated at 9 months and 15 months. The 15-year-old age group received an additional vaccination. Transplacental measles antibody (Ab) decreased from 10.0% at 6 months to 0% at 9 months. Measles Ab was positive in 52.9% (14 months), 89.4% (18 months), 60.8% (96 years), 45.0% (10 years) and 96.8% (15 years). To increase Ab levels, a booster vaccination is recommended, administered either with the second DPT booster or at pre-high school age.

Prévalence des anticorps antirougeoleux chez des enfants de différents âges à Chiraz (République islamique d'Iran)

RÉSUMÉ Une flambée de rougeole due à l'échec de la vaccination secondaire a conduit à effectuer une étude de la prévalence des anticorps antirougeoleux chez les enfants. Nous avons étudié 608 enfants dans sept groupes d'âge différents : 6, 9, 14 et 18 mois et 6, 10 et 15 ans. Les enfants des deux groupes d'âge les plus jeunes n'avaient pas été vaccinés ; le reste des enfants avaient été vaccinés à l'âge de 9 et 15 mois. Le groupe des enfants de 15 ans avait eu une vaccination supplémentaire. Les anticorps transplacentaires diminuaient, passant de 10,0 % à l'âge de 6 mois à 0 % à l'âge de 9 mois. Dans les groupes d'âge étudiés, la proportion des enfants présentant des anticorps antirougeoleux par âge était de 52,9 % (14 mois), 89,4% (18 mois), 60,8 % (6 ans), 45,0 % (10 ans) et 96,8 % (15 ans). Afin d'augmenter les taux d'anticorps, une vaccination de rappel est recommandée, à administrer soit avec le deuxième rappel DTC soit à l'âge correspondant au cycle d'enseignement pré-secondaire.

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Introduction

Prevention of measles using vaccination is still the most important task in developing countries. The disease is a substantial cause of mortality and morbidity in children. It is highly contagious but preventable [1]. Mortality has declined dramatically since the introduction of a live attenuated vaccine. Despite an 85% decrease in mortality, however, outbreaks of measles have been reported due to secondary vaccine failure in older age groups (10–24 years), e.g. in a study of measles epidemiology by the Iranian Minister of Health and Medical Education in 1998 [2]. This has led some countries, including the United States of America, to introduce an additional dose of vaccine in school-age children. In the Islamic Republic of Iran, the decline in measles incidence due to the vaccination programme has been noticed in children; cases in older age groups are, however, still emerging. This might be due to immigration from neighbouring countries such as Afghanistan and Pakistan, which have a vaccine coverage of less than 80% (unpublished report, Ministry of Health and Medical Education, 1988).

Our study was conducted to disclose the prevalence of measles antibodies in different age groups and to evaluate the necessity of administering additional doses of vaccine. The study was prompted by an outbreak of measles in our country in 1997.

Methods

Over the period 2001–02 we enrolled 608 children into the study in 7 different age groups. Details of the groups and their vaccination history are given in Table 1. The children were selected by random cluster sampling of children referred to the Motahari out-patient clinic or from primary

schools in Shiraz. The epidemiological data including sex, age, socioeconomic status, number of family members and vaccination history were obtained. For antibody (Ab) testing, 5 mL of blood was drawn and serum was separated and frozen at -20°C . The sera were examined using an enzyme-linked immunosorbent assay IgG kit (Morbillio, Radim SpA, Pomezia, Italy). Samples with optical density (OD) lower than the cut-off control ($\text{OD} < 0.200$) were considered non-reactive for measles IgG antibodies. Samples with OD higher than the cut-off control ($\text{OD} > 0.700$) were considered reactive for measles IgG antibodies. Samples with absorbance values $\pm 10\%$ of the cut-off ($\text{OD} = 0.200$ to 0.700) control were considered questionable and were re-tested for confirmation.

Results

We enrolled 608 children, 52% male and 48% female, in the study. Table 2 shows

Table 1 Vaccination history for children in seven different age groups

| Group | No. | Age | Vaccination history |
|-------|-----|------|---|
| 1 | 70 | 6 m | No vaccination |
| 2 | 62 | 9 m | No vaccination |
| 3 | 70 | 14 m | Vaccinated at 9 m |
| 4 | 66 | 18 m | Vaccinated at 9 m and 15 m |
| 5 | 97 | 6 y | Vaccinated at 9 m and 15 m |
| 6 | 149 | 10 y | Vaccinated at 9 m and 15 m |
| 7 | 94 | 15 y | Vaccinated at 9 m, 15 months and 9 m prior to the study |

m = months. y = years.

Table 2 Prevalence of measles antibody (Ab) in children in seven different age groups in Shiraz

| Age | Total No. | Ab positive | | Ab negative | | P-values between different age groups | |
|-------|-----------|-------------|------|-------------|-------|---------------------------------------|---------|
| | | No. | % | No. | % | | |
| 6 m | 70 | 7 | 10.0 | 63 | 90.0 | | |
| 9 m | 62 | 0 | – | 62 | 100.0 | 6 m and 9 m | 0.014 |
| 14 m | 70 | 37 | 52.9 | 33 | 47.1 | 9 m and 14 m | 0.00001 |
| 18 m | 66 | 59 | 89.4 | 7 | 10.6 | 18 m and 6 y | 0.00006 |
| 6 y | 97 | 59 | 60.8 | 38 | 39.2 | 6 y and 10 y | 0.016 |
| 10 y | 149 | 67 | 45.0 | 82 | 55.0 | 10 y and 15 y | 0.00001 |
| 15 y | 94 | 91 | 96.8 | 3 | 3.2 | All age groups | 0.00001 |
| Total | 608 | 320 | 50.7 | 288 | 49.3 | | |

m = months.

y = years.

the frequency of measles Ab prevalence in each age group. Antibody prevalence was higher in girls, although the result was not statistically significant. The Ab prevalence was significantly different in all consecutive age groups ($P = 0.00001$). The P -values for the different age groups are shown in Table 2. Number of family members, socioeconomic status and literacy of parents were not significant (data not shown).

Transplacental IgG from mothers declined from 10.0% at 6 months to 0% at 9 months of age in non-vaccinated children. Although this is unusual and we do not have good explanation for it, it is possible the titre of measles Ab in our pregnant women was very low due to low contact with wild measles viruses. However, in infants more than 9 months old, the prevalence of Ab increased owing to vaccination at 9 months and 15 months of age, and declined over time thereafter.

Primary vaccine failure is defined as a no detectable antibody after vaccination. It can be caused by interaction of maternal antibody to the vaccine by immunological response, technical problems, and so on. Primary vaccine failure in our study was

47.1% in the 14-month-old group, reducing to about 10.6% in the 18-month-old group due to the second dose of vaccine given at 15 months. Primary vaccine failure was 55% at age 10, reducing to 3.2% at 15 due to the third vaccine administration.

Discussion

Measles is a highly contagious, preventable disease. The incidence has shown a remarkable decline in our county over recent years due to routine administration of live, attenuated vaccine at the ages of 9 months and 15 months, but several reports of disease outbreak in older age groups have been documented [2,3]. The presence of measles Ab indicates previous infection, active immunization or, at ages below 9 months, maternal Ab transmission, all of which offer immunity.

Our study was conducted to determine the pattern of Ab prevalence in different age groups of children. In this study, transplacental Ab was detected in only 10.0% of 6-month-old infants, declining to 0% at 9 months. This finding is in accord with pre-

vious studies from Iran [4,5]. The decline of maternal antibody in infants in different geographic areas is dependent on socioeconomic states, catabolism of antibody, amount of antibody transmission to fetus, level of maternal antibody, and so on. In some studies it was shown to be between 0% and 10% at about 11 months of age [2,4]. Therefore, a high percentage of children at 6 months of age are also susceptible in an outbreak of the disease. It has been documented that the Schwarz type vaccine that is used in the Islamic Republic of Iran is not so effective for 6-month-old infants [6,7]. The absence of Abs during outbreaks was 47.1% at 14 months, 1 month before the second vaccination and 10.6% 3 months afterwards. This finding was in accordance with previous studies [8–10]. High primary vaccine failure at 9 months of age might be related to trans-placental Ab from mothers [8].

Other possible factors responsible for this high primary vaccine failure include nutritional status of children [11], acute disease during vaccination [12–14] and concomitant administration of gamma globulin [15], race, environmental factors [16,17], sex [18] and immunity status of those being vaccinated [19,20]. In our study, sex and literacy were not statistically important factors in primary vaccine fail-

ure. Measles Ab was positive in 89.4% of the 18-month-old children and 60.8% at 6 years of age, which was statistically significant ($P < 0.001$). In the 10-year-old group, only 45.0% of the children were positive for measles Ab ($P = 0.016$). This Ab-waning phenomenon is reported to be about 2%–20% in several studies [21–24]. The presence of Ab may be due to the vaccine effect or to previous infection with wild virus. The waning of Ab titre is greater in subjects who produce lower initial Ab titres. Accordingly, a single vaccination produces more significant Ab waning [25]. An important observation was the significant rise in the Ab titre of the 15-year-old age group following the administration of an additional booster dose of the vaccine, compared to the 10-year-old age group ($P < 0.00001$) (Table 2). The necessity for an additional immunization is also emphasized in a report from Singapore [26] and in other countries [27,28]. Therefore, an additional dose of measles vaccine is recommended for Iranian children around high-school age.

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Measles mortality reduction

Measles remains a leading cause of death among young children, despite the availability of a safe and effective vaccine for the past 40 years. More than half a million people, the majority of them children, died from measles in 2003; in the Eastern Mediterranean Region (EMR) there were an estimated 69 000 deaths from measles. WHO and UNICEF have developed a joint Strategic Plan for Measles Mortality Reduction and Regional Elimination 2001-2005. The overriding goal of this plan is to reduce the number of global measles deaths (from the 1999 level) by 50% by the end of 2005. The priority countries in EMR are Afghanistan, Djibouti, Pakistan, Somalia and Sudan. The four-pronged strategy for sustainable measles mortality reduction is based on: providing strong routine immunization; providing a "second opportunity" for measles immunization to all children; surveillance; improvement in the clinical management of measles cases. Thus, from 1999 to 2003, more than 350 million children globally received measles vaccine through supplementary immunization activities. Moreover, improvements were made in routine immunization over this period. These accelerated activities have resulted in a significant reduction in estimated global measles deaths. Overall, global measles mortality decreased by 39% between 1999 and 2003. Given the progress made to date, it is expected that the 2005 global measles mortality reduction goal will be achieved.

Source: WHO Fact sheet No. 286

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