Original Article

Epidemiological Investigation of Measles in Sera of Healthy People in Heilongjiang Province, China

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SUMMARY: Serological samples of healthy people were collected to obtain the levels of measles antibodies in different groups of people in Heilongjiang Province, China. Using quantitative enzyme-linked immunosorbent assays to measure the antibody levels, we found the lowest antibody positive rate and the lowest geometric mean concentration values in healthy people aged 15–39. This group is the population at high risk for adult measles in Heilongjiang Province, and is the focus of measles elimination work. The new challenges for the eventual elimination of measles will be to address immunization strategies in this segment of the population in order to control the incidence.

INTRODUCTION

Before the implementation of measles vaccinations, the incidence of measles was almost equivalent to the birth rate in Heilongjiang Province. Together with the promotion and application of measles vaccines, the subsequently successful immunization program resulted in a dramatic decline in the incidence of measles to 0.7 per million in 2004. Since 2005, the incidence of measles underwent a substantial rebound in that province. Furthermore, the age at onset of emergence changed, as a considerable proportion of infected patients were adults, which suggested that the level of province-specific population immunity might be problematic. To investigate the immune status of the population of Heilongjiang Province, the sera of 126 healthy people in the Meilisi district were collected for epidemiological investigation by enzyme-linked immunosorbent assay (ELISA) and hemagglutination-inhibition (HI) tests.

Expanded Program on Immunization (EPI) implementation was initiated in Heilongjiang Province in 1983. In the first years, the rate of measles vaccination was low, and the number of reported cases of measles was at a high level. After 1992, the coverage of measles vaccinations was stabilized at a high level, and there were a low number of reported cases of measles. The age of the target population used to calculate the coverage was 8-month-old children, an age after the first dose of basic measles immunization. The age composition of measles incidence has changed, with a bidirectional shift transfer to an older age group and an infant group who have not yet reached the age of primary immunization (Fig. 1).

MATERIALS AND METHODS

Epidemiological survey for antibodies to measles in the sera of healthy people: (i) Random sampling methods of serological specimens: The cross-sectional survey method was taken in the Nangang district in Harbin city, the Meilisi district in Qiqihar city, Yian county in Qiqihar city, the Lishu district in Jixi city, Baoqing county in Shuangyashan city, the Datong district in Daqing city, and Huachuan county in Jiamusi city, which are all seven national disease surveillance points. Two units were randomly selected as monitoring points in each township. The selected target population (aged, 1–59) was comprised of 1,050 individuals who were divided into 10 age groups: 1–2 years old (n = 70), 3–5 years old (n = 107), 6–9 years old (n = 137), 10–14 years old (n = 131), 15–19 years old (n = 83), 20–24 years old (n = 83), 25–29 years old (n = 123), 30–34 years old (n = 105), 35–39 years old (n = 105), and ≥40 years old (n = 106).

(ii) Sera sample collection: Information concerning the history of measles vaccination was collected on-site, and 2 ml of venous blood was aseptically collected for serum separation.

(iii) Detection methods: An ELISA kit (batch: SX.X.D.M; Institut Virion/Serion GmbH, Würzburg,
Germany) was used for the quantitative detection of the levels of the measles IgG antibody. A positive result was detected when antibody levels exceeded 150 mIU/ml.

Detection of antibodies using HI: (i) Source of serological samples: Serological samples were collected from healthy people in the Meilisi district, and 126 serological samples were collected for measles IgG antibody level testing. An HI test was used to detect IgG antibodies to measles.

(ii) Test methods and reagent sources: HI test reagents were used according to the Ministry of Health "EPI Technology Management and Regulation." The hemagglutinin was purchased from Beijing Institute of Biological Products, and values ≥1:2 were considered positive.

Statistical methods: The database was established using EpiData 3.0, and the analyses were done using SPSS12.0 software (SPSS, Inc., Chicago, Ill., USA). The antibody positive rate was analyzed by a χ² test; and the antibody level was compared by an F test.

RESULTS

The result of measles IgG antibody levels in different age groups of healthy people: The rates of the positive detection of antibodies to measles ranged from 87.62–97.81% in the 10 age groups, with an overall positive rate of 93.90%. The geometric mean concentration (GMC) values were 0.51–1.83 IU/ml, with an average GMC of 0.77 IU/ml. As shown in Table 1, the positive rates and GMC values of the 15–39-year-old group were lower than those of the <15-year-old group and that of the ≥40-year-old group (χ² = 20.81, P < 0.001; F = 30.959, P < 0.001).

Comparison of the detection methods: ELISA and HI tests were used to detect antibodies to measles in 126 serological samples from healthy people in the Meilisi district. The antibody titer of 108 serological samples from different age groups were statistically analyzed (18 samples with antibody values <0.05 IU/ml and >5 IU/ml were deleted, and so the data was not available for statistical analysis). As the antibody titer increased, the corresponding mean IU value increased (Table 2). There was no significant difference in positive rates between the <15-year-old group and the 15–39-year-old group (χ² = 18.94, P < 0.000). With correlation analysis, a correlation coefficient of r = 0.76 (P < 0.001) was found (Fig. 2), demonstrating a close correlation between these two methods.

DISCUSSION

Measles is a vaccine-preventable disease, and measles vaccine is the most effective method of prevention. According to the Field Guidelines for Measles Elimination, which is provided by the World Health Organization Western Pacific Region (1), the measles vaccination rate should be ≥95% in order to eliminate measles. Our monitoring results indicate that the rates of positive antibody test to measles in the <15-year-old group exceeded 95%. This group also had a high concentration of measles antibodies, indicating that the measles vaccination rate of children in the province is high. The measles vaccination coverage data in our province showed that the rates of measles vaccination have remained at 95% and above. Serological surveillance in the province indicates that the measles antibody levels of healthy people exhibit a phenomenon of being lower in the middle groups and higher in the end groups. The measles antibody positive rate and GMC values were high in the <15-year-old group, low in the 15–39-year-old group, and high in the ≥40-year-old group. This phenomenon

<table>
<thead>
<tr>
<th>Age group</th>
<th>No. of samples</th>
<th>No. of positives (%)</th>
<th>GMC (IU/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;15</td>
<td>123</td>
<td>112 (91.06)</td>
<td>0.53</td>
</tr>
<tr>
<td>15–20</td>
<td>83</td>
<td>76 (91.57)</td>
<td>0.59</td>
</tr>
<tr>
<td>20–25</td>
<td>123</td>
<td>112 (91.06)</td>
<td>0.53</td>
</tr>
<tr>
<td>25–30</td>
<td>105</td>
<td>96 (91.43)</td>
<td>0.59</td>
</tr>
<tr>
<td>30–35</td>
<td>105</td>
<td>92 (87.62)</td>
<td>0.51</td>
</tr>
<tr>
<td>Subtotal</td>
<td>499</td>
<td>451 (90.38)</td>
<td>0.55</td>
</tr>
<tr>
<td>≥40</td>
<td>106</td>
<td>102 (96.23)</td>
<td>0.81</td>
</tr>
<tr>
<td>Total</td>
<td>1,050</td>
<td>986 (93.90)</td>
<td>0.77</td>
</tr>
</tbody>
</table>

There is no significant difference of positive rates between <15-year-old group and 15–39-year-old group (χ² = 18.94, P < 0.000).

Table 2. Comparison of these two detection methods

<table>
<thead>
<tr>
<th>No. of samples</th>
<th>HI test Antibody titer (1:1)</th>
<th>Quantitative ELISA (IU/ml)</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>2</td>
<td>0.31</td>
<td>1.14</td>
</tr>
<tr>
<td>11</td>
<td>4</td>
<td>0.45</td>
<td>0.34</td>
</tr>
<tr>
<td>30</td>
<td>8</td>
<td>0.74</td>
<td>0.46</td>
</tr>
<tr>
<td>28</td>
<td>16</td>
<td>1.09</td>
<td>0.56</td>
</tr>
<tr>
<td>23</td>
<td>32</td>
<td>1.82</td>
<td>0.68</td>
</tr>
<tr>
<td>13</td>
<td>64</td>
<td>3.09</td>
<td>1.41</td>
</tr>
</tbody>
</table>

HI, hemagglutination-inhibition; ELISA, enzyme-linked immunosorbent assay; SD, standard deviation.

Fig. 2. Correlation analysis between HI test and ELISA test.
is due to the history of implementation of the measles vaccine in the province, and the change of natural infection risk matches the characteristic age of measles incidence in our province. Apparently, the 15–39-year-old group is the high-risk measles incidence group in the province, and it is the focus group of future measles elimination. The development of immunization strategies to control the incidence of measles in this segment of the population will be the new challenge of measles elimination. In developed countries, after measles outbreaks were effectively controlled in young children, measles cases moved to adults and persons that had not yet accessed measles vaccine (2,3). An increase in the proportion of the incidence of measles in adults is a common phenomenon in regions of high vaccination rates (4). After extensive use of measles vaccine in Beijing, Shanghai, and Shandong, the incidence of measles was controlled at a relatively low level for many years, but the proportion of adult infections significantly increased (5–7).

Serological surveillance of measles cases indicates that IgG antibody levels of healthy people in the 15–39-year-old group were lowest among the age groups in our province, with values <0.6 IU/ml. Whether or not a measles IgG antibody level of 0.6 IU/ml can be used as a reference value of the threshold for measles protection requires further research.

A comparison of the results of the HI test and quantitative ELISA revealed that these methods showed a close correlation, with corresponding mean IU values increasing with the increase in antibody titer. This study showed that with a quantitative ELISA detection of measles IgG at a concentration of 0.6 IU/ml, the corresponding HI antibody titer was under 1:8.

Serosurvey is the only measure of the overall level of population immunity (1,8). This investigation applied ELISA in order to obtain the population immunity levels rapidly (9). Naiying et al. (10) compared the gold standard plaque-reduction neutralization test with commercially available kits of quantitative ELISA in order to detect measles IgG antibody. They demonstrated that the kit made by the Institut Virion\Serion had the best qualitative and quantitative detection. This kit was easy to operate, had rapid access of results, and is therefore suitable for large-scale serological sample testing.

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Conflict of interest None to declare.

REFERENCES