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Identify the susceptibility profile to measles in the general population: Serological survey of measles antibodies in Shaanxi province, China, in 2016

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ABSTRACT

The reported coverage with two doses of the measles vaccine (MCV) in Shaanxi Province, China, is greater than 95%, but the measles incidence over the whole province remains high. Cross-sectional serological surveys of measles antibodies in Shaanxi Province were conducted in 2016 to assess the population's immunity. The measles IgG levels were measured in serum samples using ELISA. The geometric means concentration (GMC) levels and seroprevalence rates with 95% CIs were calculated by region, gender, and age. A total of 3574 serum samples were collected from participants aged from 2 months to 49 years. The GMC of measles antibodies was 471.3 mIU/ml (95% CI: 445.9–498.2 mIU/ml), and the seroprevalence was only 85.9% (95% CI: 84.8–87.1%). A significant difference in the GMC ($P < .05$) but not the seroprevalence ($P > .05$) was observed among the 3 regions. The report measles incidences were high in individuals aged 0–7 months (33.2/100 000) and 8–17 months (26.8/100 000). Although both measles immunity (90.7%) and MCV coverage (89.7%) were low in children aged 8–17 months, the measles seroprevalence in adults was high at greater than 90%. These results revealed that further actions may be taken to increase vaccination coverage in children aged 8 months to 5 years over the whole province and teenagers in the south region. In particular, timely administration of the first MCV dose should be emphasized to prevent measles epidemics in children aged 8–17 months. Vaccination strategies may be varied by age and region.

1. Introduction

Measles is a contagious but vaccine-preventable disease. Measles was eliminated in the United States in 2000 [1,2]. The World Health Organization in the Western Pacific Region (WPR) has set a goal for measles elimination by 2012 [3]. Since a large proportion of measles cases in the WPR are reported by China, the interruption of measles transmission in China is crucial to achieve measles elimination in this region [4]. The national plan for measles elimination in China was drafted to be consistent with this initiative, with the key points including reaching 95% immunity to the measles virus in every cohort born after 2006, conducting supplementary immunization activities (SIAs) in children aged 8 months-14 years, and strengthening the routine surveillance system for measles and rubella [5]. Currently, a routine two-dose measles-containing vaccine is offered to children at 8 months (measles-rubella vaccine, MR) and between 18 and 24 months (measles-mumps-rubella vaccine, MMR) in China [6,7]. However, the number of measles cases showed yearly increases from 2013 to 2015 [8–11].

Shaanxi Province, which is located in the western region of China, is a less developed province compared to the eastern provinces. The measles epidemiology in Shaanxi Province is different from that in the eastern region [6]. For example, although the measles incidence is relatively high in adults and relatively low in children aged 8 months to 5 years in the eastern provinces [9,12,13], the measles incidence in adults in Shaanxi Province is relatively low, and a higher incidence of measles is observed in

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children aged 0–5 years. Additionally, data concerning the immunity of the population to measles virus in the less developed regions of China, such as Shaanxi Province, are limited. Serological surveillance is a core component of integrated measles surveillance and can provide direct evidence of a population's immunity profile to the measles virus.

The objectives of this study were to assess the immunity to measles in the general population in Shaanxi Province, China, to explore the susceptible or high-risk population, to identify the target population and to identify appropriate immunization activities that may benefit the goal of measles elimination in the less developed regions of China.

2. Materials and methods

2.1. Serological survey

A cross-sectional survey for IgG antibodies to measles virus was conducted in the general population of Shaanxi Province. The whole province was stratified into 3 regions (north, center, and south) based on variations in the geography and socioeconomic status. One county was randomly sampled in each region, and 3 townships or communities were selected randomly in each county. In each selected township or community, a list of the households was obtained from the local government, then the households were selected by systematic sampling methods. All the subjects (resident or temporary resident) in each selected household were invited to participate in this survey. And the participants were selected to be proportionally representative by gender and age as follows: 0–7 months, 8–17 months, 18–35 months, 3–5 years, 6–12 years, 13–17 years, and 18–49 years.

This study was approved by the Biomedical Ethics Committee of Xi'an Jiaotong University Health Science Center. All participants or their parents signed written informed consent forms and were invited to fill out a questionnaire containing questions about their gender, age or birth date, and vaccination status. The measles-containing vaccine (MCV) vaccination status of participants $\leq$12 years were obtained by participants' recall and then verified by checking the Vaccination Certificates or Vaccination Cards in immunization sites. If the Vaccination Certificate and Vaccination Card were lost, the vaccination status should be considered as unknown. The vaccination status of participants $\geq$13 years were obtained by the participants' recall or checking the Vaccination Certificate if available.

The MCV investigated coverage is defined as the percentage of participants who receive one or more doses MCV in the investigated participants. The MCV reported coverage is defined as the percentage of participants who receive one (8 months to 17 months of age) or more doses MCV (18 months to 12 years of age) in the participants. For all the participants, the immunization history with unknown status was excluded from the coverage analysis.

2.2. Measles case surveillance and reporting

Measles is a class B infectious disease in China. All cases diagnosed by hospital staff should be reported to the National Notifiable Disease Reporting System (NNDRS), which is a web-based computerized reporting system.

2.3. Laboratory assay

Sera were separated from blood samples and then stored at −20 °C prior to testing. A commercial ELISA (SERION ELISA Classic Anti-Measles Virus IgG, InstitutVirion/Serion GmbH) was used to detect human IgG antibodies against measles virus in the serum samples. The ELISA results were first expressed as the optical density (OD) at 405 nm and then transformed to the antibody concentration (mIU/ml) using SERION software; the antibody concentration was categorized as negative or positive using fixed cut-off values. Equivocal samples were retested prior to categorization. An antibody concentration $\geq$200 mIU/ml was categorized as positive, and a concentration <200 mIU/ml was considered negative.

2.4. Statistical analysis

To fully describe the measles immunity profile of the general population, the measles IgG status was described according to socio-demographic characteristics using basic descriptive statistics, including frequencies, counts and proportions. The geometric mean concentrations (GMCs) and seroprevalence rates with 95% confidence intervals (95% CIs) were compared after stratification by region, gender, and age. The age-specific measles incidence was calculated as the number of measles cases per 100,000 individuals in each age group, and the population denominators were provided by the National Bureau of Statistics of China. Comparisons of GMCs were performed through analysis of variance (ANOVA). The SNK-q test was applied for multiple comparisons. Comparisons of the seroprevalence rates by region, gender, and age were performed using the χ^2 test. The Cochran-Mantel-Haenszel χ^2 test (CMH χ^2) was applied to analyze the trend in seroprevalence between years. Data quality control was conducted using Epidata software for suitable edit checks and validations. R 2.10.0 statistical software was used for the analysis [14]. $P < .05$ was considered significant.

3. Results

A total of 3574 serum samples were collected from participants aged from 2 months to 49 years. As shown in Table 1, the GMC of measles antibodies for the whole province was 471.3 mIU/ml (95% CI: 445.9–498.2 mIU/ml), and the seroprevalence was only 85.9% (95% CI: 84.8–87.1%). The GMC ($P < .05$), but not the seroprevalence ($P > .05$), significantly differed between the 3 regions. Neither the GMC nor the seroprevalence showed significant differences between males and females ($P > .05$). Among the 7 age groups, the lowest GMC (73.5 mIU/ml) and the lowest seroprevalence (44.6%) appeared in infants less than 7 months of age who had not received MCV. The highest GMC (1317.7 mIU/ml) and highest seroprevalence (98.3%) appeared in children 18–35 months and 3–5 years of age, respectively (Table 1).

As shown in Table 2, the coverages of at least 1 dose of the MCV for children 8 months to 12 years of age were 91.5%, 84.6%, and 92.9% in the center, north, and south regions, respectively. Tables 3 and 4 show the GMC and seroprevalence stratified by age in the different regions, respectively. A similar changing trend in the GMC and seroprevalence with age in each region was observed compared to the whole province. With the exception of the 6–12-year-old age group, significant differences in the GMC were observed among the 3 regions in the age groups. Significant differences in the seroprevalence rates were found among the 3 regions in participants with each following age group: 0–7 months, 13–17 years, and 18–49 years.

Most of the reported cases in Shaanxi Province occurred in participants aged 0–7 months and 8–17 months with high incidence of 33.2/100,000 and 26.8/100,000, respectively, which was consistent with the seroprevalence rates calculated in this study (Fig. 1). All the reported cases aged 0–7 months were too young to vaccinate MCV; while the majority of cases aged 8 months to 12 years

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