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A hospital-associated measles outbreak among individuals not targeted for vaccination in eastern China, 2014

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ABSTRACT

Background: An outbreak of measles occurred in early 2014 among individuals not targeted for vaccination—adults, and infants too young to vaccinate, in Xiangshan County, Zhejiang Province, in eastern China.
Objective: We conducted an investigation to identify risk factors responsible for this outbreak and to provide evidence-based recommendations for measles elimination strategies in China.
Methods: Measles was diagnosed using national standard case definitions. In a case-control study, 20 randomly selected measles patients were matched with controls selected from the same village or community as each case in a 1:2 case-to-control ratio. Controls were matched on age, within 5 years, and gender. We compared exposure histories during the 7–21 days before rash onset of the case and the same time period for the matched controls. We also conducted a measles antibody seroprevalence survey of a convenient sample of residual serum obtained from healthy patients during routine care in a hospital.
Results: The outbreak consisted of 45 measles cases, with an attack rate of 8.9/100,000 total population. Among cases, 91.1% (41/45) were adults (ranged 23–51 years) who had unknown vaccination histories; the other cases were infants younger than 8 months of age. The case-control study showed major risk factors to be a visit to Hospital X (OR_{MH} = 7.3, 95% CI: 1.8–30.7) and treatment in an IV room in Hospital X (OR_{MH} = 11.0, 95% CI: 1.3–96.1). The seroprevalence survey showed that 88.8% of adults had measles IgG antibodies, and that 100% of children 2–19 years of age were seropositive.
Conclusions: The outbreak was primarily among age groups not targeted for vaccination—primarily adults, but with some children too young to vaccinate. Visiting a hospital was the major risk factor for measles transmission. We conclude that in addition to maintaining high 2-dose coverage with measles vaccine, working with hospital infection control programs to implement evidence-based strategies to prevent or limit hospital transmission is an important action for eliminating measles in eastern China.

1. Introduction

The incidence of measles in China has been greatly reduced through more than 35 years of nationwide measles vaccination efforts [1]. When the Expanded Program on Immunization started in China in 1978, a 1-dose measles-containing vaccine (MCV) strategy was used, and since 1986, the program has used a 2-dose MCV immunization strategy: The first dose at the age of 8 months; the second dose at the age of 7 years. In 2006, the age of administration of the second dose was changed from 7 years to 18 months. In 2005, the China Ministry of Health established a goal to eliminate measles in China by 2012 (i.e., to reduce measles incidence to below 1/1000,000, excluding imported cases), consistent with the World Health Organization Western Pacific Region's time-bound goal for measles elimination [2]. To achieving this goal, China strengthened measles surveillance and improved the measles vaccination effort with a goal of

Abbreviations: MCV, measles-containing vaccine; IgM, immunoglobulin M; IgG, immunoglobulin G; ELISA, enzyme-linked immunosorbent assay; RT-PCR, reverse transcription-polymerase chain reaction; RNA, ribonucleic acid; CDC, center for disease control and prevention; IV room, intravenous rehydration room; GMT, geometric mean titres; EPI, expanded program on immunization; OR, odd ratio; CI, confidence interval.

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attaining and sustaining MCV first and second dose coverages above 95%.

In eastern China's Zhejiang Province, MCV coverage levels are determined using an administrative records methodology, and 2-dose coverage has consistently been reported to be >98% since 2006 [3,4]. In 2012, Zhejiang Province reported only 52 measles cases to the national Measles Surveillance System, the official, Internet-based information system for disease control and prevention [5]. In early 2014, without any change in the national Measles Surveillance System, a measles outbreak was detected in Xiangshan County (County X), which is located in peninsula, eastern China's Zhejiang Province, and has a population of 506,904 (in 2013) with the area is 6510 km^2. We conducted an investigation of this outbreak to identify risk factors for measles and to provide evidence to support recommendations for measles elimination strategies in China.

2. Methods

2.1. Case definition and investigation

Measles cases were diagnosed and classified using standard case definitions in the Chinese Measles Surveillance Guidelines [6]. A laboratory-confirmed case was a suspected case that either tested positive for measles-specific IgM by ELISA or for measles RNA by RT-PCR, or from which measles virus was isolated in a clinical specimen. A clinically-diagnosed case was a suspected case without laboratory testing, but which was epidemiologically linked to a laboratory-confirmed case during the incubation period.

2.2. Data collection

In China, measles cases are required to be notified through the Measles Surveillance System. The investigators attempted to find out all the measles cases through passive surveillance system and active search by reviewing medical records in different hospitals and interviewing anyone in close contact to cases for clinical symptoms. And then try to obtain the following information about cases: demographic data, illness onset, vaccination history, history of contact with measles patients, and history of a hospital visit during the incubation period (7–21 days before rash onset). We also got a shot at review the electronic medical records of all measles patients in the hospital computerized information system to determine whether they visited the hospital, and if so, when.

2.3. Case-control study

High exposure rate of measles cases to Xiangshan County First People's Hospital (Hospital X) and its intravenous rehydration room (IV room) for treatment during their incubation period. We therefore hypothesized that hospital transmission was a major risk factor in this measles outbreak. To test that hypothesis, we conducted a case-control study comparing exposure histories to health facilities and public places, travel histories, patients contact histories, and so on. A random selection of measles case-patients were matched with controls, selected from the same village or community as the case, in a 1:2 case-to-control ratio. Controls were matched on age, within 5 years, and gender. For cases, the exposures of interest were during 7–21 days before rash onset; the same time period was used for each case's 2 matched controls.

2.4. Prevalence of measles antibodies

In order to evaluate the prevalence of measles antibodies rapidly, we conducted a seroprevalence study using a convenience sample of residual serum specimens from hospitals in County X. Serum specimens were obtained from healthy individuals who visited the hospital for a health examination. Specimens were transported to the county CDC for measles-specific IgG testing [6]. The collection of serum specimens was carried out in February 2014; demographic information including age, gender, and location of residence were collected, but subjects' immunization status and history of measles were not obtained. These data were analyzed after determining seropositivity and geometric mean titres (GMT) in age-stratified groups.

2.5. Data analysis

Data were analyzed using SPSS for Windows (ver. 13.0; SPSS). The Mantel–Haenszel χ^2 test was used to determine the significance of differences between categorical variables. Differences between groups were considered significant at a level of $P < 0.05$. All P values are 2-tailed.

2.6. Ethical review committee

Testing the residual blood specimens for measles antibody was approved by the Ethical Review Committee of Zhejiang Province CDC. Identifying data were not obtained on individuals whose serum was tested for measles antibodies. The outbreak investigation and case-control study were considered a response to a public health emergency and determined to be exempt from institutional review board review by Zhejiang Province CDC. Individual-identifying data from the investigation and case-control study were not retained.

3. Results

3.1. Setting

County X is located on a peninsula in Zhejiang Province. Historically, County X has had high measles vaccination coverage among targeted children. Estimated coverage of both MCV1 and MCV2 from 2011 to 2013 was above the national target of 95% for measles elimination. There have been very few measles cases in County X since 2001.

3.2. Outbreak description

From December 20, 2013 to February 28, 2014, a total of 56 suspected measles cases were reported in County X, of which 45 were either laboratory confirmed ($n = 43$) or clinically diagnosed ($n = 2$) cases; 11 suspected cases were not confirmed as measles. The estimated attack rate was 8.9/100,000, which was more than 50 times the overall attack rate in Zhejiang Province (0.17/100,000) during the same period of time. Of the 45 measles cases (with 16 males and 29 females, the incidence rate was 6.3/100,000 and 11.5/100,000 respectively, gender ratio was 0.55:1), 91.1% (41/45) were among adults, age range between 23 and 51 years of age. Vaccination status was unknown for these adult cases. The other 4 cases were children under age 8 months, with a highest measles incidence rate of 142.9/100,000, who were therefore not age-eligible for MCV1 (Table 1).

The epidemic curves showed that cases had occurred sporadically until the end of January, 2014, when the case count increased dramatically, and an outbreak was suspected. 8336 contacts of cases were vaccinated immediately for who either had not been fully vaccinated against measles or who had unknown measles vaccination status. Measles cases were isolated. Following these 2 measures, the outbreak stopped (Fig. 1).

Measles cases were seen in 13 of the 18 townships or urban sub-districts of County X. Among the cases, 86.7% (39/45) were local residents who had not traveled far from home. The other 6