Measles transmission among adults with spread to children during an outbreak: Implications for measles elimination in China, 2014

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1. Introduction

Before licensure of measles vaccine (MV) in 1965, the annual measles incidence in China fluctuated between 10,000 and 50,000 cases per million population [1]. Establishment of the national Expanded Program on Immunization (EPI) in 1978 enabled a one-dose routine MV schedule, with the dose administered at 8 months of age. In 1986, a 2-dose MV schedule was recommended – one dose at 8 months followed by a second at 7 years of age. The recommended age for the second dose was lowered to 18 months in 2005 [2].

In addition to routine measles vaccination, in 2006 China began closing immunity gaps among children using province-wide, catch-up, supplementary immunization activities (SIAs). These campaigns were followed by a large nationwide SIA in 2010 [3,4]. As of September 2010, every birth cohort between and including the 1995 and the 2009 cohorts have been targeted with an SIA that vaccinated children regardless of their prior vaccination history [5]. Some provincial SIAs targeted cohorts as early as the 1990 birth cohort.

Continuous use of the 2-dose measles-containing vaccine (MCV) vaccination policy for 25 years, coupled with the comprehensive SIA strategy, has led to a marked decrease in measles, so that by 2012, the annual incidence was at its lowest point ever of 4.6 cases
per million population [6]. However, accumulation of susceptible children in new birth cohorts has allowed a resurgence of measles that started at the end of 2012 [5], reaching 20.4 per million in 2013 [6], and 38.8 per million in 2014.

Measles typically is a disease that mainly affects children; in the pre-vaccine era, over 90% of children had measles by their 15th birthday [7]. With a greater than 99.5% decrease in the incidence of measles during the elimination effort in China, the age distribution of measles case-patients has changed. In recent years, relatively few cases have been reported from age-groups that were targeted by SIAs. Instead, the majority of cases have been occurring among young children <24 months of age and adults [6,8]. Among all reported measles cases, the percentage of cases in the over 15-year-old age group was less than 10% in the early 1990s [9,10], increased to 27% in the first 10 months of 2013 [5], and further increased to over 40% in 2014 [11]. Some provinces have been having measles outbreaks among adults.

One of the stated research needs for global measles elimination is to identify the roles of infants less than 9 months old, adolescents, and adults in measles virus transmission [12]. In our traditional assessment, adult measles is highly correlated with the incidence in children. The great reduction of measles incidence rates in every age-group in 2011 and 2012 – including among children and adults – seems to support this assessment [6,8]. Such an assessment implies that high immunization rates among children will provide adequate herd immunity to prevent measles among adults and infants too young to vaccinate – a key part of the strategy for measles elimination. However, we have seen measles outbreaks among adults without children acting as measles virus reservoirs in recent years in China, raising our concern that susceptible adults could alone sustain measles virus transmission in community settings. We report a typical measles outbreak among adults in China that occurred in 2014, describing a pattern of measles virus transmission from adult to adult and then to children, in Kulun (KL) County. We describe sources of infection and the effect of outbreak response immunization, and we suggest control measures targeting adults.

2. Methods

2.1. Setting

Kulun (KL) County is one of the eight counties in Tongliao prefecture, Inner Mongolia Autonomous Region, a less-developed western province. The county has a population size of 167,200 (5.3% of the total population in Tongliao prefecture, and 0.7% of Inner Mongolia); 2.1% are children less than 2 years of age, and 82.7% are 15 years or older. Three rounds of SIAs had been conducted in KL: a catch-up SIA in April 2009 targeting birth cohorts of May 1994 through August 2008 as part of an Autonomous Region-wide campaign; a follow-up SIA in September 2010 targeting birth cohorts between October 2005 and 2009 as part of the nation-wide campaign; and a 2nd round follow-up SIA in 2012 targeting birth cohorts between 2008 and 2011, as part of an Autonomous Region-wide campaign. Thus, all birth cohorts from 1994 through 2011 have been covered by at least one SIA, regardless of target children’s prior vaccination histories.

In 2009, there was a large measles epidemic in KL County, with 279 cases reported (52.7% of these were ≥15 years old), representing a measles incidence of 152.9 per 100,000 population. After the outbreak, only three cases were reported (in November 2011, and May and June 2013) until another outbreak started in December 2013 that continued into 2014. Over 150 measles cases were reported by March 31, 2014, representing an incidence of 89.7 per 100,000 population; among the cases, >75% were among individuals 15 years or older. The disease pattern raised our concern about the source(s) of infection and transmission routes (from whom and to whom), and prompted an evaluation of the effectiveness of outbreak response immunization in such an adult outbreak setting. We conducted a field investigation in April, 2014.

2.2. Outbreak investigation and description

In accordance with the Chinese Measles Surveillance Guidelines [13], all suspected measles cases were reported through a computerized, real-time reporting system. Variables obtained included age, sex, address of residence, date of onset, occupation, MCV vaccination history, and measles-specific immunoglobulin (IgM) testing results [14]. A suspected measles case was defined using World Health Organization (WHO) criteria as a person with fever, rash, and one or more of the following symptoms: cough, coryza, or conjunctivitis. All suspected measles cases were classified as laboratory confirmed, epidemiologically confirmed, clinically compatible, or discarded measles cases [13].

During the field investigation, we conducted a retrospective active case search to find additional measles cases; suspected cases found were reported through the measles surveillance system. MCV vaccination statuses were checked by reviewing vaccination certificates and SIA records. Case data were analyzed to describe person, place, and time characteristics of the outbreak.

2.3. Source of infection and transmission chain determination

We evaluated all laboratory and epidemiological-link confirmed measles cases that had onset during the first 2 months of this outbreak (before March 2014) to determine source of infection and early-stage transmission patterns. In-house interviews of all individuals confirmed to have had measles were conducted to gather an activity history from 21 days before their rash onset through 5 days after rash onset, to describe the “incubation period” (7–21 days prior to rash onset, when they get infected) and the “transmissibility period” (5 days before through 5 days after rash onset). Queried activities included contact with other fever and rash illness patients, places visited, and hospitals and clinics visited. A source of measles virus infection was categorized as: (a) an imported measles case, defined as exposure to measles virus outside the KL County during the seven to 21 days prior rash onset in which a thorough investigation of contacts excludes a local source of infection; (b) a family-contact acquired infection, defined as one or more measles cases occurring during their transmissibility period within the same family during the 7–21 days prior to rash onset; (c) a nosocomial measles case, defined as having a clinic/hospital visit during 7–21 days prior to rash onset in which a thorough investigation of contacts excludes other sources of infection; or (d) a community acquired infection, defined as contact with measles cases in the same or neighboring villages, or in schools, workplaces, or other locations outside of healthcare facilities or the home. Cases with a clear, common infection source were epidemiologically linked to each other.

2.4. Ethical considerations

This field investigation did not involve endangered or protected species, and no human subjects’ specimens were obtained. Such outbreak investigations are considered by China CDC’s Ethical Review Committee to be exempt from IRB review as they are considered public health program evaluation. Individual identifying data were not retained in analytic data sets.
3. Results

3.1. Outbreak description

In total, 292 suspected cases were identified in this outbreak; 280 cases were confirmed, and 12 were excluded. Among the 280 confirmed cases, illness onset dates were between 29 December 2013 and 19 June 2014 (Fig. 1). Among all cases, 148 (52.8%) were among males; 183 (65.4%) were laboratory confirmed with a positive serological test for measles IgM, and the remaining 97 (34.6%) cases were linked epidemiologically to laboratory-confirmed cases. Among the 195 villages of KL County’s six townships, 143 (73.3%) had reported measles cases, and the median number of cases per village was 2 (range: 1–7). The age at onset of measles ranged from 1 month to 61 years. The majority (220, 77.6%) were adults, aged 20 years or above, 24 (8.6%) were 8–23 months of age, and 22 (7.9%) were less than 8 months of age (Table 1). At time of the outbreak, 29.2% of the 24 cases among children 8–23 months of age were documented to have received an MCV dose, and 75.0% of the twelve 2–9 year olds had received ≥1 dose. Both of the 15–19 year olds who had measles had been vaccinated. Among 220 ≥20 year olds with measles, <5% had documentation showing receipt of MCV (Table 1).

3.2. Transmission chain identification

Among the 107 individuals with measles rash onset before March 2014 that we attempted to re-visit, 83 (77.6%) were successfully interviewed to determine the most likely transmission settings. Among those interviewed, 41 (49.4%) were categorized as being community acquired cases, 24 (28.9%) were nosocomial cases, 13 (15.7%) were family-contact cases, and 5 were imported cases from outside the county (Fig. 2). Among the 17 individuals with onset of measles before February 2014, three were categorized as imported cases, two had been infected within their family, eight had been infected in the community, and three had been infected in a hospital in late January. After February 2014, more nosocomial infections were seen, along with continuous community and family transmission.

Fifty-eight (69.9%) of the 83 people that we interviewed had measles infections that were clearly linked (Fig. 2), especially in the outbreak’s first three generations. The outbreak started with adult-to-adult transmission in family and community settings, and then a small number of young infants and children became infected. Nosocomially-infected cases occurred in late January – one month after the first cases was reported. The first case led to at least six generations, infecting eight others. Among the 44 clearly determined transmission linkages, 37 (84.1%) were from adults to other age-groups (29 were adult to a different adult age group, seven were adult to children, and one was adult to a young infant), six were young infant to other age groups (four were infant to adult, and two were infant to child transmission), and one was child-to-child transmission.

3.3. Outbreak response immunization

During January through March – the first three months of the outbreak – only limited outbreak response immunization activities were implemented. These were non-selective vaccination efforts in which all age-eligible children and adults living near a measles case were targeted regardless of their prior MCV vaccination history. At the early stage of the outbreak on January 10 and 11, public health officials conducted three of these non-selective activities, vaccinating 35 children 8–59 months old, 156 children 5–19 years old, and 1480 adults with measles vaccine. Further ORI was not conducted until 28–29 of January when 97 adolescents 15–19 years old and 68 adults were vaccinated. In the first two weeks of February, no ORI was conducted even though the number of measles cases continued to increase.

As the outbreak continued, ORI was intensified. From 18 February through 12 March, ORI activities were conducted every day, as soon as a measles case was reported. During these 3 weeks, 4235 children and adolescents 5–19 years old and 570 adults were vaccinated. From 7 April through 20 May, large ORI activities targeting children and adults were conducted, with 9757 children and adolescents 5–19 years old and 27,625 adults vaccinated. In total, 0.8% of 8–59-month-old children, 51.3% of 5–19-year-old children and adolescents, and 30.2% of 20–49 year olds were vaccinated during these non-selective ORI activities in KL County (shown visually in Fig. 1). The last case of the outbreak occurred in mid-June.

4. Discussion

KL County is known to have high MCV coverage among children 2–19 years of age through routine immunization and SIAs among
these age cohorts. We have described an outbreak of measles that occurred primarily among adults that was sustained by adult-to-adult transmission. Transmission did not remain confined to adults, as measles virus was eventually transmitted from adults to infants too young to receive MCV, followed by transmission to unvaccinated young children born after the historic SIAs. Measles virus transmission occurred mainly in community and family settings during the early stage of the outbreak – immediately after importation to the county. Healthcare-facility-acquired infections appeared to accelerate transmission, enlarging the scale of the outbreak. Outbreak response immunization that targeted both children and adults was necessary, and apparently was effective, at decreasing the magnitude and duration of the outbreak.

Areas approaching measles elimination have a marked decreased overall incidence of measles. It is not surprising, then, that adults form an increased proportion of susceptibles and have a relatively higher burden of infection compared with MCV-targeted age groups [15]. This is becoming the emerging pattern of outbreaks in China in our context of the past 50-years’ measles vaccination policy and subsequent decrease in measles incidence rates. A significant proportion of the Chinese birth cohorts of the 1970s, 1980s, and early 1990s (current 20–50 year olds) apparently remained susceptible to measles, and now comprise a substantial immunity gap in the Chinese population.

Our assessment of the emerging pattern is supported by three points. First, these age cohorts were not well protected by MCV routine immunization when they were infants and toddlers. Before 1986, a less effective liquid MV [16] was used, and only one dose was administered to infants aged >8 months. Although the 2-dose schedule using lyophilized MV was introduced in 1986 [3], routine immunization coverage was not very high. For example, the national target goal for immunization was 85% at township level in 1995 [17], and the estimated average MCV1 coverage during 2000–2009 was 86.3% [3]. Second, the markedly decreased measles incidence in China has reduced exposure to wild measles virus of unvaccinated individuals in these birth cohorts, leaving many without immunity that follows infection. Following widespread use of MV starting in 1965, the

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**Table 1**

<table>
<thead>
<tr>
<th>Age group</th>
<th>Total case no.</th>
<th>Incidence (per 100,000)</th>
<th>No. of cases by MCV history</th>
<th>% of vaccinated</th>
<th>Description of eligibility for MCV doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–4 years</td>
<td>55</td>
<td>614.3</td>
<td>31 9 5 10</td>
<td>–</td>
<td>Not eligible for MCV</td>
</tr>
<tr>
<td>0–7 months</td>
<td>22</td>
<td>2318.2</td>
<td>22 0 0 0</td>
<td>–</td>
<td>1–2 routine dose MCV***</td>
</tr>
<tr>
<td>8–23 months</td>
<td>24</td>
<td>938.2</td>
<td>13 6 1 4</td>
<td>29.2</td>
<td>2 routine-dose, the 2012 SIA dose</td>
</tr>
<tr>
<td>2–4 years</td>
<td>9</td>
<td>165.2</td>
<td>13 6 1 4</td>
<td>77.8</td>
<td>2 routine-dose, the 2009 SIA dose**</td>
</tr>
<tr>
<td>5–9 years</td>
<td>4</td>
<td>28.5</td>
<td>13 6 1 4</td>
<td>6.7</td>
<td>2 routine-dose, the 2009 SIA dose</td>
</tr>
<tr>
<td>10–14 years</td>
<td>0</td>
<td>0.0</td>
<td>0 0 0 0</td>
<td>–</td>
<td>2 routine-dose, the 2009 SIA dose</td>
</tr>
<tr>
<td>15–19 years</td>
<td>2</td>
<td>23.6</td>
<td>0 1 1 0</td>
<td>100.0</td>
<td>2 routine-dose, the 2009 SIA dose</td>
</tr>
<tr>
<td>20–24 years</td>
<td>11</td>
<td>100.2</td>
<td>6 0 0 0</td>
<td>0.0</td>
<td>2 routine-dose</td>
</tr>
<tr>
<td>25–29 years</td>
<td>20</td>
<td>137.6</td>
<td>7 1 0 0</td>
<td>12.0</td>
<td>2 routine-dose</td>
</tr>
<tr>
<td>30–34 years</td>
<td>57</td>
<td>437.5</td>
<td>27 1 2 0</td>
<td>3.2</td>
<td>1 routine-dose, liquid vaccine**</td>
</tr>
<tr>
<td>35–39 years</td>
<td>62</td>
<td>388.2</td>
<td>36 2 0 0</td>
<td>5.0</td>
<td>Born before EPI started</td>
</tr>
<tr>
<td>40–44 years</td>
<td>44</td>
<td>269.5</td>
<td>25 2 0 0</td>
<td>7.4</td>
<td>Born before EPI started</td>
</tr>
<tr>
<td>45–49 years</td>
<td>19</td>
<td>120.1</td>
<td>6 0 0 0</td>
<td>17.0</td>
<td>Born before EPI started</td>
</tr>
<tr>
<td>≥50 years</td>
<td>7</td>
<td>16.2</td>
<td>7 0 0 0</td>
<td>0.0</td>
<td>Born before EPI started</td>
</tr>
<tr>
<td>Total</td>
<td>280</td>
<td>167.5</td>
<td>145 16 8 111</td>
<td>8.6</td>
<td></td>
</tr>
</tbody>
</table>

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*8–17-month-old children are eligible for 1 dose MCV, and 18–23-month-old children are eligible for 2 doses.

**5–6 year-old children are eligible for both 2010 and 2012 SIA, 7–9-year-old children are eligible for 2010 SIA.

**China used lyophilized MV since 1986, and before that liquid MV was used.

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Fig. 2. Timeline demonstrating chain of measles transmission in the 83 cases, by date of rash onset and transmission setting, KL County, Inner Mongolia Autonomous Region, China, 2013–2014 (red represents adult of ≥20 years old, blue represents infants of <8 months old, green represents children aged 8 month through 19 years).
measles incidence per 100,000 total population started to decrease, from over 1000 to approximately 500 in the early 1970s down to 250 in 1978 when EPI was established [3]. The average incidence further decreased to 52.9 during the 1980s and to 7.6 during the 1990s [3,18]. Third, by using combined province-wide catch-up SIAs and a nationwide follow-up SIA strategy, each province had covered their 1995–2009 birth cohorts with SIA-based immunization by 2010. Some provincial SIA targets were as early as the 1991 birth cohorts. However, susceptible individuals born before 1995, who are now over 20-year-old adults, were not reached by SIAs; nor were child born after the 2010 national SIA.

Recent provincial serological survey-based evidence has shown protection levels among adults to be lower than among children. Surveys conducted in Tianjin (91.2% seropositive in the 1972–1981 birth cohorts) [19], Fujian province (88.3% positive among 19–24 years olds) [20], and Jiangsu province (89.3% positive among migrants over 20 years of age) [21] showed that seropositive levels among adults were the lowest among all age-groups – with the exception of infants too young to vaccinate and some preschool age groups. The changing measles epidemiology in China shows that following the nadir in 2012, measles has increased in incidence among both adults and very young children – in both absolute and relative terms [5]. Now, adult measles outbreaks are reported frequently [22,23].

Our report adds to the literature that measles virus transmission among adults has contributed to the recent resurgence of measles in China. Our study raises the distinct possibility that adult susceptibility may have to be reduced in order to eliminate measles. A 2013 national and international consultation on measles elimination in China concluded that it is not clear whether adult susceptibility jeopardizes elimination of measles in China [24]. The recent and ongoing outbreaks among adults appear to be providing clarity and evidence for action.

The complicated and variable measles vaccination policies since the 1960s, coupled with the wide age range of adults that appear to leave significant susceptibility to measles, makes campaigns targeting adults difficult and inefficient: most adults are immune but cannot prove their vaccination status through records. Thus, a realistic and possibly important vaccination strategy to target adults is outbreak response immunization (ORI). The conduct of ORI is generally recommended in most outbreak settings in middle- and low-income countries [25]. During the early stages of the outbreak in KL County, ORI activities were few, mainly targeted children, and were non-selective. They apparently had little impact as virus transmission continued, adult-to-adult. Only after the necessity of targeting adults through ORI was recognized and implemented in April did the outbreak begin to decelerate. Although it is difficult to determine the contribution of ORI targeting adults to stopping the outbreak, the epidemic curve appears to show an impact of this ORI, especially since the usual seasonal peak of measles in China is April to May [5,6,8].

This outbreak also demonstrated that a rapid response, even with relatively low coverage, can avert more cases than higher coverage with a delayed response [26]. A question raised by the response results is whether children should be targeted non-selectively by SIAs [27]. A strategy of only vaccinating children who cannot show documentation of two MCV doses may be more efficient and easier to explain to parents of fully vaccinated children. Some unvaccinated children were almost certainly vaccinated in the non-selective SIAs, but only when the immunity gap among adults was addressed did the outbreak stop.

As the epidemiology of measles continues to evolve, epidemiologists in China will have to monitor measles outbreaks carefully to determine whether gaps in immunity among adults threaten measles elimination. We recommend that public health officials stay alert for adult-to-adult transmission of measles in outbreaks, and that they consider vaccinating adults as part of outbreak response immunization.

**Competing interests**

The authors declare that they have no competing interests.

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**Authors’ contribution**

Dr. Chao Ma, Huaqing Wang, Shaohong Yan and Qiru Su led the field investigation and wrote of this manuscript. Dr. Zhijie An and Shaopei Tang participated the field investigation. Dr. Yulong He and Guangfei Fan coordinated the case interview. Dr. Lance Rodewald and Lixin Hao helped drafting the manuscript.

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**References**


