Measles Imported to the United States by Children Adopted From China

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abstract

In July 2013, the National Immunization Program of China was notified by the US Centers for Disease Control and Prevention that measles was detected in 3 newly adopted, special needs children with cerebral palsy (CP) from China. We report an investigation of measles transmission in China that led to infection of these children. Interviews were conducted with welfare institute staff and panel physicians; health records of the potentially exposed population were reviewed; and immunization coverage was assessed among institute residents. Five residents with CP, all unvaccinated against measles, among who were the 3 adoptees, were linked epidemiologically into 3 generations of measles transmission antecedent to the US outbreak. In a random sample of residents, first dose of measles containing vaccine (MCV1) and MCV2 coverage was 16 of 17 (94%) and 7 of 11 (64%) among children with CP, and 100% (32 of 32) and 96% (21 of 22) among children without CP. Vaccinators reported reluctance to vaccinate children with CP because the China pharmacopeia lists encephalopathy as a contraindication to vaccination. Panel physicians reported to investigators no necessity of vaccination for adoptees to the United States if US parents sign an affidavit exempting the child from vaccination. We recommend that the China pharmacopeia vaccine contraindications be reviewed and updated, the United States should reconsider allowing vaccination exemptions for internationally adopted children unless there are true medical contraindications to vaccination, and US pediatricians should counsel adopting parents to ensure that their child is up-to-date on recommended vaccinations before coming to the United States.

Measles is a highly contagious disease that causes outbreaks among susceptible individuals and can spread rapidly in confined settings such as schools and residential facilities. China has a goal to eliminate measles and uses a 2-dose measles vaccination policy, with the first dose at 8 months of age by using measles-rubella vaccine, and a second dose at 18 to 24 months of age by using measles-mumps-rubella vaccine. Although substantial progress has been made toward elimination of measles in China, with overall high measles containing vaccine (MCV) measles coverage, indigenous measles transmission has yet to be interrupted.1 When measles virus circulates in any country, there is the potential to spread the infection to other countries, including countries that have already eliminated indigenous measles transmission, such as the United States.2 In July 2013, the National Immunization Program of the Chinese Center for Disease Control and Prevention (China CDC) was notified by the US Centers for Disease Control and Prevention (US CDC) that measles was detected in 3 newly adopted, special needs children with cerebral palsy (CP) from Henan province in China. The 3 children had no documentation of measles vaccination. In combination

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with information from US CDC, we confirmed that 2 of 3 cases were from Z welfare institute, and another one was from P welfare institute. All 3 cases previously lived in J rehabilitation hospital before recently returning to their own welfare institutes, where they prepared for the emigration process. We report the results of our investigation to determine the routes of transmission, identify gaps in immunity among children living in the welfare institute, understand the risk of measles exportation, and make recommendations to prevent exportation of measles among adopted children.

METHODS
Case Data Collection
Measles is nationally notifiable to a case-based, laboratory-supported surveillance system through the Internet in China. Local CDC staff is responsible for case investigation and collection and transportation of blood specimens. Measles cases are diagnosed by using the case definition in the Chinese National Measles Surveillance Protocol, which is similar to the World Health Organization (WHO) definition. A suspected case of measles is defined as any person with fever and rash and 1 or more of the following symptoms: cough, coryza, or conjunctivitis. Epidemiologic investigations are conducted, and serum specimen are collected and sent to a measles laboratory and tested for measles-specific immunoglobulin M (IgM) by using a commercial enzyme-linked immunosorbent assay. The measles surveillance system in Henan province is evaluated by the China CDC and was shown to improve between 2009 and 2011 and has exceeded the WHO measles surveillance quality indicators requirements since 2013 (China CDC, unpublished data).

Active Search of Cases
To determine routes of transmission, we conducted an active search for suspected measles cases in places where exposure of measles may have happened. We reviewed health records of residents in Z welfare institute and J rehabilitation center, and we also required staff in P welfare institute to actively search for additional measles cases.

Identification of Gaps in Immunity in Z Welfare Institute
To identify gaps in immunization, we conducted a coverage survey by reviewing a random sample of vaccination records of children who lived in Z welfare institute. Among 301 children aged 1 to 4 years, 49 children’s immunization records were reviewed to determine dates of receipt of MCV1, MCV2, hepatitis B vaccine (HBV) 1–3, oral polio vaccine (OPV) 1–3, and diphtheria-tetanus toxoids-pertussis vaccine (DPT) 1–3. Proportions vaccinated were calculated for children with and without CP, respectively.

Staff Interviews
We conducted interviews of the institute health care staff concerning vaccination policy and barriers to vaccination. Among the interviewees were staff serving as “panel physicians.” People of any age immigrating to America are requested to have a medical examination by panel physicians in agencies that are appointed by the United States. The agency responsible for conducting medical examinations for these children, Guangdong International Travel Healthcare Center, is located in Guangdong province and has panel physicians contracted by the US Department of State. We interviewed panel physicians who examined the adopted children who became cases in this outbreak. We also interviewed staff from the travel company that helped the adopting parents navigate the complicated adoption process.

RESULTS
Outbreak Settings
This measles outbreak occurred in ZY county, located in Z prefecture, Henan province. In China, provinces are divided into prefectures, and prefectures are divided into counties. According to the fifth National Population Census in 2000, ZY county had an average population density of 2997 persons per square kilometer. During the first half of 2013, 84 measles cases were reported from Z prefecture (incidence of 0.97/100 000), among which, 13 cases were reported from ZY county (incidence of 2.15/100 000; China CDC, unpublished data). The Z welfare institute is located in ZY county, has been operating since 2008, and covers 5.1 acres. It had over 750 children in July 2012, among whom 98% were children with special needs. Approximately 480 children were ≤7 years old, and among them, 33% (159) had been diagnosed with CP, and 17% (81) had been diagnosed with brain injury. The J rehabilitation hospital, located in another prefecture, is a privately owned hospital, providing rehabilitation service to children with CP, mainly by using traditional Chinese medicine treatments.

Outbreak Profile
Five measles cases, including the 3 adoptees above, were identified and laboratory-confirmed with positive measles IgM or positive reverse-transcriptase polymerase chain reaction. All 5 cases had CP, and none had been vaccinated against measles. Among the 5 cases, 2 were girls and 3 were boys, all between 2 and 3 years of age. Four (cases A, B, D, and E) were from Z welfare institute in Z prefecture, and 1 (case C) was from P welfare institute in P prefecture. Cases A, B, and C were adopted by American families; case D and E remained in the Z welfare institute. Because cases A, B, and C were diagnosed in America, illness information of the 3 cases was provided by the US CDC.

The index case (case D) developed measles before onset of the other 4 cases. She was noted to have rash...
onset on June 24, and had a fever at that time. Case E was noted to have rash and fever on July 5. When case A was seen by a panel physician on June 29, he was afebrile and his rash consisted of new and previously existing rashes. His rash was diagnosed as contact dermatitis. The next day he had fever, and the rash progressed from head to trunk. We estimate that the rash onset was June 29. Case B developed fever on June 29, and her rash onset was July 1. Case C developed fever on July 10 and rash on July 14 (Fig 1). The source of measles transmission to the index case was not able to be identified. Case D was away from the institute from June 9 to June 11, but no suspected exposure to measles was identified. There were occasional visitors to the welfare institute.

Possible Routes of Transmission

The index case (case D) lived with cases A, B, and E in a 22-child dormitory from June 21 to 23, corresponding to the contagious period of case D. Among the 22 children, 5 were not vaccinated against measles, although 4 (A, B, D, and E) were age-eligible for measles vaccination. The fifth unvaccinated child was younger than 8 months old and did not develop measles. Case C was exposed to cases A and B during the adoption and emigration process from June 24 to July 3, when they departed to the cities from which they would travel by air to the United States. These dates overlapped with the contagious period of cases A and B (Fig 1). No other cases were discovered through active search in Z and P welfare institutes, and J hospital. No airline passengers were reported to have acquired measles.

Estimation of Coverage

Coverage levels among children in the institute were 98% (48 of 49) for MCV1 and 85% (28 of 33) for MCV2. Among the 17 children with CP, coverage for MCV1 and MCV2 were 94% (16 of 17) and 64% (7 of 11), respectively. Among children without CP, coverage for MCV1 and MCV2 was 100% (32 of 32) and 96% (21 of 22). Coverage for HBV, OPV, and DPT were lower among children with CP. Coverage of MCV ranked highest among the 4 vaccines assessed. These coverage rates did not include outbreak response doses (Table 1).

Outbreak Response

On July 1, Z welfare institute isolated case D because of her illness; case E was isolated on July 10, when staff learned that measles was detected in cases A and B. Rooms occupied by children with measles were disinfected, and active searches were conducted for additional cases in the institute. Two hundred of the 402 children residing in the institute, who were screened as in good health and appropriate for vaccination by health workers in the institute, were vaccinated with measles vaccine regardless of vaccination history; no adverse events after immunization were reported.

The J rehabilitation hospital also strengthened surveillance for measles after notification of possible measles transmission from Z welfare institute. Ninety-two of 187 children with CP being treated in the hospital were determined to be in good health and were vaccinated with measles vaccine on July 25; no adverse events after immunization were reported.

Interview Findings

Vaccination services for the institutes were provided by local community health service clinics. Clinic health care providers reported feeling reluctant, or even that it was illegal to vaccinate children with CP, because China’s current pharmacopoeia lists “one suffering from encephalopathy, uncontrolled epilepsy or other progressive neurological diseases” as a vaccination contraindication. Encephalopathy is an umbrella term denoting a group of diseases that includes CP. However, considering the high risk of measles transmission and that these residents did not have parents to request vaccination for their children, in 2011 the Z rehabilitation began to vaccinate children with CP who were in good health to protect the
TABLE 1 Vaccination Coverage Rate in Children in Z Welfare Institute

<table>
<thead>
<tr>
<th></th>
<th>Children With CP</th>
<th></th>
<th>Children Without CP</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vaccinated/Checked</td>
<td>Coverage, %</td>
<td>Vaccinated/Checked</td>
<td>Coverage, %</td>
</tr>
<tr>
<td>HBV1</td>
<td>13/17</td>
<td>76.5</td>
<td>31/32</td>
<td>96.9</td>
</tr>
<tr>
<td>HBV2</td>
<td>10/17</td>
<td>58.8</td>
<td>29/32</td>
<td>90.6</td>
</tr>
<tr>
<td>HBV3</td>
<td>7/17</td>
<td>41.2</td>
<td>17/32</td>
<td>53.1</td>
</tr>
<tr>
<td>OPV1</td>
<td>12/17</td>
<td>76.5</td>
<td>31/32</td>
<td>96.9</td>
</tr>
<tr>
<td>OPV2</td>
<td>10/17</td>
<td>58.8</td>
<td>31/32</td>
<td>96.9</td>
</tr>
<tr>
<td>OPV3</td>
<td>8/17</td>
<td>47.1</td>
<td>28/32</td>
<td>87.5</td>
</tr>
<tr>
<td>DPT1</td>
<td>4/17</td>
<td>23.5</td>
<td>31/32</td>
<td>96.9</td>
</tr>
<tr>
<td>DPT2</td>
<td>2/17</td>
<td>11.8</td>
<td>30/32</td>
<td>93.8</td>
</tr>
<tr>
<td>DPT3</td>
<td>1/17</td>
<td>5.9</td>
<td>24/32</td>
<td>75.0</td>
</tr>
<tr>
<td>MCV1</td>
<td>16/17</td>
<td>94.1</td>
<td>32/32</td>
<td>100.0</td>
</tr>
<tr>
<td>MCV2</td>
<td>7/11</td>
<td>63.6</td>
<td>21/22</td>
<td>95.5</td>
</tr>
</tbody>
</table>

Coverage rates did not include outbreak response doses given. Checked, vaccination card had been checked.

children from measles. Cases D and E were not vaccinated because of health concerns (eczema and chronic diarrhea). The J rehabilitation hospital does not vaccinate children with CP because of the pharmacopoeia’s statement on encephalopathy. Cases A, B, and C had been living in J rehabilitation hospital for more than 1 year before returning to their residential welfare institutes, and these 3 children had not been vaccinated against measles.

The agency that is responsible for conducting medical examinations for immigrants including adoptees has a policy to screen for measles and other notifiable infectious diseases. However, the about-to-be adopted children did not have easily diagnosed cases of measles because some features were not present (no fever in 1 case and no rash in another case). Thus, measles had not been detected before departure. Measles vaccination history is reportedly of not much concern for adoptees because of a US policy that allowed exemption of vaccination for internationally adopted children aged ≤10 years if their adopting parent(s) signs an affidavit indicating that the child will receive vaccination within 30 days of entry into the United States.6

DISCUSSION

The 5 measles cases, all of whom had CP and none of whom had been vaccinated against measles, were epidemiologically linked as a single, 3-generation, outbreak, which was, in turn, linked to a US outbreak, which involved the adoptive mother of case B.3 Measles cases reported in ZY county indicated that measles was circulating in the community where Z welfare institute was located. The undervaccination that we identified made circulation of measles in the institute possible, and the confined spaces in which many children lived together increased the ease of transmission.

A difference in vaccination coverage between children with and without CP reveals an important problem with false contraindications to measles vaccination that might be a more generalized problem in China. “One suffering from encephalopathy, uncontrolled epilepsy or other progressive neurological diseases” is listed in the China pharmacopoeia as a contraindication for MCV (Supplemental Table 2) and some other attenuated live vaccines. In China, the pharmacopoeia is the authoritative source of indications and contraindications to vaccination. Interviews of health care providers helped identify reasons that some children were not vaccinated. A consistent reason given was the contraindication list in the pharmacopoeia, and a fear that it might be illegal to vaccinate children with CP, because providers consider CP to be an encephalopathy. In addition, providers said that children with special needs such as CP might be vulnerable to other diseases that could be mistaken for vaccine side effects. Providers reported unwillingness to risk incorrect association with harmful side effects with vaccines. These concerns have been reported by others.6–8 The fear of side effects resulted in even lower coverage of vaccines other than MCV and OPV. China has a national goal to eliminate measles and remain polio free, which may be why coverage with MCV and OPV was the highest among recommended vaccines.

The interviews with panel physicians helped us understand additional risks for measles importation to the United States, including allowing parents to waive vaccination requirements for children younger than 10 years of age, and nonclassic measles symptoms during the emigration physical examination leading to a missed diagnosis of measles. Our experience adds to risks reported by others.5,9–11 We believe that the United States should reconsider the vaccination exemption policy for internationally adopted children that makes it easier to waive vaccination than to vaccinate. Pediatricians in the United States should be aware that newly adopted children can import measles. Pediatricians could counsel adopting parents to ensure that the child they are adopting is up-to-date on all immunizations before coming to the United States, and that parents should not waive the requirements for vaccination before adoption. Pediatricians in the United States should be reassured that vaccines made and used in China are manufactured with international-standard, current Good Manufacturing Practices. The WHO is confident in the safety, quality, and effectiveness of vaccines made and used in China because regulatory oversight of Chinese vaccines has passed WHO/international
CP is not rare in China. There were ~500,000 children with CP, aged younger than 15 years old according to a 6-province study conducted in 1997–1998.13 In China, children with CP and other special needs often reside in welfare institutes and rehabilitation hospitals. In recent years, China has reported several measles outbreaks that occurred in welfare institutes among children with CP.14–18 Differences in gaps in immunity between children with and without CP have also been identified by others,19 and reluctance to vaccinate children with CP has been described. Measles still circulates in China and other countries,20 and this poses a challenge for the elimination of measles.

Responding to imported measles outbreaks in areas where endemic transmission has been eliminated can be expensive.21 Although this outbreak resulted in only 1 additional case in the United States, public health officials had to track over 200 exposed individuals.3 The undervaccination of children with CP may imply that other special needs children could be in need of timely and complete vaccination to prevent them from acquiring vaccine-preventable diseases.

We think that the following recommendations should be considered: (1) contraindications for measles vaccination and other live attenuated vaccines in the China pharmacoeaia should be reviewed for supportive evidence, and if no supportive evidence is found, the contraindication list should be updated; (2) it is important to improve Chinese vaccination providers’ ability to differentiate true contraindication from disease symptoms that are not contraindications, perhaps through education and training; (3) detection of measles through fever/rash screening by the panel physicians should be strengthened through education and training and assurance of access to measles diagnostic laboratory services; (4) welfare institutes and adoption agency should improve their ability to detect contagious diseases such as measles; and (5) adoption parents should be encouraged to ensure their newly adopted children are fully vaccinated before emigration to the United States.

There are some research questions raised by this investigation: (1) What is the impact of missed opportunities to vaccinate due to use of false contraindications to vaccination in China? (2) How confident are providers about their determination of contraindications? (3) How much do noncausal adverse events after vaccination impact vaccination coverage? There are limitations to our investigation. Due to limited time and human resources, we were not able to count the number of contacts of cases and identify their vaccination status. The sample for coverage estimation that helped us identify immunity gaps was relatively small. Preoutbreak coverage may have been lower than 94% because cases were excluded from the sampling frame. A larger coverage survey, perhaps combined with a seroprevalence survey, could be considered for future investigations.

CONCLUSIONS

Five measles cases were epidemiologically linked as a single outbreak, which was, in turn, linked to a US outbreak. In Z welfare institute, MCV coverage was lower in children with CP than children without CP. Some contraindications listed in China’s pharmacepoeia may play a significant role in impeding vaccination. WHO guidelines do not list static neurologic conditions such as CP as a contraindication to vaccination. We recommend that the China pharmacepoeia contraindications to vaccination be reviewed for supportive evidence. We also recommend the United States to reconsider allowing vaccination exemptions for internationally adopted children, and US pediatricians should counsel adopting parents to ensure that the child they are adopting is up-to-date on all immunizations before coming to the United States. We recommend education for panel physicians on measles diagnostic practices.

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