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A varicella outbreak in a school with high one-dose vaccination coverage, Beijing, China☆

Li Lu[a], **Luodan Suo**[a], **Juan Li**[a], **Lijun Zhai**[b], **Qingxiu Zheng**[b], **Xinghuo Pang**[a], **Stephanie R. Bialek**[c], and **Chengbin Wang**[c,*]

[a]Beijing Center for Disease Control and Prevention, Beijing, PR China

[b]Dongcheng District Center for Disease Control and Prevention, Beijing, PR China

[c]Centers for Disease Control and Prevention, Atlanta, USA

Abstract

Background—Varicella vaccine is available in the private sector in China, with a single dose currently recommended for children aged ≥12 months. We investigated a varicella outbreak in a school in Beijing with high varicella vaccination coverage to describe the outbreak, examine risk factors for vaccine failure, and calculate vaccine effectiveness.

Methods—A varicella case was defined as an acute generalized maculopapular rash without other apparent cause in a student without prior varicella attending the elementary school during August 30–December 28, 2010. Varicella among vaccinated students (breakthrough varicella) was defined as varicella occurring >42 days after vaccination. Students' vaccination status was verified with immunization records and clinical presentations were collected from health care practitioners.

Results—Of the 951 students, 934 (98%) had no prior varicella history. Among these students, 916 had received 1 dose of varicella vaccine and 2 had received 2 doses (98% vaccination coverage) before the outbreak. A total of 87 cases occurred during the outbreak; most had breakthrough varicella (86/87, 99%) and mild disease (83/87, 95%). Age at vaccination (<15 months vs.≥15 months) and time since vaccination before outbreak (<5 years vs. ≥5 years) were not associated with development of breakthrough varicella. Single-dose varicella vaccination was 89% effective in preventing any varicella and 99% in preventing moderate/severe varicella.

Conclusion—Single-dose varicella vaccination is highly effective in reducing varicella incidence and mitigating disease severity, but not high enough to prevent outbreak. A two-dose program might help to prevent varicella outbreaks in Beijing.

Keywords

Varicella outbreak; Varicella vaccine effectiveness

☆The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention, U.S. Department of Health and Human Services.

*Corresponding author at: Centers for Disease Control and Prevention, 1600 Clifton Road NE, MS A-34, Atlanta, GA 30333, USA. Tel.: +1 404 639 7655; fax: +1 404 417 0795. cwang1@cdc.gov (C. Wang).

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1. Introduction

Varicella (chickenpox) is a highly contagious disease caused by infection with varicella zoster virus (VZV), and is characterized by a generalized pruritic vesicular rash. Although varicella is usually self-limiting and resolves within a week, severe complications, including death, can occur [1].

Varicella vaccines are now widely available globally for prevention and control of varicella. In China, varicella vaccine first was licensed for use as single dose in 1998. The vaccine has been shown to be highly effective in preventing varicella disease [2]. Currently, the vaccine is available for private purchase but is not included in national or provincial routine immunization programs. To control school-based outbreaks, single-dose vaccination has been provided free of charge by Beijing government since 2006 to unvaccinated students in Beijing schools. The vaccine is offered immediately after an outbreak is detected, a strategy which in some settings has been demonstrated to be effective [3,4].

In September 2010, the Beijing Center for Disease Control and Prevention (CDC) was notified of an outbreak in an elementary school. Because almost all students in the school had received varicella vaccine before the outbreak, most cases were among vaccinated students. Beijing CDC investigated this outbreak to (1) describe its epidemiology, (2) delineate transmission patterns, (3) examine varicella vaccine effectiveness (VE), and (4) assess whether age at vaccination or time since vaccination were related to vaccine failure. This article summarizes findings from this investigation and discusses the implications for varicella outbreak control and vaccination policy in Beijing, China.

2. Methods

2.1. Outbreak setting

The outbreak occurred in a public elementary school for Grades 1 and 2 (hereafter referred to as “School A”) in Beijing. During the outbreak, School A had 951 students. The 3-story school building includes 22 classrooms, 11 for each grade, with 7–8 classrooms on each floor. Mixing of students occurred in the classrooms, hallways, play areas, on school buses, and at after-school activities (e.g., drawing, dancing, and martial arts groups).

2.2. Case definition and data collection

A case of varicella was defined as an acute generalized maculopapular rash without other apparent cause that occurred during August 30–December 28, 2010 in a student attending School A [5]. Varicella among vaccinated students (breakthrough varicella) was defined as a varicella-like rash that developed >42 days after vaccination [5]. We used reports from the school nurse and the infectious disease surveillance system of Beijing CDC to identify cases. Parents of all students attending School A received and returned a questionnaire to provide information on history of varicella before the outbreak, and, for students with disease during the outbreak, disease severity, complications, and sources of exposure. Varicella cases were categorized as mild (<50 lesions) and moderate/severe (≥50 lesions). The vaccination status of each student before the outbreak was obtained from school records.

2.3. Outbreak control measures

Students with varicella were excluded from school until lesions crusted or faded. On September 13 and October 14, 2010, varicella vaccinations were provided free of charge to unvaccinated students without a history of varicella. After-school activities were suspended and the classrooms, indoor play area, and school buses were disinfected when the outbreak was detected.

2.4. Statistical analyses

Sociodemographic factors and vaccination status of cases vs. non-cases students were compared and tested with Pearson Chi-square test, Fisher exact test, or Student's *t*-test as appropriate. Vaccination coverage at the start of the outbreak was calculated as the proportion of vaccinated students among those without a history of varicella. VE for all varicella disease and for moderate/ severe disease was calculated using the equation: (1 − attack rate among vaccinated students/attack rate among unvaccinated students without a history of varicella) × 100%. Because few students were unvaccinated and only 1 unvaccinated student was infected, we used historical attack rates among unvaccinated children in a child care center in the United States [6] to calculate VE. We evaluated potential risk factors for breakthrough disease among single dose varicella vaccine recipients; specifically, age at vaccination and time since vaccination before outbreak were categorized as <15 months vs. ≥15 months and <5 years vs. ≥5 years, respectively, as used in prior reports [7,8]. All data were analyzed by using SAS V9.2 (SAS Institute, Cary, NC).

3. Results

3.1. Study population

Among the 951 students in School A, 17 who had a history of varicella before the outbreak were excluded for further analysis (Fig. 1). No staff or faculty developed varicella during the outbreak and all analyses were restricted to students. Among the 934 students without disease history, 16 were unvaccinated and 918 had received vaccine before the outbreak (2 of these had received 2 doses). During the outbreak, 11 of the unvaccinated students received vaccine and were excluded from further analysis; three of them developed rash at 1, 14, and 28 days after vaccination, respectively. Among the 923 students included in the study, the average age was 7.0 years (range: 5.9–8.6), 52.7% were male, and 50.6% were in Grade 1.Overall vaccination coverage at the start of the outbreak among students without a history of varicella was 98.3% (range by classroom, 93–100%). Vaccination coverage was marginally higher in Grade 2 than in Grade 1 (99.1% vs. 97.5%, $P = 0.05$). Among single-dose recipients ($n = 916$), the average age at vaccination was 22 months and the average time since vaccination before the outbreak was 5.1 years.

3.2. Outbreak

The outbreak lasted approximately 4 months, from August 30 through December 28, 2010. Among the 923 students included in the study, there were 87 cases with 86 among vaccinated students and 1 in an unvaccinated student (Fig. 1). The overall attack rate was 9.4%. Four peaks of cases occurred in this outbreak at intervals of approximately two weeks: October 11–15, October 24–29, November 7–15, and November 24–29 (Fig. 2). The

primary case was a previously vaccinated Grade 1 student who was exposed to a neighborhood playmate who had varicella. The student developed fever 1 week later on August 29 and rash with <50 lesions on August 30. He likely transmitted the disease to 3 classmates and another student, all on the first floor of the school building. The first peak of cases (n = 18) clustered on the first and second floors, and with just one case in a third floor classroom. Thereafter, disease spread throughout the school building, with the following 3 peaks of cases mainly clustered on the second and third floors, with sporadic cases occurring on the first floor. Among the 22 classrooms in School A, three Grade 1 and one Grade 2 classrooms had attack rates higher than 20% (range: 22–23.8%), with 9–10 cases per class. Among the other classrooms, 2 had no cases, 7 had only 1 case, 7 had 2–5 cases, and the other 2 had 7 and 8 cases, respectively. Two of the 4 unvaccinated students who were not infected were in a class without any cases during this outbreak.

3.3. Case characteristics

Most cases had mild disease (83, 95.4%) and were vaccinated (86, 98.9%); and 52 (59.8%) had fever. All the moderate/severe cases (n = 4) were single-dose vaccine recipients from different classes of two grades. No cases developed complications or were hospitalized due to varicella. School exposure was the source of infection for all cases, with the exception of the primary case and one case with hospital exposure. Most cases were among students in Grade 1 (55, 63.2%), and the average age was 6.8 years (range: 6–8.2 years) (Table 1). Cases and non-cases did not differ in vaccination status (P = 0.63), gender (P = 0.24), or age (P = 0.10). Compared with noncases, cases were more likely to be in Grade 1 (63.2% vs. 49.3%, P = 0.01) (Table 1).

3.4. Vaccine effectiveness and risk factors for breakthrough disease

Among the 916 students who had received a single dose of varicella vaccine before the outbreak, 86 developed breakthrough varicella, of whom 4 developed rash with ≥50 lesions; thus, the overall attack rate was 9.4% and the attack rate for moderate/severe disease was 0.4% among these single-dose recipients. The attack rate was 20% among the 5 unvaccinated students with the only case being mild. Using historical attack rates of any disease (88%) and moderate/severe disease (55%) among unvaccinated children in children care center [6],we calculated single-dose VE of 89.3% for preventing any varicella and 99.3% for preventing moderate/severe varicella. In single-dose recipients, age at vaccination (<15 months vs. ≥15 months) and time since vaccination (<5 years vs. ≥5 years) were not associated with breakthrough varicella in this outbreak (P = 0.78 and 0.44, respectively) (Table 1).

4. Discussion

In our investigation of a varicella outbreak that lasted for 4 months in a Beijing elementary school where one-dose varicella vaccine coverage before the outbreak was nearly 100%, disease was introduced by a vaccinated student and occurred almost exclusively among vaccinated students exposed at school. This study confirms that children vaccinated with a single-dose of varicella vaccine may both contract and transmit varicella, and high single-dose varicella vaccination coverage may not provide sufficiently high population immunity

to prevent outbreaks [10–13]. This study also demonstrates, as have others, that single-dose varicella vaccination is highly effective in preventing cases and mitigating the severity of breakthrough cases that occurs [9].

In the United States, the first county to implement a universal varicella vaccination program, a single-dose regimen led to dramatic declines in varicella incidence, near elimination of severe disease and reduced the number, size, and duration of outbreaks [10]. During the single-dose varicella vaccination era in the United States, attack rates in school settings with high and low varicella vaccination coverage differed dramatically, from 9% to 15% in schools with coverage levels higher than 95% to 55% in a school with vaccination coverage of just 45% [6,11–14]. In China, comparisons of areas with high varicella vaccination coverage to those with low coverage or no varicella vaccination also clearly demonstrate the impact of varicella vaccination on reducing attack rates during outbreaks. In the outbreak reported here, in which one-dose coverage was high, the attack rate was less than 10%, with no severe outcomes. Elsewhere in China, in kindergartens and elementary schools where vaccination coverage was very low, average attack rates of more than 50% have been reported during outbreaks [15–17]. Given the effectiveness of varicella vaccine in preventing varicella and severe outcomes, hundreds of cases, and perhaps some complications and hospitalizations, likely were prevented among students in School A due to single-dose varicella vaccination. High vaccination coverage also provides indirect protection to unvaccinated students; among the 4 students who were not vaccinated before or during the outbreak and who attended school throughout the outbreak, 2 sat in a classroom where no infections occurred, and they did not become infected. The experience from this outbreak provides further evidence that varicella vaccine is the most effective tool for preventing and controlling varicella infection and mitigating disease severity and severe complications.

However, single-dose varicella vaccine effectiveness, while high, does not provide high enough population immunity to interrupt endemic disease transmission and prevent outbreaks completely. For this reason, the United States changed from a routine 1-dose varicella vaccination program for children to a universal 2-dose program in 2006 [18], in that the 2-dose varicella vaccination was 70% more effectively in preventing breakthrough disease than single-dose vaccination [19]. One goal of this revised policy was to prevent varicella outbreaks that continued to occur despite high single-dose vaccination coverage [18] Since implementation of the universal 2-dose program in the United States, further reductions have been seen in both varicella disease burden [20,21], and the number of outbreaks [21]. More data are needed to assess the effectiveness of 2-dose varicella vaccination and its impact on the rate of breakthrough disease and reduction in number of outbreaks.

Post-exposure varicella vaccination can be effective in preventing illness or modifying varicella severity if administered within five days after exposure [18]. Thus timely vaccination when an outbreak is detected may help to reduce size and duration of varicella outbreak, which may be resulted from the combined protective effect from pre- and post-exposure vaccination since not all students were exposed at the start of an outbreak. However, with the increase in the number of schools with high single-dose varicella

vaccination coverage among their students and fewer students eligible to receive their first dose of vaccine during outbreak response efforts, Beijing may need to consider other options to further reduce varicella spread in school populations. Prior to implementation of the universal two-dose varicella vaccination program in the United States, a second dose of varicella vaccine was recommended for outbreak control in settings with high one-dose varicella vaccination coverage [22].

Policy makers from other countries are likely to consider the U.S. experience with one- and two-dose routine varicella vaccination programs in addition to disease burden, vaccine cost, and vaccine availability in deciding whether to implement one-dose or 2-dose varicella vaccination programs. In addition to public health and socioeconomic considerations, the World Health Organization emphasizes that varicella vaccination programs should only be implemented if high vaccination coverage (85–90%) can be maintained [23]. Sustained high coverage is essential to prevent an epidemiologic shift in disease incidence which may lead to more varicella among adolescents and adults, who are more prone to develop severe disease [24].

The current study has limitations. We relied on clinical diagnosis of cases and did not require laboratory confirmation. Although varicella is still a common disease in Beijing and clinical practitioners are very experienced in diagnosing varicella, misdiagnosis is possible because breakthrough varicella is often less severe. In addition, the mild clinical presentation of breakthrough varicella makes under-reporting likely in the absence of thorough case finding efforts, particularly in this setting in which most cases occurred in vaccinated students who had mild disease with few lesions [14]. The attack rates of unvaccinated children in U.S. school settings that we used to calculate VE may underestimate effectiveness since schools in Beijing may be more crowded and more favorable for facilitating varicella transmission. The lower household exposure due to the ‘One Child’ policy and the possibility of higher community exposure for children in China than in the U.S. may lead under- or over-estimates of varicella VE in the current study as a result of our use of a historical attack rate. Unfortunately, there are no comparable published attack rates from China available to us. The small number of unvaccinated students ($n = 5$) and unvaccinated case ($n = 1$) also make it impossible to get a reliable VE estimate using the attack rate in the unvaccinated students from this school, and we had to resort to the historical attack rate among unvaccinated in school setting [6].

In summary, we found that one-dose varicella vaccination in Beijing, while effective for preventing varicella, and extremely effective for preventing severe disease, is not sufficiently high enough to prevent outbreaks in settings where exposure is intense. The single-dose free vaccination strategy becomes less effective for outbreak control in highly vaccinated settings. More aggressive measures, such as 2-dose regimen, may be an option to prevent varicella outbreaks, but policy changes will need to be based on consideration of disease burden, social impact, program cost, affordability, vaccine supply, and sustainability.

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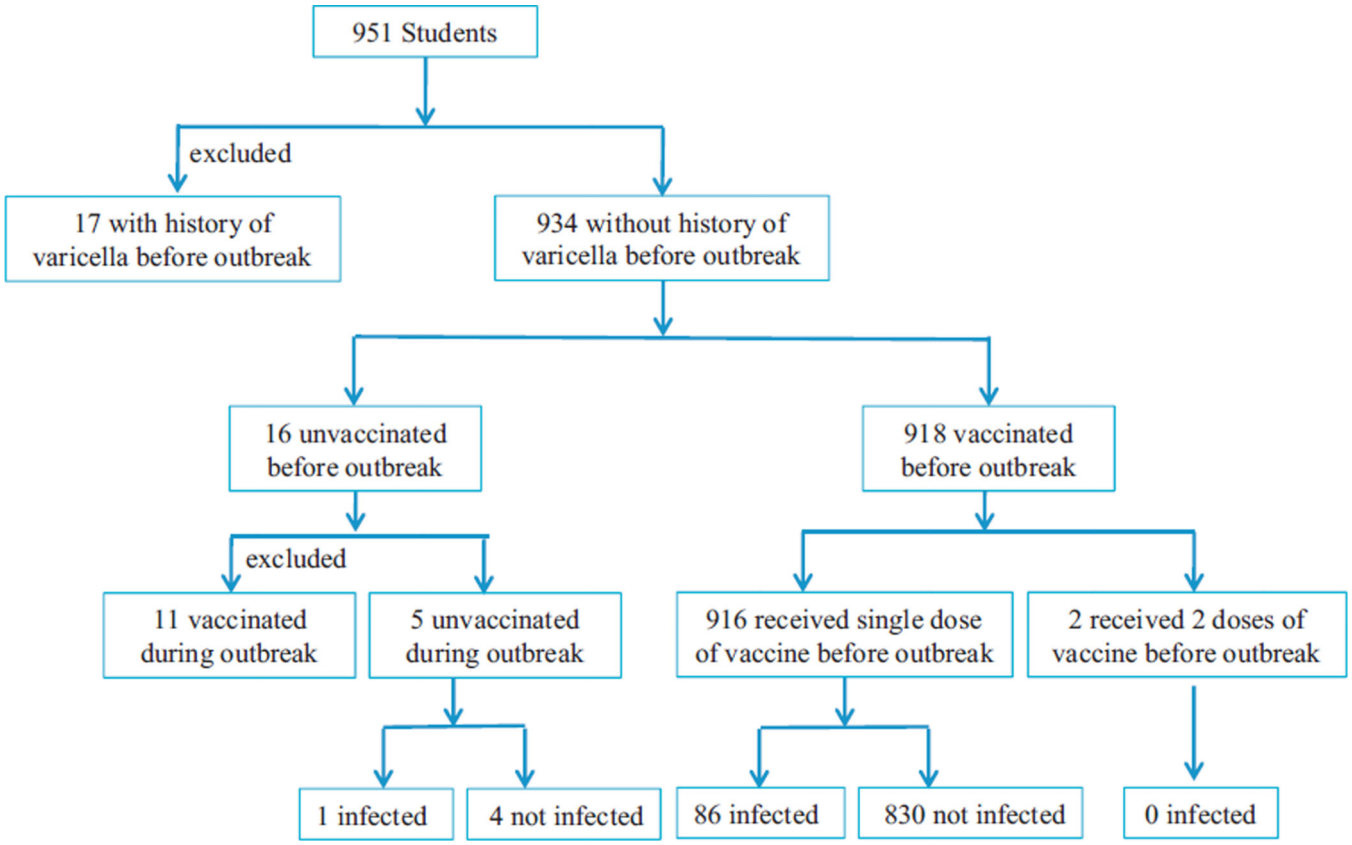

Fig. 1.
Vaccination and varicella case status, varicella outbreak in School A, Beijing, 2010.

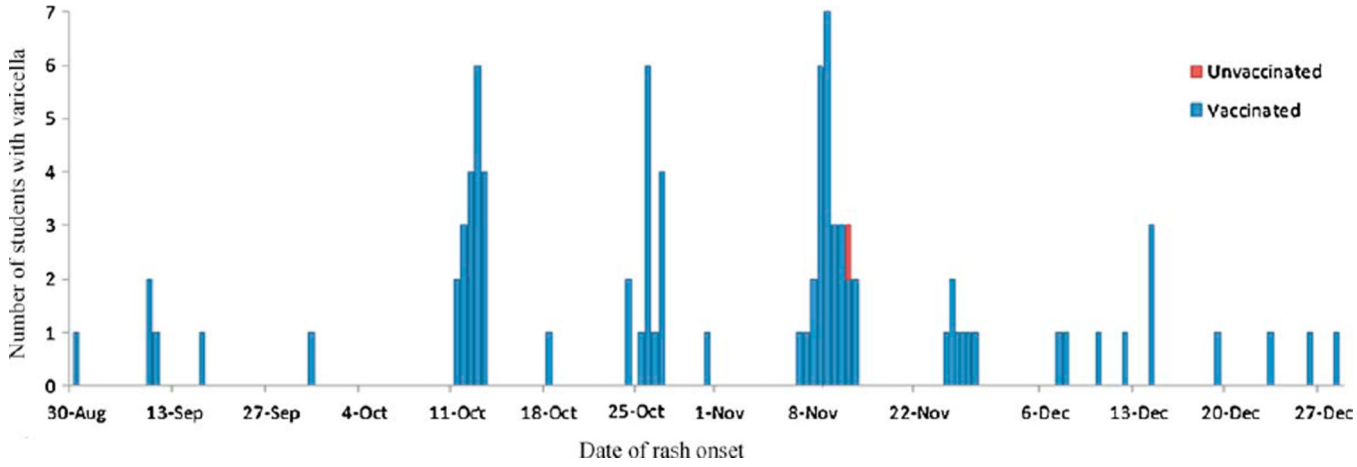

Fig. 2.

Varicella cases by date of rash onset and vaccination status (n = 87), School A, Beijing, August 30–December 28, 2010.

Table 1

Comparison of students with and without varicella during a varicella outbreak, School A, Beijing, 2010.

	Students with varicella (*n* = 87)	Students without varicella (*n* = 836)	*P* value
Gender			0.24
Male	51(10.5)	435(89.5)	
Female	36(8.2)	401(91.8)	
Age in years before outbreak			
Mean (SD)	6.8 (0.6)	7.0 (0.7)	0.10
Vaccination status before outbreak			0.63
Unvaccinated	1(20.0)	4(80.0)	
1-Dose	86(9.4)	830(90.6)	
2-Dose	0 (0.0)	2(100.0)	
Grade			0.01
1	55(11.8)	412(88.2)	
2	32(7.0)	424(93.0)	
Age at vaccination[a]			0.78
<15 months	30(9.0)	302(91.0)	
≥15 months	56(9.6)	528(90.4)	
Time since vaccination before outbreak[a]			0.44
<5 years	30(8.5)	325(91.5)	
≥5 years	56(10.0)	505(90.0)	

[a] Single-dose varicella vaccine recipients only.