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Identification and Control of a Poliomyelitis Outbreak in Xinjiang, China

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ABSTRACT

BACKGROUND

The last case of infection with wild-type poliovirus indigenous to China was reported in 1994, and China was certified as a poliomyelitis-free region in 2000. In 2011, an outbreak of infection with imported wild-type poliovirus occurred in the province of Xinjiang.

METHODS

We conducted an investigation to guide the response to the outbreak, performed sequence analysis of the poliovirus type 1 capsid protein VP1 to determine the source, and carried out serologic and coverage surveys to assess the risk of viral propagation. Surveillance for acute flaccid paralysis was intensified to enhance case ascertainment.

RESULTS

Between July 3 and October 9, 2011, investigators identified 21 cases of infection with wild-type poliovirus and 23 clinically compatible cases in southern Xinjiang. Wild-type poliovirus type 1 was isolated from 14 of 673 contacts of patients with acute flaccid paralysis (2.1%) and from 13 of 491 healthy persons who were not in contact with affected persons (2.6%). Sequence analysis implicated an imported wild-type poliovirus that originated in Pakistan as the cause of the outbreak. A public health emergency was declared in Xinjiang after the outbreak was confirmed. Surveillance for acute flaccid paralysis was enhanced, with daily reporting from all public and private hospitals. Five rounds of vaccination with live, attenuated oral poliovirus vaccine (OPV) were conducted among children and adults, and 43 million doses of OPV were administered. Trivalent OPV was used in three rounds, and monovalent OPV type 1 was used in two rounds. The outbreak was stopped 1.5 months after laboratory confirmation of the index case.

CONCLUSIONS

The 2011 outbreak in China showed that poliomyelitis-free countries remain at risk for outbreaks while the poliovirus circulates anywhere in the world. Global eradication of poliomyelitis will benefit all countries, even those that are currently free of poliomyelitis.

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The World Health Assembly established the Global Polio Eradication Initiative in 1988.[1,2] The World Health Organization (WHO) Western Pacific region, including China, was certified as a poliomyelitis-free region in 2000.[3] However, the transmission of wild-type poliovirus has not yet been stopped in Afghanistan, Pakistan, or Nigeria. Globally, some countries have had outbreaks of imported wild-type poliovirus, and in others the circulation of outbreak strains has been reestablished.[4]

China has the world's largest population (1.347 billion in 2011).[5] By 1963, live, attenuated oral poliovirus vaccine (OPV) was being administered in annual campaigns conducted during the winter. OPV has been included in the Expanded Program on Immunization since 1978, and the incidence of cases of poliomyelitis has declined dramatically. A surveillance system for acute flaccid paralysis was established in 1991. National immunization days (conducted in two rounds, 1 month apart) or subnational (regional) immunization days have been conducted throughout China since 1993. The last indigenous wild-type poliovirus was isolated in September 1994.[6,7]

Poliomyelitis has appeared in China several times since the indigenous transmission of wild-type poliovirus was interrupted. Cases of infection with wild-type poliovirus imported from Myanmar were identified in 1995 and 1996, and wild-type poliovirus originating in India was detected in Qinghai Province in 1999.[8] Type 1 circulating vaccine-derived polioviruses were isolated from two patients with acute flaccid paralysis and four close contacts of patients with acute flaccid paralysis in Guizhou Province in 2004.[6]

We describe an outbreak of wild-type poliovirus that occurred in the Xinjiang Uygur Autonomous Region (Xinjiang) in 2011, which had been certified as poliomyelitis-free 10 years earlier. Our report illustrates the processes of detection, evaluation, and response, as well as the challenges of managing an outbreak of imported wild-type poliovirus.

Methods

Definitions

Cases of poliomyelitis were defined as any child younger than 15 years of age with acute flaccid paralysis, or any person of any age with paralytic illness if poliomyelitis is suspected. Any person who had acute flaccid paralysis and provided a stool sample in which wild-type poliovirus was detected was considered to have a laboratory-confirmed case. Clinically compatible cases of poliomyelitis were defined as cases in which the disease was diagnosed clinically but not confirmed because a stool specimen was missing or was inadequate, or cases in which the only viruses isolated in stool specimens were related to those used in vaccines (<1% nucleotide substitutions in the region of *VP1*, the gene encoding poliovirus type 1 capsid protein VP1). Close contacts were defined as persons who lived with or shared a toilet with an infected person during the infectious period of the disease, medical staff members who cared for patients, and others who came into contact with infectious material from patients. All cases of acute flaccid paralysis recorded in hospital surveillance reports were reported daily to the relevant county branch of the Chinese Center for Disease Control and Prevention (hereafter referred to as county CDC), and the results of surveillance were reported regardless of whether a new case of acute flaccid paralysis was identified. The study was initiated by the Chinese Ministry of Health, and the requirement for informed consent was waived.

Surveillance System

Surveillance for poliomyelitis is conducted by means of surveillance for cases of acute flaccid paralysis. Cases are reported by hospitals to their county CDC within 2 days after they have been identified. County-level CDC staff are responsible for case investigation, collection and transportation of stool specimens, and follow-up. Two specimens, each weighing 5 g or more, are obtained from patients with acute flaccid paralysis within 14 days after the onset of paralysis, with the second specimen collected at least 24 hours after the first specimen. If it is determined that the acute flaccid paralysis is not the result of poliomyelitis, it is categorized as nonpoliomyelitis acute flaccid paralysis.

In accordance with the requirements of the "Technical Guideline for Emergency Response to Epidemics Caused by Imported Wild Poliovirus or Events Related to Vaccine-Derived Poliovirus" (Part A in the Supplementary Appendix, available with the full text of this article at NEJM.org), stool specimens were collected from convenience samples obtained from five close contacts of each affected patient and from 30 to 50 healthy persons younger than 5 years of age who resided in

the neighborhoods where the patients with wild-type poliovirus infection resided. In addition, 25 environmental samples were collected before the first round of supplementary immunization (3 sewage samples obtained from 3 waste-water treatment plants in Kashgar, and 12 sewage samples obtained from 6 waste-water treatment plants and 10 river-water samples obtained upstream and downstream from 3 local rivers in Hotan).

After immunization, physicians and vaccination providers were required to report adverse events (including fever, diarrhea, allergic reaction, paralysis, or death) to the county CDC. County CDCs verified the events and reported the data to the online surveillance system. Serious adverse events were defined as events involving hospitalization, death, life-threatening illness, or permanent disability on the basis of WHO guidelines. Mild events included fever and localized redness and swelling, sometimes accompanied by general discomfort, fatigue, poor appetite, and tiredness.

ASSESSMENT OF STOOL SPECIMENS

Isolation and primary identification of the poliovirus were performed by means of a microneutralization assay with the use of poliovirus type-specific rabbit polyclonal antiserum (provided by the Dutch National Institute for Public Health and the Environment) in accordance with standard procedures at the Xinjiang CDC.[9] Sequencing analysis of the poliovirus type 1 capsid protein VP1 was performed in accordance with the standard methods used by the Chinese CDC. Phylogenetic dendrograms were constructed from entire *VP1* coding-region sequences with the use of the maximum-likelihood method and MEGA software, version 5.0.[10]

RAPID ASSESSMENT OF VACCINATION COVERAGE

After confirmation of the poliomyelitis outbreak, a rapid assessment of OPV coverage was conducted for children younger than 5 years of age in counties in which poliovirus had been detected and in neighboring counties of Hotan. Three townships and three villages per township were assessed, including the township in which a patient infected with wild-type poliovirus type 1 had been identified and two townships selected at random from the same county. Convenience samples were collected from at least 50 children selected from these townships. Their OPV immunization status was determined by checking their hospital immunization records or hand-held immunization cards.

RESULTS

DETECTION OF THE OUTBREAK

The index patient was a 16-month-old girl born on March 17, 2010, who lived in the county of Hotan. The patient and her family had no history of travel outside Xinjiang. The onset of paralysis had occurred on July 3, 2011. The patient was hospitalized 2 days later, and the case was reported at that time. Epidemiologic investigations were conducted, and two adequate stool specimens were obtained from the patient. Specimens were obtained from three additional patients with acute flaccid paralysis in Hotan and were submitted to the CDC in Xinjiang between July 25 and August 4. Poliovirus type 1 was isolated from the stool samples from all four patients by the CDC in Xinjiang, and the four isolates were sent to the Chinese CDC.

On August 25, the CDC confirmed the presence of the wild-type poliovirus strain in all four patients. Genetic sequencing showed that the four strains diverged from the *VP1* region of the type 1 Sabin strain by 20.9 to 21.3% (i.e., 20.9 to 21.3% of the nucleotide sequences were different from those in the Sabin strain) and were 99.2 to 99.6% homologous with one another. The Chinese government informed the WHO about the outbreak on August 26, and the WHO confirmed that it had been caused by a wild-type poliovirus imported from Pakistan on the basis of evidence showing a high degree of homologous nucleotide sequencing in the viruses isolated in Hotan and in Pakistan (Fig. 1).

OUTBREAK PROFILE

Between July 3 and October 9, 2011, investigators confirmed 21 cases of infection with wild-type poliovirus in southern Xinjiang: 13 in Hotan, 6 in Kashgar, 1 in Bazhou, and 1 in Akesu (Fig. 2 and 3). They also confirmed 23 clinically compatible cases of poliomyelitis, with 19 in Hotan, 3 in Kashgar, and 1 in Akesu.

The incidence rates of wild-type poliovirus infection and clinically compatible poliomyelitis were highest among children younger than 1 year of age (3.46 and 1.15 cases per 100,000 population, respectively). The incidences were also higher among males than among females (Table 1).

Of the 21 cases of infection with wild-type

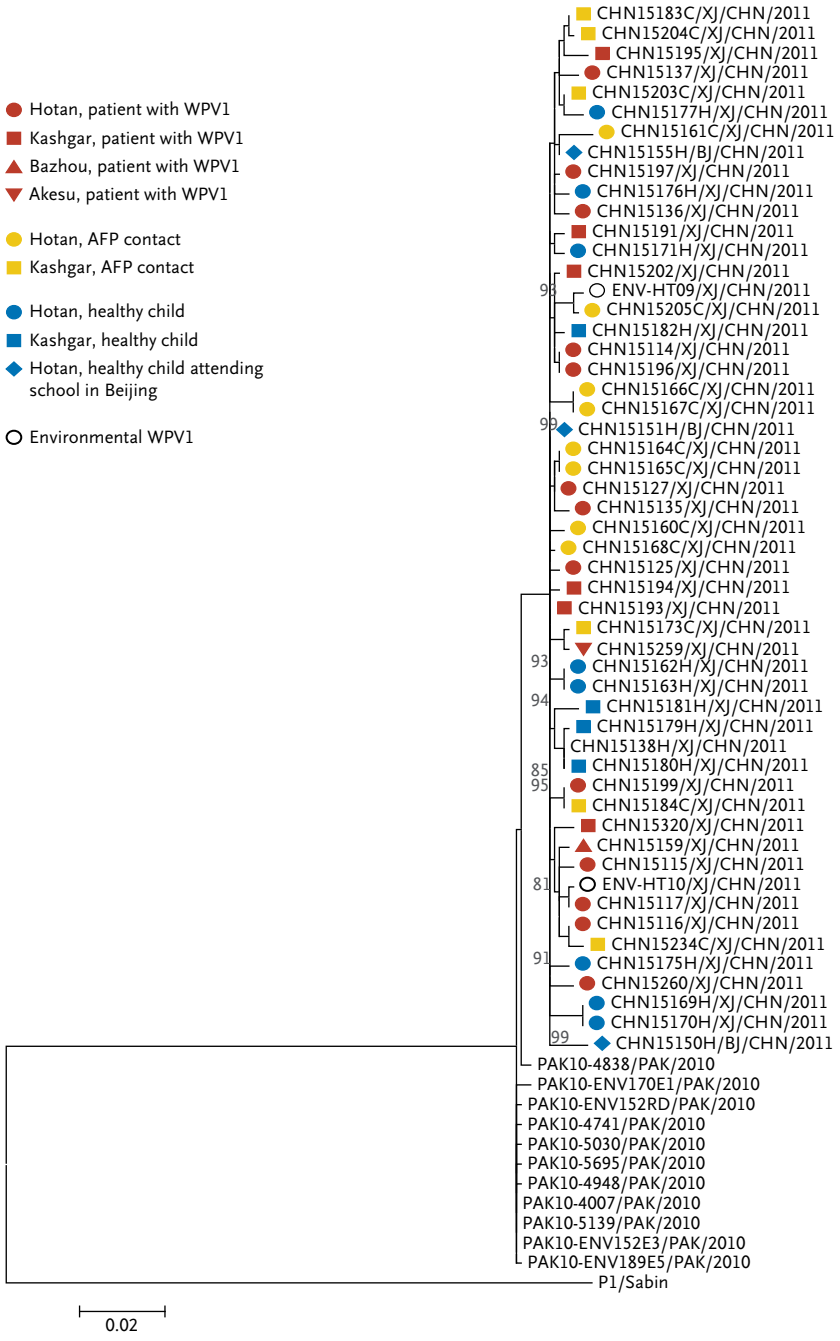

Figure 1. Phylogenetic Tree Constructed with the Use of Maximum Likelihood on the Basis of *VP1* Sequences of Wild-Type Poliovirus Type 1 Detected in Xinjiang, China.

The wild-type poliovirus detected in Xinjiang was genetically linked to the virus identified in Pakistan in 2010. This was the sole evidence of importation.

poliovirus, 10 occurred in persons younger than 15 years of age and 11 in persons between 15 and 53 years of age. Of the 10 affected children, 3 had not received OPV, 2 had received one or two doses, and 5 had received three or more doses, indicating primary vaccination failure.[11,12]

Wild-type poliovirus was isolated from 14 of 673 contacts of persons with acute flaccid pa-

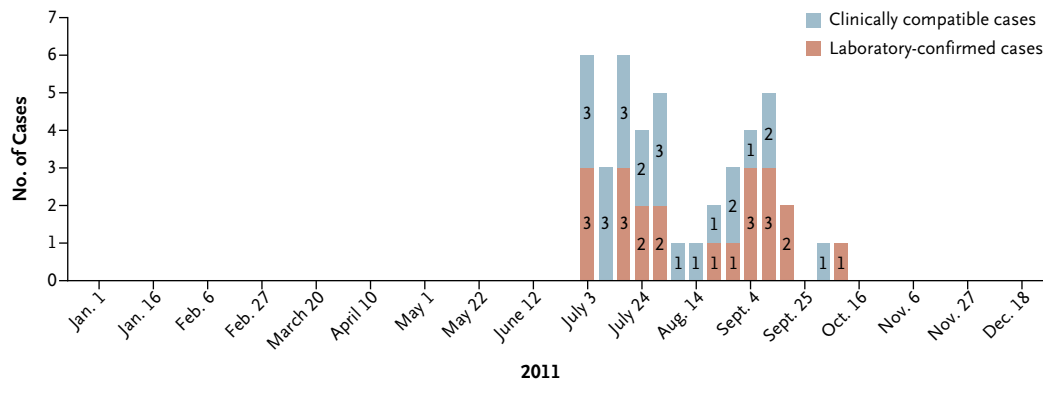

Figure 2. Distribution of Laboratory-Confirmed Cases of Wild-Type Poliovirus Infection and Clinically Compatible Cases According to Week of Paralysis Onset in Xinjiang.

There were 21 laboratory-confirmed cases of wild-type poliovirus infection and 23 clinically compatible cases, all of which were identified between July 3 and October 9, 2011. No additional cases were identified after October 2011 or during the first 6 months of 2012.

ralysis (2.1%) and from 13 of 491 healthy persons (2.6%) in Hotan, Kashgar, Bazhou, and Akesu. Three wild-type poliovirus strains were isolated in Beijing among healthy students from Hotan. One sewage sample from Hotan sewage and one sample of river water from Hotan were positive for wild-type poliovirus. A total of 53 wild-type poliovirus isolates were obtained (Fig. 1).

PUBLIC HEALTH EMERGENCY RESPONSE

The China Ministry of Health and the Xinjiang provincial government immediately launched a level 2 public health emergency response, the highest level of response to a public health emergency that the ministry is authorized to initiate. The leadership for the outbreak response was designated by August 26, 2011, and the lead group from the ministry worked on all aspects of coordination, technical matters, and media communications.

The Xinjiang government convened an emergency-response meeting for a poliomyelitis epidemic on August 30. More than 1000 health workers were trained in response immunization and surveillance by August 31. By September 2, more than 5 million doses of trivalent OPV had been shipped by air from Beijing to Xinjiang. By September 8, the first vaccination campaign was launched in Xinjiang.

RISK ASSESSMENT

A total of 2340 children younger than 5 years of age in five Hotan counties were selected at random for the purpose of surveying OPV coverage after the outbreak was confirmed. The third dose of OPV was administered by means of routine immunization in 78.8 to 90.9% (mean, 86.0%) of the population in the five counties.

Before the first round of supplementary immunization, 2611 serum samples had been obtained from healthy persons of any age in southern Xinjiang to test for neutralizing antibody against poliovirus. The rate of a positive test for antibody against type 1 poliovirus (titer ≥1:4) was 90.4%, and the antibody geometric mean titer was 1:39. The rates of positive antibody tests among children younger than 5 years of age were 80.0 to 92.0%, and the antibody geometric mean titers were 1:40 to 1:106, which were considered to be relatively low (Part B in the Supplementary Appendix).

INTENSIFICATION OF SURVEILLANCE

After the outbreak was confirmed, the government of Xinjiang implemented a daily reporting system of surveillance for cases of acute flaccid paralysis. In southern Xinjiang and in Urumqi, public and private hospitals at the township level and above were included in the surveillance for acute flaccid paralysis, and monitoring was expanded to include persons of all ages in the entire population. In other Xinjiang prefectures, public and private hospitals at the county level and above were included in surveillance for acute flaccid paralysis. A search for cases of acute flaccid paralysis that had occurred since January 2010 was per-

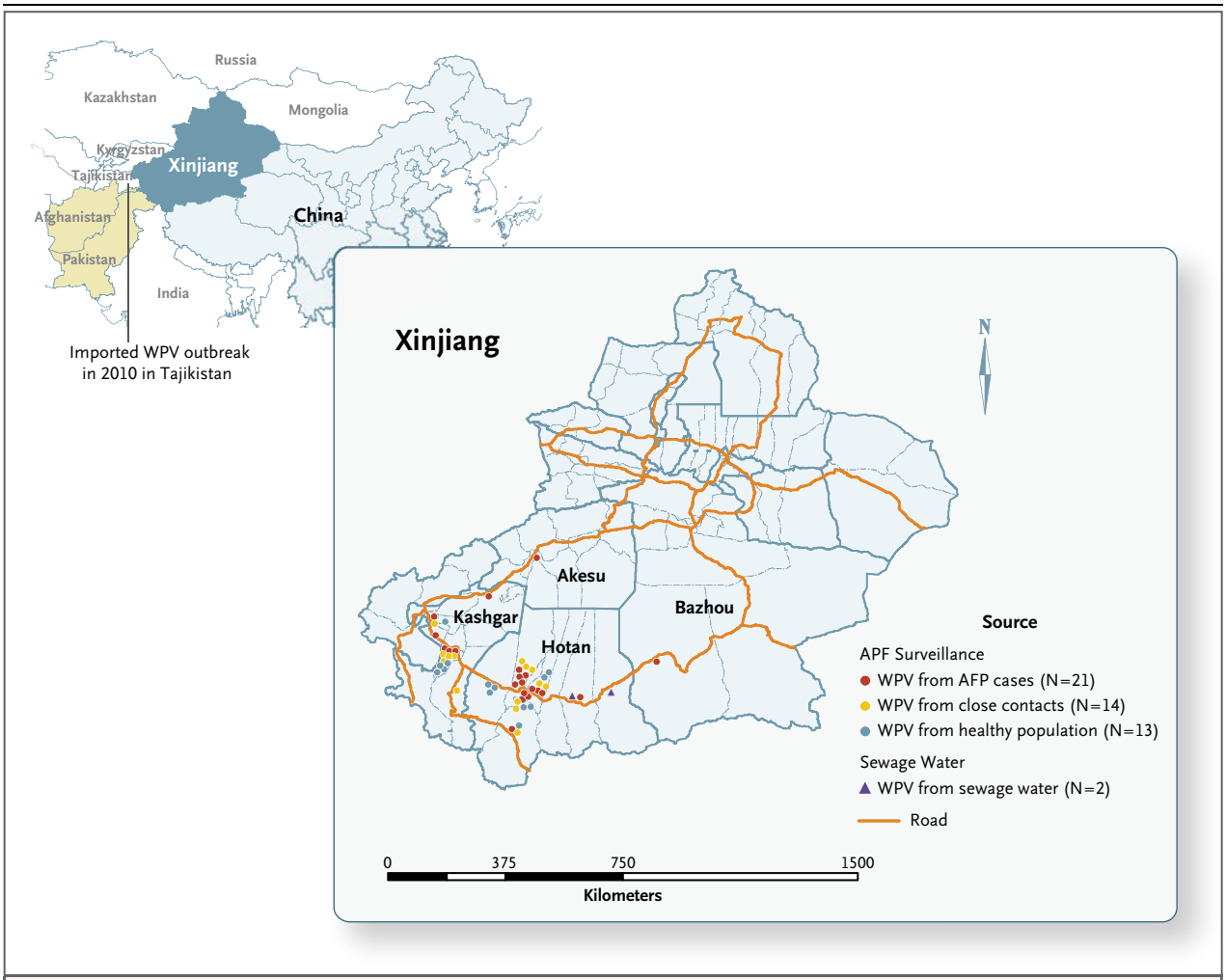

Figure 3. Regional Distribution of Wild-Type Poliovirus (WPV) Isolated from Patients with Acute Flaccid Paralysis (AFP), Close Contacts, the Healthy Population, and Sewage Water in Xinjiang in 2011.

formed, and a total of 410 cases were identified (122 in children and 288 in adults); 121 of these cases were detected through routine surveillance, and 289 were added as a result of retrospective searching. Of these additional cases of acute flaccid paralysis, 15 were classified as clinically compatible with poliomyelitis and 9 were confirmed cases of poliomyelitis on the basis of laboratory testing; all were included as outbreak cases.

SUPPLEMENTARY IMMUNIZATION

As the understanding of the epidemiologic nature of the outbreak evolved, the targets for supplementary immunization were refined. When supplementary immunization was initiated, the target population was limited to children younger than 15 years of age, because at that time, all the affected patients who had been identified were in this age cohort. When affected adults were subsequently identified in southern Xinjiang, the age range was increased to include all people younger than 40 years of age; OPV was administered regardless of the vaccination history.

Public health messages and information about the vaccination campaign were reported repeatedly on television, on the radio, and in newspapers. Before vaccination campaigns began, text messages were sent to mobile-phone subscribers and to local political and religious leaders, community elders, and volunteers, asking them to help

Table 1. Incidence Rates of Wild-Type Poliovirus Infection and Clinically Compatible Cases in Xinjiang Province, According to Demographic Characteristics.*

Characteristic	WPV Infection	Incidence Rate	Clinically Compatible Cases	Incidence Rate	Total	Incidence Rate
	no. of cases	*no./100,000*	*no. of cases*	*no./100,000*	*no. of cases*	*no./100,000*
Age						
<1 yr	6	3.46	2	1.15	8	4.62
1–4 yr	4	0.64	4	0.64	8	1.28
5–14 yr	0	0	1	0.07	1	0.07
15–39 yr	10	0.22	14	0.31	24	0.52
≥40 yr	1	0.04	2	0.07	3	0.11
Sex						
Male	14	0.29	20	0.41	34	0.70
Female	7	0.15	3	0.06	10	0.21
Prefecture in Xinjiang						
Hotan	13	0.65	19	0.94	32	1.59
Kashgar	6	0.15	3	0.08	9	0.23
Akesu	1	0.04	1	0.04	2	0.08
Bazhou	1	0.08	0	—	1	0.08
Total	21	0.10	23	0.11	44	0.20

* The incidence rates were calculated on the basis of the population in southern Xinjiang, where the wild-type poliovirus (WPV) was isolated.

spread the message. In rural communities, artists put on plays to warn the community about poliomyelitis and the dangers of not being vaccinated. Community leaders went from house to house to provide information about the vaccination campaign.

Campaigns for children were initiated in schools and kindergartens at the end of August 2011. Each child's ear or finger was marked with indelible ink after vaccination to indicate that the child had received OPV. All bazaars and markets had vaccination teams ready to vaccinate every child in the area. Teams also went from house to house to check on and vaccinate infants being kept at home.

Five rounds of supplementary immunization were conducted in Xinjiang from August 2011 to April 2012, with a total of 43.7 million doses of OPV administered (Table 2). Adults received OPV during four rounds of supplementary immunization conducted in southern Xinjiang. Monovalent OPV type 1 (OPV1) was used during the third and fourth rounds, with approximately 20 million doses administered. Trivalent OPV was used in the final round, since it is used for routine immunization. A total of 422 mild adverse events were reported after immunization; no moderate or severe adverse events thought to be related to vaccination were reported.

INTERRUPTION OF TRANSMISSION

The outbreak of imported wild-type poliovirus in Xinjiang was stopped 1.5 months after laboratory confirmation of the index case. The reported incidence rates of nonpoliomyelitis-related acute flaccid paralysis in Xinjiang in 2011 and 2012 exceeded 2 cases per 100,000 population among children younger than 15 years of age (on the basis of data gathered by means of routine surveillance), and the timeless indicators of the surveillance system for acute flaccid paralysis met WHO requirements. The reported coverage rates were more than 98% for each round of supplementary immunization in Xinjiang. Externally surveyed coverage rates were assessed in three randomly selected villages in each county and three ran-

Table 2. Dates of Supplementary Immunization Rounds, Target Population, Numbers of Persons Immunized, and Vaccine Types Used for Emergency Vaccination in Xinjiang, 2011–2012.

Vaccination Round	Date	Target Population	No. Immunized	Vaccine
			millions	
1	Aug. 29–31, 2011	Students in primary and middle schools in Hotan	0.1	Trivalent OPV
	Sept. 8–12, 2011	Children <15 yr of age in southern Xinjiang and Urumqi, children <5 yr of age in other prefectures	4.2	Trivalent OPV
	Sept. 13–26, 2011	Persons 15–39 yr of age in southern Xinjiang	5.3	Trivalent OPV
2	Oct. 8–12, 2011	Children <15 yr of age in southern Xinjiang and Urumqi, children <5 yr of age in other prefectures	4.2	Trivalent OPV
3	Nov. 15–22, 2011	Persons <40 yr of age in southern Xinjiang, children <15 yr of age in Urumqi, children <5 yr of age in other prefectures	9.4	Monovalent OPV type 1
4	March 17–25, 2012	Persons <40 yr of age in southern Xinjiang, children <15 yr of age in other prefectures	10.2	Monovalent OPV type 1
5	April 16–25, 2012	Persons <40 yr of age in southern Xinjiang and Urumqi, children <15 yr of age in other prefectures	10.3	Trivalent OPV

domly selected villages in each township. Convenience samples were obtained from 10 adults and 10 children in these villages. Coverage rates for each round of supplementary immunization exceeded 95% in all counties.

After the first, second, and third rounds of supplementary immunization, 603, 599, and 597 blood samples, respectively, were collected from the healthy population in southern Xinjiang. The rate of a positive test for neutralization antibody against type 1 poliovirus (titer ≥1:4) ranged from 97.8 to 99.3%, and the geometric mean titer ranged from 1:267 to 1:281; the values for both measures were greater than the values before the outbreak (Part B in the Supplementary Appendix).

DISCUSSION

This report documents an outbreak of imported wild-type poliovirus in China, which was certified as a poliomyelitis-free region in 2000. Evidence of the circulation of wild-type poliovirus was limited to four prefectures in southern Xinjiang, and the outbreak was interrupted 1.5 months after laboratory confirmation of the index case. The response in Xinjiang met the criteria of the 2006 World Health Assembly resolution[13] on outbreaks of wild-type poliovirus: the investigation and local responses began within 72 hours after confirmation of the outbreak; five rounds of supplementary immunization were conducted to control the outbreak, with the first round starting within 4 weeks after the confirmation of the outbreak and three rounds occurring after the last cases were reported; the reported and surveyed coverage rates for all five rounds of supplementary immunization were greater than 95%; the surveillance system for acute flaccid paralysis in Xinjiang was enhanced; and the incidence of nonpoliomyelitis-related acute flaccid paralysis exceeded 2 cases per 100,000 population in 2011 and 2012.

China used control measures recommended by the WHO to interrupt the transmission of wild-type poliovirus. Key response measures were the declaration of a public health emergency, enhancement of the sensitivity of surveillance for acute flaccid paralysis, the conduct of epidemiologically targeted vaccination campaigns, the use of monovalent OPV1 for two rounds of sup-

plementary immunization, close collaboration with international agencies such as the WHO and the U.S. Centers for Disease Control and Prevention, and provision of adequate resources to mount the response.

The use of monovalent OPV1 during the outbreak represented its first use in China. The increased efficacy of monovalent OPV1, as compared with the trivalent vaccine, is attributable to the absence of interference among the three serotypes of Sabin vaccine strains. The higher per-dose efficacy of monovalent OPV1 facilitates a more rapid increase in population immunity during an outbreak in the posteradication era.[11,14] Although monovalent OPV1 was licensed for use in China, it was not produced in China. Its administration was carried out with technical assistance from the WHO.

The outbreak investigation and response required substantial resources. China's central government and the Xinjiang government each allocated ¥160 million (approximately $26 million in U.S. dollars) for control of the outbreak. Health authorities and authorities in other government sectors collaborated extensively in performing case surveillance and reporting in schools and nurseries, producing and transporting vaccine, and transporting specimens and equipment. More than 500 public health experts went to Xinjiang to support local health workers, government officials, and the approximately 500,000 volunteers who worked in the vaccination campaigns and to assist in improving the surveillance for acute flaccid paralysis.

Until wild-type poliovirus transmission is interrupted globally, poliomyelitis-free countries will continue to be at risk for viral importation. Several poliomyelitis-free countries have had outbreaks after the importation of wild-type poliovirus.[15-18] As seen in the Democratic Republic of the Congo,[19,20] Namibia,[21] and Albania,[22] a country that has had no wild-type poliovirus transmission for a long time and has a relatively low rate of vaccination coverage may face outbreaks characterized by a large proportion of cases in adults.[21-27]

Some challenges still need to be addressed in the China immunization program, particularly in remote and undeveloped areas where routine immunization remains weak and where it is difficult to implement supplementary immunization. Reported coverage rates may overestimate actual coverage rates in areas where some persons eligible for vaccination are not being registered by local health staff during supplementary immunization. Weakness of routine immunization was also evident from the lower antibody titers and seropositive rates among children 4 years of age or younger than among those who were older.

Maintaining poliomyelitis-free status requires substantial effort: high coverage with poliomyelitis vaccines, frequent risk assessments, sensitive laboratory-supported surveillance for acute flaccid paralysis, and preparedness for outbreak detection and response. China's response, although effective, incurred direct costs and opportunity costs. The global eradication of poliomyelitis will benefit all countries, including those that have been certified as poliomyelitis-free.

In summary, an imported wild-type poliovirus circulated in 2011 in southern Xinjiang after a period of 10 years during which China had been poliomyelitis-free. Prompt, extensive control measures were implemented through multisectoral cooperation under the leadership of government at all levels. The timely conduct of five large rounds of supplementary immunization, in which trivalent OPV and monovalent OPV1 were used, stopped the circulation of wild-type poliovirus and interrupted its transmission in southern Xinjiang. The response most likely prevented poliomyelitis from spreading to other parts of China.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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