

## Outbreak Reports

## Detection and Initial Response to a Type 2 Vaccine-Derived Poliovirus — Sichuan Province, China, 2019

Jiushun Zhou<sup>1,✉</sup>; Ning Wen<sup>2,✉</sup>; Yong Zhang<sup>3,✉</sup>; Qi Qi<sup>1</sup>; Chunxiang Fan<sup>2</sup>; Dongmei Yan<sup>3</sup>; Xiaoping Zhu<sup>1</sup>; Lixin Hao<sup>2</sup>; Shuangli Zhu<sup>3</sup>; Yu Liu<sup>1</sup>; Xiaozhen Ma<sup>1</sup>; Chao Ma<sup>2</sup>; Lei Nan<sup>4</sup>; Yong Chen<sup>5</sup>; Qianli Ma<sup>1</sup>; Cheng Wang<sup>1</sup>; Kun Deng<sup>4</sup>; Lei Cao<sup>2</sup>; Ge Shao<sup>6</sup>; Xianxiang Ding<sup>6</sup>; Hong Yang<sup>2</sup>; Zhijie An<sup>2</sup>; Lance E. Rodewald<sup>7</sup>; Aiqiang Xu<sup>8</sup>; Huaqing Wang<sup>2</sup>; Zijian Feng<sup>7</sup>; Zundong Yin<sup>2,✉</sup>; Xianping Wu<sup>1,✉</sup>; Wenbo Xu<sup>3,✉</sup>

### Summary

#### What is already known about this topic?

After the type 2 strain of the live, attenuated poliovirus vaccine was withdrawn globally in 2016, any identification of a type 2 poliovirus is a Public Health Emergency of International Concern. A vaccine-derived type 2 poliovirus (VDPV2) was identified in Sichuan, prompting an urgent, comprehensive investigation and response.

#### What is added by this report?

Type 2 monovalent, live, attenuated oral poliovirus vaccine (mOPV2) is being used to respond to the numerous VDPV2 outbreaks seen around the world. In contrast, the response in Sichuan used Sabin strain inactivated poliovirus (sIPV) to stop circulation of the VDPV2. In the 6 months following the vaccination response, there have been no VDPV2s detected in Sichuan, despite extensive search.

#### What are the implications for public health practices?

Further search for the VDPV2 must continue in order to determine whether transmission has been stopped. The ongoing investigation and response to the Sichuan VDPV2 is providing evidence to the Global Polio Eradication Initiative on managing VDPV2 outbreaks.

### Background

In 2015, the World Health Organization (WHO) declared that type 2 wild poliovirus was eradicated. In April 2016, the type 2 oral poliovirus vaccine (OPV) strain was withdrawn globally from trivalent live attenuated oral poliovirus vaccine (tOPV) to avoid the inherent risk of seeding type 2 vaccine-derived polioviruses (VDPV2). China withdrew OPV2 in synchrony with other tOPV-using countries, changing the routine immunization schedule to one dose of

inactivated polio vaccine (IPV) followed by three doses of bivalent (I+III) OPV (1). After OPV2 withdrawal from all countries, routine protection of subsequent birth cohorts from type 2 polioviruses only comes from IPV, which is trivalent. A very small number of VDPV2 outbreaks were anticipated following OPV2 withdrawal, and these would have to be stopped with monovalent OPV2. The detection of any type 2 poliovirus (wild, vaccine-derived, or Sabin) in any sample from any source is generally considered to be a global public health emergency (2), necessitating urgent investigation and a comprehensive response.

In June 2019, VDPV2 was detected in stool specimens from an acute flaccid paralysis (AFP) case in Liangshan Prefecture, Sichuan Province. The Chinese Center for Disease Control and Prevention (China CDC) joined Sichuan provincial and local CDCs to investigate and respond. We report investigation results and responses to date.

### Investigation

The AFP case was of a 4-year-old boy born in November 2014 in a remote village of Leibo county, Liangshan Prefecture, Sichuan Province (Figure 1). Illness onset was April 25, 2019, when both of his legs and his left arm were found to be paralyzed 7 days after symptoms first appeared. By vaccination record and the parents' recall, the child had received tOPV in March 2015 and May of 2015, approximately one year prior to the switch from tOPV to bOPV.

Stool specimens were collected on May 17 and 18, 2019. The provincial CDC laboratory found a type 2 poliovirus; China CDC confirmed the VDPV2 and determined it had 28 nucleotide changes from the vaccine strain and shared 9 nucleotide changes with a VDPV2 isolated from sewage in Urumchi, Xinjiang Autonomous Region on April 18, 2018 (the Xinjiang VDPV2 had 13 nucleotide changes from the vaccine strain) (3). The child recovered without residual

paralysis and was discharged from the hospital. His subsequent stool specimens were negative for VDPV2 (Table 1).

We tested stool specimens for poliovirus from children under 5 years old in the affected child's neighborhood and village and the hospital that treated

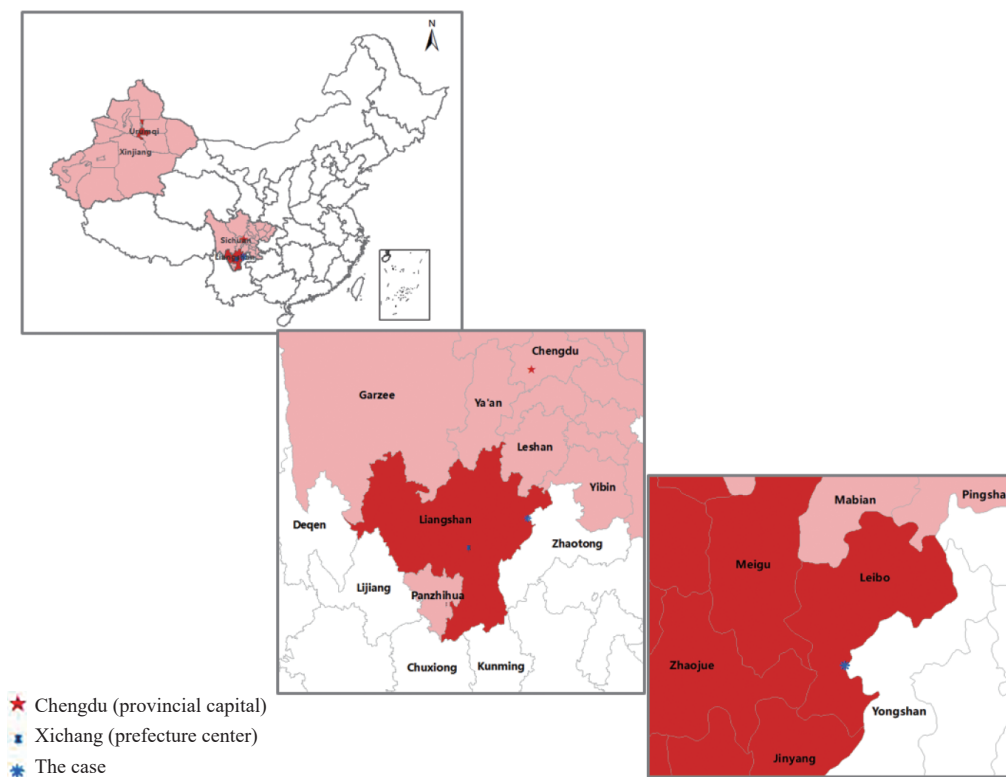


FIGURE 1. Location of the 2 VDPV2 events - Sichuan (2019) and Xinjiang (2018).

TABLE 1. Stool sample results from the acute flaccid paralysis (AFP) case, his contacts, and one other child.

	Sample	AFP case	Contact 1	Contact 2	Healthy child
1 <sup>st</sup>	Collection date	2019.5.7	2019.6.14	2019.6.27	2019.8.18
	Isolation result	PV type 2	PV type 2	PV type 2	PV type 2
	Nucleotide changes*	28	27	33	27
2 <sup>nd</sup>	Collection date	2019.5.18	2019.6.27	2019.7.7	2019.9.18
	Isolation result	PV type 2	NPEV	NPEV	Negative
	Nucleotide changes	28	— <sup>†</sup>	— <sup>†</sup>	— <sup>†</sup>
3 <sup>th</sup>	Collection date	2019.6.17	2019.7.7	2019.7.15	2019.9.25
	Isolation result	NPEV	NPEV	Negative	Negative
4 <sup>th</sup>	Collection date	2019.6.22	2019.7.15	2019.7.24	2019.10.9
	Isolation result	Negative	Negative	Negative	Negative
5 <sup>th</sup>	Collection date	2019.6.30	2019.7.24	— <sup>§</sup>	2019.10.18
	Isolation result	NPEV	Negative	— <sup>§</sup>	Negative
6 <sup>th</sup>	Collection date	2019.7.7	— <sup>§</sup>	— <sup>§</sup>	— <sup>§</sup>
	Isolation result	NPEV	— <sup>§</sup>	— <sup>§</sup>	— <sup>§</sup>

Abbreviation: PV=Poliovirus, NPEV=Non-polio enterovirus.

\* Nucleotide changes from vaccine strain.

<sup>†</sup> Because no poliovirus was detected, no further comparisons were necessary.

<sup>§</sup> Two negative results indicated that no further specimens and testing were needed.

him. Among 160 healthy children investigated, specimens from 2 children who lived 4 kilometers from the residence of the AFP case were positive for VDPV2s—one with 27 nucleotide changes and the other with 33 changes. We detected another VDPV2, with 27 nucleotide changes, in a healthy child in Leibo county who lived 5.5 kilometers from the initial child during investigation of 300 other healthy children (Table 1).

We assessed polio vaccine coverage in the village and surrounding townships among 88 children 1–5 years old in the village and 164 children <6 years old in 4 surrounding townships. In the village, 53.4% (47/88) had no history of polio vaccination, 35.2% (31/88) received 1 dose, 6.8% (6/88) received 2 doses, 3.4% (3/88) received 3 doses, and 1.1% (1/88) received 4 doses. In the surrounding townships, 65.0% (106/164) received 3 or more doses of polio vaccine.

We conducted retrospective searches for AFP cases in Liangshan on June 12 and five surrounding prefectures on June 17. The provincial medical investigation team reviewed 31,631,487 in-patient and out-patient records from 778 hospitals, going back to May 1, 2016. Among the 279 AFP cases found, 10 had not been reported previously. These newly-identified AFP cases were reviewed by provincial polio experts, and polio was diagnostically excluded from all 10. AFP “zero case reporting”, which is requiring absence of cases to be reported every day to ensure complete reporting of any cases, was started on June 21 (August 19 in Aba) to enhance sensitivity of surveillance in Liangshan and its 6 surrounding prefectures.

## Response and Further Search

Two non-selective Supplementary Immunization Activities (SIAs) with Sabin-strain IPV (sIPV) were conducted in Liangshan Prefecture—one in June and a second in August of 2019—targeting children 2 months to 5 years old (born between 1 July 2013 and 30 April 2019). SIA vaccination rates were 95.6% (30,424/31,812, first SIA) and 98.3% (30,751/31,283, second SIA) in Leibo County. In Liangshan Prefecture, over 450 thousand children received sIPV in each SIA, with vaccination rates of 97.4% (457,719/469,964) and 98.8% (488,803/494,920).

In the six surrounding prefectures (Panzihua, Leshan, Yibin, Ya'an, Aba, and Ganzi), we conducted one selective sIPV SIA (June–October) for children 2 months to 5 years old without documentary proof of any type 2 polio vaccination. We conducted one non-

selective sIPV SIA in December, similar to the Liangshan Prefecture SIA. In total, 34,000 children were vaccinated in the selective sIPV SIAs and 780,000 children were vaccinated in the non-selective sIPV SIAs.

After testing stool samples from close contacts, 300 additional stool samples were collected between August 13 and 21 from 6 sites—3 counties bordering Leibo county and 3 townships bordering the index patient's township. Each site collected 50 samples (from 1 to 5-year-olds; 10 samples from each year cohort), and one VDPV2 was found.

We conducted environmental surveillance (ES) for poliovirus in four prefectures (Liangshan, Yibin, Aba, and Chengdu—guided by risk assessments), and 2 samples were collected in each site every month. ES has been consistently negative through December 2019, and from August 2019 to date, no type 2 polioviruses have been detected in any surveillance. We conducted serological surveys for poliovirus immunity prior to the SIAs, and the results are pending.

## Discussion

According to WHO (4), there have been 47 cVDPV2 outbreaks in 20 countries since the switch from tOPV to bOPV in April 2016. Some of these outbreaks involve more than one country. On average, 2–3 VDPV events happen in China every year (5). The Sichuan VDPV2 is the first VDPV2 that has been discovered in an AFP case since the polio vaccination switch on May 1, 2016. One VDPV2 was isolated from environmental samples in Xinjiang (April 2018) (3), but no VDPV2s were found among AFP cases in Xinjiang.

This VDPV2 outbreak followed cessation of OPV2, but despite careful investigation, we were unable to identify the source of transmission. Similarly, a putative epidemiological link between the Sichuan and Xinjiang viruses has not been established. We believe that the VDPV2 likely circulated for three years in Liangshan enabled by weak routine immunization in this remote county, which is evidenced by the vaccination coverage survey described above.

Using sIPV or requesting monovalent mOPV2 from the WHO to attempt to stop the outbreak was a difficult choice. Most countries with cVDPV2 outbreaks used mOPV2 to control their outbreaks. However, the relative low gut immunity to type 2 poliovirus following the cessation of OPV2 vaccination

carries the implicit risk that Sabin-strain lineages can survive to become cVDPV2s in the future, necessitating outbreak response with monovalent OPV2 and thereby potentially seeding new lineages (6). Based on current evidence, the sIPV campaigns in Sichuan Province appear to have prevented further VDPV2 spread; however, it is still uncertain whether this IPV-only strategy will completely stop transmission. We must sustain intensive AFP and environmental surveillance to guide any possible further response to this event. Experience and data from this outbreak and our use of an sIPV response can augment the growing evidence base of the Global Polio Eradication Initiative for managing VDPV2 outbreaks.

## Acknowledgments

We thank the health care staff at provincial, county, and township levels of Sichuan for their contribution to the control of VDPV transmission. We also thank Dr. Yixing Li and Guomin Zhang, National Immunization Program, China CDC, thank for their contribution to the coverage investigation of SIAs.

This study was supported by National Science and Technology Major Project of China (2018ZX10101002-003).

# Corresponding authors: Zundong Yin, yinzd@chinacdc.cn; Xianping Wu, wwwuxp@163.com; Wenbo Xu, wenbo\_xu1@aliyun.com.

<sup>1</sup> Sichuan Provincial Center for Disease Control and Prevention,

Chengdu, Sichuan, China; <sup>2</sup> National Immunization Program, Chinese Center for Disease Control and Prevention, Beijing, China; <sup>3</sup> National Institute for Viral Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing, China; <sup>4</sup> Liangshan Yi Autonomous Prefectural Center for Disease Control and Prevention, Xichang, Sichuan, China; <sup>5</sup> Leibo county Center for Disease Control and Prevention, Leibo, Liangshan, Sichuan, China; <sup>6</sup> Chinese Field Epidemiology Training Program; <sup>7</sup> Chinese Center for Disease Control and Prevention, Beijing, China; <sup>8</sup> Shandong Provincial Center for Disease Control and Prevention, Jinan, Shandong, China.

& Joint first authors.

Submitted: February 20, 2020; Accepted: March 06, 2020

## References

1. National Health Commission of the Peoples's Republic of China. Notification of the switch on poliomyelitis vaccine immunization strategy of national immunization programme, in China. 2016-4-29. <http://www.nhc.gov.cn/jkj/s3582/201604/5b23c513cfc4fe7848d52a98f02b1ea.shtml>. (In Chinese).
2. WHO. Standard operating procedures: Responding to a poliovirus event or outbreak version 3. Geneva (Switzerland): World Health Organization; 2019 Jan. License: CC BY-NC-SA 3.0 IGO.
3. Ning J, Yang H, Adili S, Cao L, Wang PS, Fan CX, et al. Emergency response to a type II vaccine-derived poliovirus first detected in sewage after the polio immunization strategy switch in China. *Chin J Vaccin Immun* 2019;25(4):373-7, 387. [http://lib.cqvip.com/Qikan/Article/Detail?id=7100100761&fromQikan\\_Search\\_Index](http://lib.cqvip.com/Qikan/Article/Detail?id=7100100761&fromQikan_Search_Index). (In Chinese).
4. Q&A With Michel Zaffran: cVDPV2 and The Vaccine Available to Stop it. <http://polioeradication.org/news-post/caught-between-a-rock-and-a-hard-place-cvdpv2-and-the-vaccine-available-to-stop-it/>.
5. Wen N, Fan CX, Yan DM, Zhu SL, Wang HB, Liu B, et al. The epidemiology characteristics analysis of vaccine-derived poliovirus and cases in China, 2001–2013. *Chin J Vaccin Immun* 2014;20(3):210-5. [http://www.wanfangdata.com.cn/details/detail.do?\\_type=perio&idzgjhmy201403004](http://www.wanfangdata.com.cn/details/detail.do?_type=perio&idzgjhmy201403004). (In Chinese).
6. McCarthy KA, Chabot-Couture G, Famulare M, Lyons HM, Mercer LD. The risk of type 2 oral polio vaccine use in post-cessation outbreak response. *BMC Med* 2017;15(1):175. <http://dx.doi.org/10.1186/s12916-017-0937-y>.