An imported case of vaccine-derived poliovirus type 2, Spain in the context of the ongoing polio Public Health Emergency of International Concern, September 2021

María Dolores Chirlaque López1,2,3,*, María Cabrerizo3,4,*, Bernardo R. Guzmán Herrador5, Josefa Masa-Calles3,4, María Ester Alarcón-Linares1, Ana Allende7, Esteban Aznar Cano6, María Isabel Barranco Boada1, Elena Cantero Gudino5, Sonia Fernández-Balbuena5, Ana Fernández Dueñas4, María Dolores Fernández-García6, Laura García Hernández4, Visitaición García Ortúzar5, Noemi López-Perea6, Eduardo Martínez-Salcedo4,5, Antonio Moreno-Docón1,4, María Ordobás Gavín13, Inmaculada Rodero Garduño10, María José Sierra Moros1,4,4,4, Fernando Simón Soria5,4, Aurora Limia Sánchez9, Berta Suárez Rodríguez10.

1. Department of Epidemiology, Murcia Regional Health Council, Murcia, Spain
2. IMIB-Arrixaca, Murcia University, Murcia, Spain
3. CIBER in Epidemiology and Public Health (CIBERESP), Madrid, Spain
4. National Polio Laboratory, National Centre for Microbiology, Instituto de Salud Carlos III, Madrid, Spain
5. Coordinating Centre for Health Alerts and Emergencies (CCAES), Directorate General of Public Health, Ministry of Health, Madrid, Spain
6. National Centre of Epidemiology, Carlos III Health Institute, Madrid, Spain
7. Research Group on Microbiology and Quality of Fruit and Vegetables, Food Science and Technology Department, CEBAS-CSIC, Espinardo, Murcia, Spain
8. Immunization Programme Area, Directorate General of Public Health, Ministry of Health, Madrid, Spain
9. Epidemiology and Prevention Service, Public Health General Direction, Canary Islands Health Service, Santa Cruz de Tenerife, Spain
10. Lorca Public Health Service, Murcia, Spain
11. Neuropediatric Unit, Department of Paediatrics, University Hospital Virgen of Arrixaca, Murcia, Spain
12. Microbiology Service. Hospital Clínico Universitario Virgen de la Arrixaca, Murcia, Spain
13. Sub-Directorate General of Epidemiology, Community of Madrid, Spain
14. CIBER in Infectious Diseases (CIBERINFEC), Madrid, Spain

* These authors contributed equally to this work and share first authorship

Correspondence: Bernardo R. Guzmán Herrado (bguzman@sanidad.gob.es)

Citation style for this article:
Chirlaque López María Dolores, Cabrerizo María, Guzmán Herrador Bernardo R., Masa-Calles Josefa, Alarcón-Linares María Ester, Allende Ana, Aznar Cano Esteban, Barranco Boada María Isabel, Cantero Gudino Elena, Fernández-Balbuena Sonia, Fernández Dueñas Ana, Fernández-García Laura, García Ortúzar Visitaición, López-Perea Noemi, Martínez-Salcedo Eduardo, Moreno-Docón Antonio, Ordobás Gavín María, Rodero Garduño Inmaculada, Sierra Moros María José, Simón Soria Fernando, Limia Sánchez Aurora, Suárez Rodríguez Berta. An imported case of vaccine-derived poliovirus type 2, Spain in the context of the ongoing polio Public Health Emergency of International Concern, September 2021. Euro Surveill. 2021;26(50):pii=2101068. https://doi.org/10.2807/1560-7917.ES.2021.26.50.2101068

Case description
A child below the age of 6 years arrived in Murcia, south-eastern Spain, from Senegal at the beginning of August 2021. The patient was admitted to a hospital on a scheduled basis to continue supportive treatment of an acute flaccid paralysis (AFP) with unknown aetiology and with onset of symptoms in Senegal at the beginning of July 2021. In the second week of August, the patient was discharged from hospital after clinical improvement with the diagnosis of AFP secondary to acute anterior meningomyeloradiculitis because of enterovirus infection. During admission, enterovirus was found in a respiratory sample (later characterised as coxsackievirus B4) and in faeces. During the first days of September, the case stayed with a local family before returning to Senegal.

Case detection
The NAPPE requires surveillance for early notification and virological study of all AFP cases in children under 15 years of age [3]. However, the AFP surveillance
It was then possible to retrieve a stool sample of the case that was sent to the CNM. The presence of poliovirus (PV) was investigated by cell culture following World Health Organization (WHO) standard procedures [4,5]. A cytopathic effect was observed on the inoculated RD and L20B cells. In mid- to end-September, the virus was isolated and characterised as PV2 using the intratypic differentiation assay according to the recommended protocol [6]. Sequencing of the complete VP1 genomic region indicated that, according to the WHO-adopted criteria [7], it was a vaccine-derived poliovirus 2 (VDPV2) strain since it was 5.1% divergent from the PV2 Sabin strain in the VP1 sequence. Results were further confirmed by the Regional Reference Laboratory of the WHO/Europe for Poliomyelitis [8] at the Robert Koch Institute, Berlin, Germany.

According to the statement of the Thirtieth International Health Regulations (IHR) Emergency Committee on the international spread of PV and the ongoing PHEIC, Senegal was classified as a country with circulating VDPV2 (cVDPV2) at the time of this case’s detection in Spain. According to the WHO, the most recent detection in Senegal had been in mid-September 2021 [2]. The recent cVDPV2 outbreak detected in Senegal was linked to ongoing transmission in other areas of West Africa [9]. The case’s vaccination card showed four doses of oral polio vaccine and one dose of inactivated polio vaccine (IPV) received during the first year of life.

### National and international coordination

Following notification of the case, a national technical support group (GAT) that included all actors with a role in the management of the event was convened by the Coordinating Centre for Health Alerts and Emergencies (CCAES). Its mandate was to keep all stakeholders updated about the development of the event, discuss the information available and provide technical advice on response actions. The GAT included representatives of the CCAES and the immunisation programme area at the Ministry of Health, the CNM, the CNE and the RPHD of the Region of Murcia. A regional technical support group with all stakeholders involved in the response at the regional level was also convened in Murcia. After identifying that six contacts of the case resided in two additional regions, Madrid and the Canary Islands, representatives from RPHD of these two regions were also included in the GAT. In addition, and after proposal by the GAT, the Director General of Public Health at the Ministry of Health convened the Response Coordinating Committee (RCC) one week later (end-September). This included representatives at a higher strategic level. Actions proposed by the GAT were discussed and endorsed by the RCC.

On the same day the GAT was convened, the CCAES reported the case to the WHO Regional Office for Europe and communicated the case to the IHR focal point in Senegal, requesting additional information on the background of the case as well as on the epidemiological situation of cVDPV2. Following WHO standard operating procedures [10], the alert was classified as an event with no evidence of transmission in Spain in which VDPV2 had been detected in a human case with AFP. The case was also communicated via the Early Warning and Response System of the European Union [11].

### Table 1

| Classification | Definition/type of exposure | Measures |
|---------------|----------------------------|----------|
| Close contact |                           |          |
| I             | Cohabitants and non-cohabitants with intense direct physical contact i.e. helped with personal hygiene, helped with feeding, played with physical contact | Collection and analysis of two faecal specimens collected > 24 h apart | One dose of IPV vaccine |
| II            | Non-cohabitants with prolonged direct physical contact i.e. rehabilitation care |          |          |
| Casual contact |                           |          |
| III           | Stayed in the same room without direct physical contact | Collection of two faecal specimens collected > 24 h apart; analysis if positive samples were identified in close contacts | Considered if positive samples were identified in close contacts |
| IV            | Any other person who has not had physical contact but has had some contact with the case i.e. family member who visited the household for a short time |          |          |

IPV: inactivated polio vaccine.
Measures undertaken to respond to the event

The following measures were undertaken within the framework of the NAPPE.

Identification and classification of contacts, collection of stool samples and vaccination

Individuals who had been in contact with the case in Spain were classified into four categories according to their level of exposure, and specific actions were planned (Table 1). In Spain, there is a high immunity against polio in the general population [12,13] and since 1998, vaccination coverage at a national level has been higher than 95% [14]. In addition, coverage rates at the local level in the Region of Murcia range between 94% and 96% (data not shown). Considering this situation, and after receiving confirmation that all contacts were vaccinated according to the national immunisation programme, the RCC decided to recommend vaccination of close contacts with one dose of IPV.

Depending on the results of the close contacts’ stool cultures, the recommendations would be reviewed in order to consider the administration of an additional dose of IPV and/or extend the vaccination recommendations. A review of potential unvaccinated individuals and possible susceptible groups was carried out in the relevant area.

Twenty close contacts and 22 casual contacts were identified, 36 in Murcia and six in other Spanish regions (Table 2). All close contacts received one dose of the IPV vaccine.

Virological analysis in contacts and in wastewater

By mid- to end-November 2021, 40 stool samples from 20 close contacts had been analysed in the CNM with the same standard cell culture methods used for the AFP case, and cVDPV2 infection was excluded for all of them. The samples of casual contacts (III and IV) are currently being studied for enterovirus only by PCR. In addition, four raw wastewater samples taken from two different entry points of the wastewater treatment plant from the area where the case had stayed on 2 different days during mid- to end-September were analysed. The samples were processed and concentrated at the CEBAS-CSIC laboratory and testing for the presence of enterovirus was carried out in the CNM by cell culture and PCR techniques. All of them were PV-negative, but non-polio enteroviruses were detected by PCR: an echovirus 3 in samples collected on the first day and an enterovirus A in samples collected on the second day.

Virological results in close contacts and wastewater samples suggest no onward PV transmission following this event in Spain.

Enhanced surveillance with retrospective and prospective search for suspected cases

A retrospective search for potential additional cases has been conducted through a review of all admissions in all hospitals in the Region of Murcia since August 2021. A daily zero-reporting system was established to ensure prospective and timely reporting of all suspected cases from all hospitals in the Region of Murcia until the closure of the event. Two children with Guillain–Barré syndrome were identified and the AFP surveillance protocol was applied, resulting negative for PV.

Ethical statement

Acute flaccid paralysis is a notifiable disease in Spain. No ethical approval was sought as this study describes the public health actions undertaken under the framework of the NAPPE following the detection of an imported case of AFP because of a vaccine-derived PV2 in Spain. Written consent for the case report was obtained from the legal guardian of the child.

Discussion

The WHO European Region was declared polio-free in 2002 [15]. In light of the ongoing circulation of wild PV type 1 and cVDPV worldwide and ongoing use of live attenuated vaccines in some countries, there is a risk of introduction of wild PV, or vaccine-derived PV in countries declared polio-free such as Spain. Given the high standards of sanitation and hygiene, the high vaccination coverage and high level of immunity against PV, together with good detection and response capacities to events related to polio, the risk of transmission of PV in Spain is estimated to be low [16]. However, in the context of the NAPPE and the ongoing PHEIC, there is no room for complacency. Although indicators show that the AFP surveillance system in Spain is of good quality, its sensitivity has decreased in recent years, possibly because of a lower perception of the risk of poliomyelitis as a consequence of the absence of polio cases [17].

Conclusion

This event has shown the importance of maintaining an optimal coordination among all the components that are part of the NAPPE and reminds us that in order to sustain a status free of PV circulation we must maintain and strengthen PV surveillance systems for early detection. This includes increasing awareness among clinicians, clinical microbiologists, public health...
specialists and other actors with a role in this system as well as maintaining good vaccination coverage.

Conflict of interest
None declared.

Authors’ contributions
MDCL led the investigation in the Region of Murcia. MC led the laboratory investigation at central level. BSR coordinated the national technical support group. BRGH drafted the first version of the manuscript. MDCL, MC, BGH, JM-C, MEA, EAC, MIBB, ECG, SF-B, AFD, MDF-G, LGH, NL-P, MOG, IRG, MJSM, FSS, ALS, and BSR are members of the national technical group. AA, AM-D, EM-S and VGO had a role in the event management in the Region of Murcia. All authors revised the manuscript.

References
1. Ministry of Health, Social Services and Equality. Plan de acción en España para la erradicación de la poliomielitis. [Action plan in Spain for Polio eradication]. Madrid: Ministry of Health, Social Services and Equality; 2016. Spanish. Available from: https://www.mscbs.gob.es/profesionales/saludPublica/preVaccPromocion/PlanPolio/do...poliomielitis.pdf

2. World Health Organization (WHO). Statement of the thirtieth Polio IHR Emergency Committee. Geneva: WHO; 23 Nov 2021. Available from: https://www.who.int/news/item/23-11-2021-statement-of-the-thirtieth-polio-ihr-emergency-committee

3. Masa-Calles J, Torner N, López-Perea N, Torres de Mier MV, Fernández-Martínez B, Cabrerozio M, et al. Acute flaccid paralysis (AFP) surveillance: challenges and opportunities from 18 years’ experience. Spain, 1998 to 2015. Euro Surveill. 2018;23(47):1700423. https://doi.org/10.2807/1560-7917.ES.2018.23.47.1700423 PMID: 3042263

4. World Health Organization (WHO). Polio Laboratory Manual, 4th edition. Geneva: WHO; 2004. Available from: http://apps.who.int/iris/bitstream/10665/68762/1/WHO_IVB_04.10.pdf

5. World Health Organization (WHO). An alternative test algorithm for poliovirus isolation and characterization, Polio Laboratory Manual 4th edition. Geneva: WHO; 2004. Available from: http://polioeradication.org/wp-content/uploads/2017/05/NewAlgorithmForPolivirusIsolationSupplement.pdf

6. Gerloff N, Sun H, Mandelbaum M, Maher C, Nix WA, Zaidi S, et al. Diagnostic assay development for Poliovirus eradication. J Clin Microbiol. 2018;56(2):e01624-17. https://doi.org/10.1128/JCM.01624-17 PMID: 29212703

7. Global Polio Eradication Initiative (GPEI). Classification and reporting of vaccine-derived polioviruses (VDPV). GPEI guidelines. Geneva: GPEI; 2016. Available from: https://polioeradication.org/wp-content/uploads/2016/09/Reporting-and-Classification-of-VDPVs_Aug2016_EN.pdf

8. Robert Koch Institut (RKI). WHO Reference Laboratories. Regional Reference Laboratory of the WHO/Europe for Poliomyelitis. Berlin: RKI; 2021. [Accessed: 13 Dec 2021]. Available from: https://www.rki.de/EN/Content/Institute/International/reference_labs/ref_lab_node.html

9. World Health Organization (WHO). Statement of the twenty-eighth polio IHR emergency committee. Geneva: WHO; 21 May 2021. Available from: https://www.who.int/news/item/21-05-2021-statement-following-the-twenty-eighth-ihr-emergency-committee-for-polio

10. World Health Organization (WHO). Standard operating procedures; Responding to a poliovirus event or outbreak version 3. Geneva: WHO; Jan 2019. Available from: https://polioeradication.org/wp-content/uploads/2016/07/sop-polio-outbreak-response-version-2019-310.pdf

11. European Centre for Disease Prevention and Control (ECDC). Early Warning and Response System of the European Union (EWRS). Stockholm: ECDC; 2021. Available from: https://www.ecdc.europa.eu/en/publications-data/early-warning-and-response-system-european-union-ewrs

12. Limia Sánchez A, Olmedo Lucerón C, et al. 2nd seroprevalence study in Spain; 2019-2020. Rev Esp Salud Pública; 2021;95:e202103059. Spanish. Available from: https://www.mscbs.gob.es/biblioPublic/publicaciones/recursos_propios/resp/revisa_cdrom/VOL95/C_ESPECIALES/R95C_202103059.pdf

13. Ministry of Health, Social Services and Equality. 2 Estudio de Seroprevalencia en España. [2nd seroprevalence study in Spain]. Madrid: Ministry of Health, Social Services and Equality; 2020. Spanish. Available from: https://www.mscbs.gob.es/profesionales/saludPublica/preVaccPromocion/vacunaciones/comoTrabajamos/docs/EstudioSeroprevalencia_EnfermedadesInmunoprevenibles.pdf

14. Ministry of Health, Social Services and Equality. Coberturas de vacunación. Datos estadísticos. [Vaccine coverage. Statistical data]. Madrid: Ministry of Health, Social Services and Equality; 2020. Spanish. Available from: https://www.mscbs.gob.es/profesionales/saludPublica/preVaccPromocion/vacunaciones/calendario-y-coberturas/coberturas/home.htm

15. World Health Organization Regional Office for Europe (WHO/Europe). Certification of the Region’s polio-free status in 2002. Copenhagen: WHO/Europe. [Accessed: 20 Nov 2021]. Available from: https://www.euro.who.int/en/health-topics/communicable-diseases/poliomyelitis/activities/certification-and-maintenance-of-polio-free-status-in-the-european-region/european-regional-commission-for-the-certification-of-poliomyelitis-eradication/certification-of-the-regions-polio-free-status-in-2002

16. World Health Organization Regional Office for Europe (WHO/Europe). Report of the 33rd Meeting of the European Regional Certification Commission for Poliomyelitis Eradication. Copenhagen: WHO/Europe. 2019. Available from: https://www.euro.who.int/__data/assets/pdf_file/0016/414205/33rd-RCC-eng.pdf

17. National Centre of Epidemiology and National Centre for Microbiology Instituto de Salud Carlos III (ISCIII). Plan de acción en España para la Erradicación de la Poliomielitis. Vigilancia de la Parálisis Flácida Aguda y Vigilancia de Enterovirus en España, Informe año 2020. [Action Plan in Spain for polio eradication. Surveillance of acute flaccid paralysis and surveillance of enterovirus in Spain, 2020 report]. Madrid: ISCIII; 5 Nov 2021. Spanish. Available from: https://www.isciii.es/queHacemos/Servicios/VigilanciaSaludPublicaRENAVE/EnfermedadesTransmisibles/Documents/archivos%20A-Z/POLIO/Resultados_Vigilancia_Polio/Informes_Anuales_Polio/Informe_PFA_EV_2020_web.pdf

License, supplementary material and copyright
This is an open-access article distributed under the terms of the Creative Commons Attribution (CC BY 4.0) Licence. You may share and adapt the material, but must give appropriate credit to the source, provide a link to the licence and indicate if changes were made.

Any supplementary material referenced in the article can be found in the online version.

This article is copyright of the authors or their affiliated institutions, 2021.