A Large Vaccine-Derived Poliovirus Outbreak on Madura Island—Indonesia, 2005

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(See the editorial commentary by Wright and Modlin, on pages 335–6.)

Between June and October 2005, 45 laboratory-confirmed type 1 vaccine–derived poliovirus (VDPV) cases were identified on Madura Island in Indonesia. Genetic sequencing data on VDPV isolates were consistent with replication and circulation for up to ~2 years. Concurrent circulation with type 1 wild poliovirus (WPV) enabled comparisons of VDPV and WPV cases and found that clinical and epidemiological features of both were similar. Attack rates for VDPV were as high as those for WPV. Of 41 VDPV case patients with known vaccination status, 25 (61%) had received zero oral polio vaccine (OPV) doses. Low population immunity due to low routine OPV coverage in rural areas and the absence of WPV circulation for more than a decade were major predisposing factors for the emergence of VDPV. Suboptimal surveillance and a limited initial immunization response may have contributed to widespread circulation. Sensitive surveillance and prompt high-quality immunization responses are recommended to prevent the spread of VDPVs.

Trivalent oral polio vaccine (tOPV), a live vaccine consisting of Sabin attenuated poliovirus strains 1, 2 and 3, is the primary tool for the global eradication of poliovirus. OPV prevents paralytic disease through stimulation of humoral immunity and induces intestinal mucosal immunity that reduces person-to-person transmission, thereby protecting both vaccine recipients and the community. Other advantages of OPV include low cost, easy administration, and suitability for use in mass campaigns in developing countries [1]. However, replicating polioviruses have a high frequency of genetic mutation and recombination with other vaccine serotypes and other enteroviruses [2–5], which rarely may result in vaccine variants reacquiring the ability of the parent wild strains to cause paralytic polio [6–8]. In settings with low population immunity, Sabin vaccine strains may be transmitted for an extended period among susceptible carriers, increasing the possibility of emergence and spread of virulent strains [6, 9].

Vaccine-derived polioviruses (VDPVs) are defined as having at least 1% nucleotide difference from their parent Sabin strains in the VP1 capsid protein region of the poliovirus genome [8]. On the basis of the average rate of poliovirus capsid evolution, a 1% divergence in the VP1 area implies that a virus has replicated for ~1 year since administration of the initiating OPV dose. VDPVs are classified into 3 categories: circulating VDPVs (cVDPVs), which are associated with sustained person-to-person transmission; immunodeficiency-associated VDPVs (iVDPVs), which have been isolated from immunodeficient persons with prolonged viral infection after exposure to OPV; and ambiguous VDPVs (aVDPVs), which either have been isolated from a single patient without immunodeficiency or are environmental isolates with an unidentified source [8]. The first documented cVDPV outbreak occurred in 2001, in Hispaniola [10]. Since then, outbreaks or extended transmission have been reported in Egypt [11], The Philip-

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pines [3, 12], China [9, 13], Madagascar [14], and the United States [15], among others [8, 16, 17]. In addition to low vaccine coverage, other risk factors for cVDPV emergence and transmission identified in these outbreaks included the absence of circulating wild poliovirus (WPV) of the same serotype as the cVDPV and poor hygienic conditions [3, 8, 10, 12].

Developing a strategy for decreasing the risks of VDPV outbreaks is a priority for the polio-eradication initiative. As global eradication of WPV nears, further understanding of the biological properties of cVDPVs and more information about conditions that enable their emergence and spread are critical for developing prevention and response strategies for future outbreaks. This report describes the epidemiological characteristics of a poliomyelitis outbreak on Madura Island, Indonesia, during 2005. With 45 patients with laboratory-confirmed paralysis caused by a cVDPV strain, this is the largest laboratory-confirmed cVDPV outbreak reported to date and is the first with cocirculation of both type 1 WPV and cVDPV.

METHODS

Background. Indonesia is an archipelago of almost 17,000 islands, with an estimated population of 219 million persons in 2005 [17]. Madura Island, located off the eastern end of Java's north coast, had an estimated population of 3.4 million and a population density of 616 persons/km^2. (Population estimates for 2005 are based on 2000 census data provided by Badan Pusat Statistik Propinsi Jawa Timur [Board of Statistics Center of East Java Province]. Geographical area data were provided by the Center for International Earth Science Information Network at Columbia University). Madura belongs to the province of East Java, whose capital, Surabaya, is a 20-min ferry ride from the west end of Madura. Despite its proximity, cultural and language barriers separate Madurese from Javanese. The human poverty index, a composite index that measures deprivations in 3 dimensions (longevity, knowledge, and standard of living) is higher in Madura (33.7) than in the province of East Java (21.7) and Indonesia (22.7) [18].

Polio immunization in Indonesia has been based exclusively on routine vaccination since 2002, with 4 tOPV doses given at 0, 1, 2, and 3–4 months of age. Immunization is usually provided at *Posyandu* (health service posts) that offer maternal and child health services. However, the availability and quality of services are low in many communities. User fees, bribes, and insufficient staff and supplies are also frequent [18]. The World Health Organization (WHO) has estimated that countrywide coverage with 3 doses of OPV during 2002–2005 was 70% [17].

Indonesia reported no WPV circulation from 1995 to 2004. The first case of type 1 WPV was recognized in West Java in May 2005, following an importation into Indonesia via Saudi Arabia of virus that originated in Nigeria [19]. In response, 2 subnational immunization campaigns with tOPV were conducted at the end of May and June in 3 provinces in West Java. As the outbreak spread to additional provinces, nationwide tOPV campaigns were conducted in August, September, and November. In November, monovalent OPV type 1 (mOPV1) was used in areas with circulating virus, including Madura. The last confirmed WPV case occurred on 20 February 2006 [19]. In August 2005, type 1 VDPV was confirmed in stool samples from 4 patients from Madura with onset of acute flaccid paralysis (AFP) in June and July.

Case ascertainment. Case patients with paralytic poliomyelitis were identified through the AFP surveillance system, which was implemented in 1995 by the Indonesian government with assistance from the WHO. Through this system, district health officers routinely investigate AFP cases reported by health care centers and hospitals, collect stool samples, and conduct a clinical reexamination 60 days after the onset of paralysis to assess residual paralysis.

Following the WHO-recommended virological classification scheme [20], we defined VDPV cases patients as those with AFP and with type 1 VDPV isolated from at least 1 stool sample and WPV case patients as those with type 1 WPV isolated from at least 1 stool sample. Those AFP case patients who (1) did not have adequate samples (i.e., 2 stool specimens collected at least 24 h apart, both within 14 days of the onset of paralysis and both arriving in the laboratory in good conditions [$>$8 g, cold-chain maintained, no desiccation, and no leakage]); (2) had residual paralysis at 60 days, died, or were lost to follow-up; and (3) had negative culture results were reviewed by an expert panel and classified as "compatible with poliomyelitis" on the basis of clinical and epidemiological evidence.

In September 2005, a team from the Indonesia Ministry of Health, the WHO, and the US Centers for Disease Control and Prevention (CDC) examined a convenience sample of VDPV and WPV case patients from Madura. The team assessed the presence of residual paralysis and obtained further information on immunization, medical history, prior travel to polio-endemic areas, and living conditions. The team conducted active searches for AFP case patients with onset of paralysis during the previous 3 months in the neighborhoods of confirmed VDPV or WPV case patients, in 2 poor and crowded urban areas (Bangkalan and Sampang districts), and in 3 of the 4 district hospitals.

Isolation and characterization of poliovirus isolates. Stool specimens were sent to the WHO-accredited laboratory in Surabaya, Indonesia, for virus isolation. Polioviruses were isolated and identified from stool suspensions by culture in L20B and RD cell cultures in accordance with standard procedures [21–23]. Poliovirus-positive cultures were sent to the Regional Reference Laboratory (Biofarma, Bandung, Indonesia) for intratypic differentiation (ITD). ITD was performed by probe hybridization with Sabin-specific probes (CDC) and by ELISA to characterize poliovirus isolates as being vaccine related or wild, in accordance with methods that have been described elsewhere [24]. Isolates with discordant ITD results

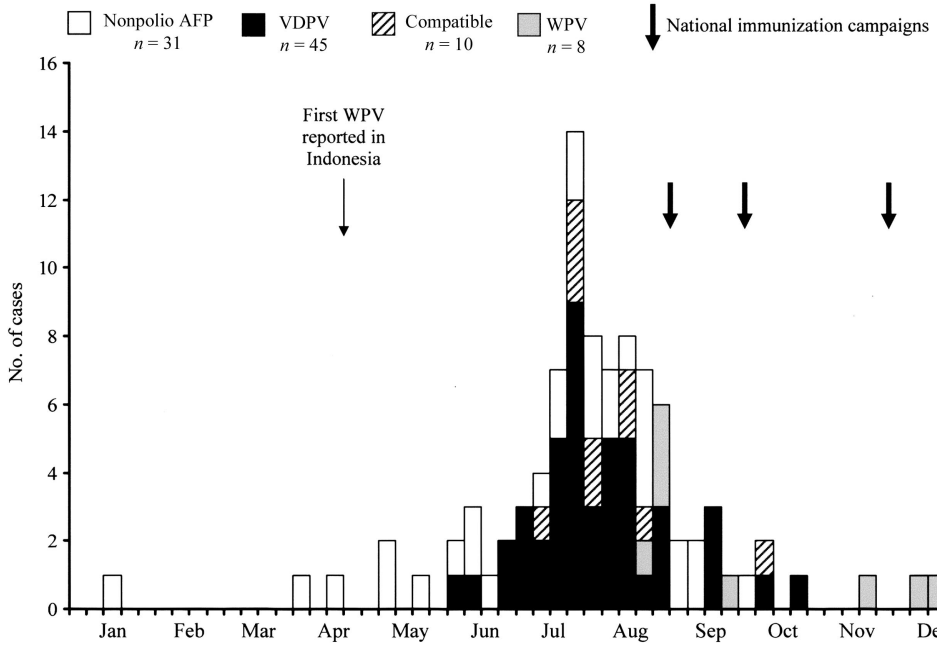

Figure 1. Classification and temporal distribution of patients with acute flaccid paralysis (AFP) on Madura Island, by week of onset of paralysis—Indonesia, 2005 ($n = 94$). VDPV, vaccine-derived poliovirus; WPV, wild poliovirus.

were sent to the Global Specialized Laboratory (Enterovirus Research Centre) in Mumbai, India, for further characterization by sequencing the VP1 coding region of the genome via automated cycle sequencing, by means of standard methods that have been described elsewhere [25].

Qualitative assessment of routine coverage and campaign coverage in high-risk areas. Because no recent vaccination-coverage surveys in Madura existed, we assessed the immunization status of children <5 years old by use of the following: (1) Indonesia government administrative coverage data for 2004 (aggregate data from the Ministry of Health, East Java Province, using the number of doses administered divided by the estimated target population); (2) vaccination status among children with nonpolio AFP in 2005 (data provided by the WHO, from case investigation forms for AFP cases for which the number of OPV doses is reported orally by parents), whose random selection allows their use as proxy for the general population; and (3) convenience surveys conducted in October 2005.

We conducted convenience surveys in the vicinity of VDPV case patients in the 4 districts of Madura and in 2 urban areas (Bangkalan and Sampang), with deliberate selection of poor, crowded, high-risk areas. In each household, information from caregivers for 1 child <5 years old was collected using a bilingual survey (English/Bahasa Indonesian) that was orally translated into Madurese by local health personnel. Instead of conducting a standard cluster survey, we interviewed an average of 5 households in each village or subvillage because (1) initial assessment showed that vaccination coverage was similar within residential clusters; (2) time and resource constraints (particularly imposed by the double language barrier and the necessity of daily training of new local staff) precluded visiting more households; and (3) we chose to prioritize gathering information over a larger area instead of precise coverage estimates.

RESULTS

Description of a VDPV outbreak on Madura. Between June and October 2005, 46 laboratory-confirmed type 1 VDPV cases were identified in Indonesia, 45 of which occurred on Madura (figure 1). Of the 45 Madura VDPV case patients, 21 (47%) were male (table 1). The median age was 2 years (range, 6 months–14

Table 1. Epidemiological and clinical characteristics of vaccine-derived poliovirus (VDPV), wild poliovirus (WPV), and polio-compatible case patients on Madura Island—Indonesia, 2005.

Characteristic	VDPV ($n = 45$)	WPV ($n = 8$)	Compatible ($n = 10$)
Male	21/45 (47)	5/8 (63)	5/10 (50)
Age, median (range), years	2 (0.5–14)	2.5 (1–10)	4 (1–8)
Children <5 years old	36/45 (80)	6/8 (75)	6/10 (60)
Fever	42/44 (95)	8/8 (100)	10/10 (100)
Asymmetry	21/45 (46)	1/8 (13)	2/9 (22)
Residual paralysis	29/45 (64)	4/5 (80)	7/9 (78)
OPV <3 doses	37/41 (90)	6/7 (86)	7/8 (88)

NOTE. Data are proportion (%) of case patients, unless otherwise indicated. Responses were missing on some case report forms. No significant difference between any groups for any characteristic were detected by 2-tailed χ^2 tests. OPV, oral polio vaccine.

years)—25 (56%) were 6–35 months old, 11 (24%) were 36–59 months old, and 9 (20%) were ⩾60 months old. Of 41 with known vaccination status, 25 (61%) reported having received zero doses of OPV, 12 (29%) reported 1 or 2 doses, and only 4 (10%) reported ⩾3 doses.

All case patients had acute onset paralysis, and 95% (42/44) presented with fever before the onset of paralysis. Paralysis was asymmetrical in 46% (21/45), and 64% (29/45) had residual paralysis 60 days after onset (table 1). Interviews of caregivers for 13 children with VDPV isolates did not identify recent travel to areas with WPV or VDPV circulation, clinical history suggestive of immunodeficiency, clinical signs of severe malnutrition, or history of intramuscular injections before paralysis. Suboptimal hygienic conditions were observed in all households, with a lack of latrines in half of the villages visited and with boiling of water for drinking reported by <40% of caregivers.

Even though VDPV cases were confirmed in all 4 districts on Madura, only 16 of 68 subdistricts of Madura were affected. A high proportion of cases appeared in clusters in the northern rural areas of the Bangkalan and Pamekasan Districts (figure 2). Only 6 occurred in the 22 most densely populated subdistricts. The overall attack rates for VDPV strains were 4.8/100,000 children <15 years old (range, 1.1–8.0 by district) and 11.4/100,000 children <5 years old (range, 2.1–17.7) (table 2). In the 16 affected subdistricts, the attack rates were 4.9/100,000 total population, 17.5/100,000 children <15 years old, 50.4/100,000 children <5 years old, and 72.1/100,000 underimmunized (<3 OPV doses) children <5 years old (table 2).

WPV cases in Madura. Because of the unique opportunity presented by the concurrent circulation of WPV and VDPV on Madura, we compared their clinical and epidemiological characteristics. Eight type 1 WPV cases were reported on Madura in 5 subdistricts across all 4 districts. The onset of paralysis was 28 August for the first case patient and 23 December for the last one (figure 1). Four WPV cases with onset during August and September were reported in Pamekasan and Bangkalan, where VDPV was circulating simultaneously (figure 2). In both districts, the onset of the last VDPV case was several weeks after the onset of the last WPV case (figure 2). The last 3 WPV cases in Madura (onset in November and December) were identified in Sumenep, in subdistricts without VDPV circulation (figure 2). Epidemiological and clinical characteristics of the 8 Madura WPV case patients differed little from those of VDPV case patients (table 1). Attack rates for WPV in the 5 affected subdistricts were 3.0/100,000 total population, 10.6/100,000 children <15 years old, 28.6/100,000 children <5 years old, and 40.9/100,000 underimmunized (<3 OPV doses) children <5 years old (data not shown).

Compatible cases. Ten AFP cases from 6 subdistricts were classified as being clinically compatible with poliomyelitis by the expert polio panel. The temporal and geographic distribution of compatible cases was more similar to that of confirmed VDPV cases than to that of WPV cases (figures 1 and 2). Eight occurred before the first confirmed WPV case; 8 occurred in subdistricts with no reported WPV circulation, and 9 occurred in subdistricts with reported VDPV circulation (figure 2).

Genetic characterization of VDPV. Genetic sequencing data on VDPV isolates were consistent with replication and likely circulation for up to ~2 years (range of VP1 divergence, 1.1%–2.2%). The earliest isolates represented at least 4 distinct genetic lineages in separate geographic clusters and were derived from a single initiating event that likely occurred sometime in 2004 (figure 2). All virus isolates showed discordant ITD results and had evidence of recombination with other species C enteroviruses in the noncapsid region, which is typical of cVDPV isolates (data not shown).

Immunization ascertainment. Since 2002, Indonesia has depended solely on routine immunization with tOPV. Provincial 2004 estimates for 3 tOPV doses were 96% for Madura (91%–99% by district) and 99% for the province of East Java. However, AFP surveillance data suggests that coverage in Madura was lower than those estimates and lower than in the rest of East Java. Of nonpolio AFP case patients <5 years old, only 30% (6/20) were fully immunized (⩾3 OPV doses) in Madura, compared with 79% (72/91) in the rest of East Java ($P < .00001$). In Madura, 45% (9/20) nonpolio AFP case patients had zero doses, compared with 4% (4/91) in the rest of East Java ($P < .0001$).

Convenience immunization assessments were conducted in 92 households—68 in rural areas (7 subdistricts) with VDPV cases and 24 in urban areas (2 subdistricts). Only 33% (29/87) of children between 4 and 59 months old reportedly received ⩾3 routine OPV doses, and 52% (47/91) received no OPV doses. These results, although not generalizable to the entire population in Madura, are consistent with coverage among nonpolio AFP case patients. We also detected higher coverage in urban areas than in rural areas, despite selecting poor, crowded neighborhoods in the urban areas (table 3). With regard to campaign coverage, 83% of the children surveyed received tOPV during the first round (30 August), and 87% received tOPV during the second round (27 September), with no significant difference between rural and urban areas (table 3).

Concern that vaccine could make the child sick was the most frequently reported barrier (71%) for routine immunization in urban settings (table 3). In rural areas, lack of knowledge about the need for or importance of immunization (38%) and distance to vaccination site (29%) were reported as frequently as concern that vaccine could make the child sick (32%). Barriers reported by the caregivers of 19 eligible children who did not receive OPV during one or both campaigns included the following: traveling at that time ($n = 4$); child was sick ($n = 3$), mother too busy ($n = 3$), child refused vaccine ($n = 1$), child had received routine OPV recently ($n = 2$), vaccination site too distant ($n = 2$), and parents unaware of the need for vaccination ($n = 1$).

AFP surveillance. The nonpolio AFP rate on Madura was 0.4/100,000 children <15 years old in 2003, 0.7 in 2004, and 3.3 in 2005, compared with the recommended standard of 1/100,000 [20]. An

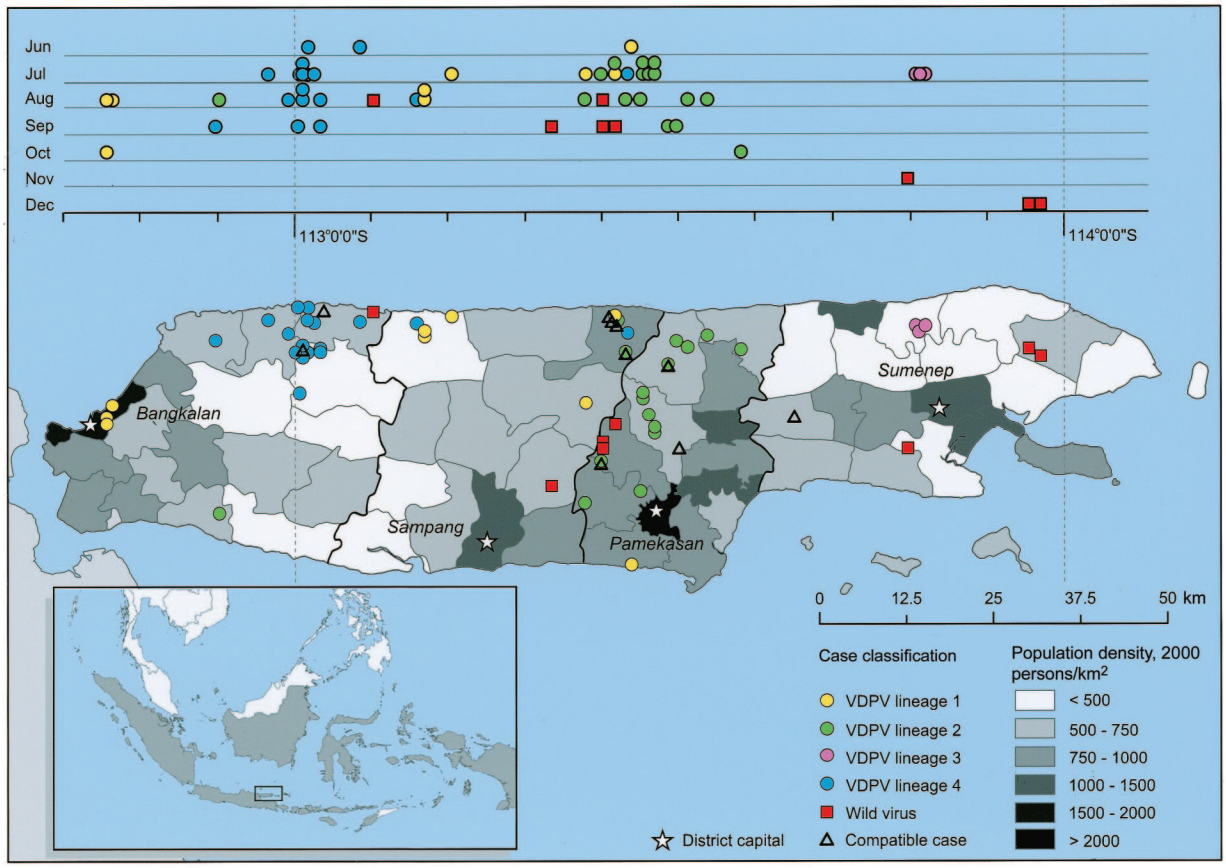

Figure 2. Vaccine-derived poliovirus (VDPV), wild poliovirus, and polio compatible cases on Madura Island, by location, date of onset, genetic lineage, and population density—Indonesia, 2005. The map was produced by the Center for International Earth Science Information Network at Columbia University, using input data from its Gridded Population of the World project (version 3). Administrative population source data were from 1990 and 2000 population censuses conducted by Badan Pusat Statistik (BPS), Indonesia (see http://www.bps.go.id/sector/population/table1.shtml for province [administrative 1 level] data). Subdistrict (administrative 4 level) population data for 2000 were purchased from the BPS. Administrative boundary source data were based on 2000 boundaries from BPS Statistics Indonesia, Statistical Services [http://www.bps.go.id].

active search conducted during the field evaluation in October 2005 identified 1 previously undetected AFP case.

Other indicators of AFP surveillance performance in 2005 were below WHO-recommended targets. The proportion of AFP cases from Madura with adequate samples between January and October was 68% (recommendation, ⩾80%). The nonpolio enterovirus isolation rate, a marker of laboratory performance and of the integrity of the reverse cold chain for specimen transport, was <1% (recommendation, ⩾10%). AFP surveillance performance was lowest in Sumenep district, which reported the fewest VDPV cases.

DISCUSSION

Low population immunity due to poor routine OPV coverage in rural areas was the major predisposing factor identified for the cVDPV outbreak on Madura. Absence of WPV circulation for more than a decade and the inadequacy of routine immunization services contributed to a buildup of susceptible children, especially in the remote rural areas of Madura. Poor hygienic conditions likely facilitated viral transmission. In addition, inadequate AFP surveillance may have delayed detection of cVDPV strains, enabling more widespread circulation for up to 2 years.

Madura had a much larger immunity gap than did the rest of East Java; almost half of Madura children had received no routine OPV doses, compared with 4% of children in the rest of East Java. The convenience survey suggested that, within Madura, the immunity gap in rural areas exceeded that of urban areas, because only 22% of rural children reported receiving ⩾3 OPV doses versus 65% of urban children, possibly explaining the preponderance of cVDPV case patients in the rural communities compared with the more densely populated urban areas. Intensified social mobilization efforts to improve knowledge of immunization benefits and to reduce the fear of side effects, coupled with a house-to-house strategy to reach children affected by barriers such as difficult access, travel, and busy caregivers, may improve coverage, especially in rural areas.

Our immunization assessment may not be representative of the entire Madura population because we selected a nonrandom

Table 2. Estimated paralytic poliomyelitis attack rates for vaccine-derived poliovirus (VDPV) on Madura Island, by district—Indonesia, 2005.

Category	Total population	Children			VDPV case patients		Attack rate for			
		<15 years old[b]	<5 years old[c]	Underimmunized[d]	All	<5 years old	Total population, per 100,000[e]	Children <15 years old, per 100,000[e]	Children <5 years old, per 100,000[f]	Underimmunized children, per 100,000[g]
District										
Bangkalan	850,679	238,190	79,113	55,379	19	14	2.2	8.0	17.7	25.3
Pamekasan	723,528	202,588	67,288	47,102	14	11	1.9	6.9	16.4	23.4
Sampang	792,843	221,996	73,734	51,614	9	9	1.1	4.1	12.2	17.4
Sumenep	1,016,935	284,742	94,575	66,202	3	2	0.3	1.1	2.1	3.0
Total	3,383,985	947,516	314,711	220,297	45	36	1.3	4.8	11.4	16.3
Category										
Affected subdistricts[h]	919,713	257,520	. . .	. . .	45	. . .	4.9	17.5	. . .	. . .
Affected subdistricts (<5 years)[i]	767,495	. . .	71,377	49,964	. . .	36	. . .	. . .	50.4	72.1

[a] Estimates for 2005 are based on 2000 census data provided by Badan Pusat Statistik Propinsi Jawa Timur (Board of Statistics Center of East Java Province).
[b] Estimated population 0–14 years old, derived by calculating 28% of the estimated total 2005 population.
[c] Estimated population 0–4 years old, derived by calculating 9.3% of the estimated total 2005 population.
[d] Estimated underimmunized children are children <5 years old who received <3 oral polio vaccine doses (70% by nonpolio acute flaccid paralysis data).
[e] Calculated by dividing the total no. of VDPV case patients by the total population.
[f] Calculated by dividing the no. of 0–4-year-old VDPV case patients by the population 0–4 years old.
[g] Calculated by dividing the no. of 0–4 year-old VDPV case patients by the susceptible population 0–4 years old.
[h] Population estimates are based on 2000 census data adjusted to 2005 (2000 census data plus 5%).
[i] Population estimates are based on 2000 census data adjusted to 2005 (2000 census data plus 5%) only for subdistricts with VDPV case patients <5 years old.

Table 3. Reported vaccination through routine immunization services and campaigns and knowledge and barriers to oral polio vaccine (OPV) immunization in rural and urban areas on Madura Island—Indonesia, 2005.

Category	Rural (n = 68)	Urban (n = 24)
Received OPV in August campaign	55/68 (81)	21/24 (88)
Received OPV in September campaign	60/68 (88)	20/24 (83)
⩾3 doses of routine OPV[a]	14/65 (22)	15/23 (65)
Zero doses of routine OPV	37/68 (57)	8/24 (35)
Reasons for not receiving routine OPV[b]		
Vaccine makes child sick	11/34 (32)	5/7 (71)
Didn't know they had to	13/34 (38)	0/7 (0)
Vaccination site far away	10/34 (29)	0/7 (0)
Mother busy/forgot it	6/34 (18)	1/7 (14)
Do you know children need immunization?	52/67 (78)	22/24 (92)
Is it hard to get routine immunization?	15/61 (25)	0 (0)
Do you know where to get routine immunization?	55/68 (81)	24/24 (100)
If yes, where do you get routine vaccination?[b]		
Posyandu	33/52 (63)	23/24 (96)
Health center/subcenter	6/52 (12)	1/24 (4)
Midwife	8/52 (15)	0/24 (0)
Chief village house	5/52 (10)	0/24 (0)

NOTE. Data are proportion (%) who answered yes. Responses were missing for some questions.

[a] Received routine OPV but unknown no. of doses in 4 surveys (1 urban and 3 rural).

[b] Open-ended questions with multiple choices available; only the most common reasons are presented.

sample. However, our routine-dose data were consistent with AFP data (e.g., 49% of survey children had received zero doses, compared with 45% in the AFP data). The absence of immunization cards or clinical records prevented verification of vaccination history for most individuals, although the potential recall bias is likely to be minimal for campaign doses because interviews were done soon after the campaigns.

This outbreak highlights the risk of cVDPV emergence and circulation in countries with high national immunization coverage but immunity gaps in subpopulations. Reasons for not vaccinating children vary among risk populations: lack of knowledge and difficult access to health care for the Madura rural population, marginalization for Roma communities in Romania [9], and religious beliefs for Amish communities in the United States [15]. These subpopulations are also at higher risk for WPV circulation after importation, as outbreaks in Roma and Amish communities have demonstrated [15, 26]. Madura was the first and most heavily affected area of WPV circulation in East Java, with 8 cases among 3 million people, compared with 2 cases among 37 million people in the rest of East Java. The presence of high-risk subpopulations may be missed when only administrative data are used to estimate coverage. Although government estimates suggested >90% coverage with 3 OPV doses in Madura, only 30% of nonpolio AFP case patients in Madura in 2005 had received ⩾3 doses, compared with 79% in the rest of East Java. AFP surveillance can help to identify high-risk areas for prioritization of routine and supplemental immunization efforts.

A second factor involved in the spread of cVDPV on Madura was the late detection of cVDPV circulation as occurred in Madagascar and The Philippines, where VDPV was circulating for up to 3 years before detection [8, 10]. Genetic sequencing demonstrated that some strains in Madura may have been circulating for as long as 2 years; cocirculation of 4 distinct lineages is consistent with widespread geographic circulation before detection. During 2003 and 2004, nonpolio AFP rates were below the goal of 1/100,000 children <15 years old and improved in 2005 because of increased awareness among health workers after WPV detection in other areas of Indonesia. The high proportion of inadequate specimens for AFP cases that were clinically compatible with poliomyelitis and the low nonpolio enterovirus isolation rate in Madura also suggest that some VDPV or WPV cases almost certainly escaped recognition.

The limited scope of the initial vaccination response may have contributed to the extent of the outbreak. The initial response in early August, after confirmation of the first 4 VDPV cases with onset in June, was limited to tOPV vaccination of ~19,000 children in the affected villages (9% of target children in those districts). Two national tOPV campaigns conducted at the end of August and September had coverage <90%. Furthermore, mOPV1, which has a 3-times higher protective efficacy against type 1 poliovirus than tOPV [27, 28], was not used until the November round.

Some have proposed that cVDPV strains may have lower virulence and attack rates than WPV strains [8] and, except for Hispaniola, prior cVDPV outbreaks have involved only a small

number of paralytic cases [3, 8, 14]. Because of cocirculation of both WPV and VDPV of the same serotype on Madura, this outbreak provided a unique opportunity to compare these viruses. Paralytic disease in this VDPV outbreak was not clinically or epidemiologically different from that caused by WPV. The attack rate for the VDPV outbreak on Madura Island (1.3/100,000 total population) is within the wide range of 0.1–52/100,000 total population reported in a review of WPV outbreaks during 1976–1995 [26], although the inability to precisely estimate susceptible population size and exposure limit the estimations of attack rates among those who are susceptible. In affected subdistricts, attack rates for VDPV were higher than those for WPV. In addition, although the last polio cases detected in Madura were WPV cases, within those districts where cocirculation occurred, the last polio cases detected were VDPV cases.

This outbreak demonstrates the need for polio-free countries to maintain high OPV coverage in high-risk subpopulations and in all districts, to prevent the spread of both endogenous cVDPV and imported WPV. Sensitive and timely AFP surveillance systems are essential to ensure quick identification of cVDPV and WPV emergence. When cVDPVs are detected, prompt investigation and an immunization response similar to that proposed for WPV importations are recommended [19]. The immunization response should be initiated within 28 days of confirmation; include at least 3 high-quality rounds of monovalent OPV specific for the poliovirus type; target a large number of children <5 years old in the affected and adjacent areas; and ensure high-coverage rounds, with house-to-house immunization and independent monitoring in high-risk areas [29].

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