After >10 years without detection of any cases of wild virus–associated poliomyelitis, a large outbreak of poliomyelitis occurred in Albania in 1996. A total of 138 paralytic cases occurred, of which 16 (12%) were fatal. The outbreak was due to wild poliovirus type 1, isolated from 69 cases. An attack rate of 10 per 100,000 population was observed among adults aged 19–25 years who were born during a time of declining wild poliovirus circulation and had been vaccinated with two doses of monovalent oral poliovirus vaccines (OPVs) that may have been exposed to ambient temperatures for prolonged periods. Control of the epidemic was achieved by two rounds of mass vaccination with trivalent oral poliovirus vaccine targeted to persons aged 0–50 years. This outbreak underscores the ongoing threat of importation of wild poliovirus into European countries, the importance of delivering potent vaccine through an adequate cold chain, and the effectiveness of national OPV mass vaccination campaigns for outbreak control.
The number of follow-up suspected poliomyelitis cases were reported. In late August the Ministry of Health requested assistance from the WHO in the investigation of the outbreak. From 1970 to 1995, national coverage of infants with the recommended schedule (1 dose of monovalent OPV or 3 doses of trivalent OPV by age 12 months) has ranged between 87% and 98%, with the exception of two periods when the vaccine supply was interrupted. In 1977, when vaccine importation from China ceased, coverage decreased to 40%. In 1990–1991, at the time of political transition, coverage declined to 80% (figure 1).

Immediate notification of clinical poliomyelitis cases to the Ministry of Health has been mandated by decree for >40 years. In 1994, the Ministry of Health established surveillance for acute flaccid paralysis, in keeping with the WHO-recommended polio eradication strategies [11]. The number of reported paralytic poliomyelitis cases decreased by the mid-1970s, and only one outbreak of poliomyelitis was detected in 1977–1978, following the abrupt decrease in coverage: 78 cases were reported, primarily from the capital city of Tirana and surrounding districts and among children 6–23 months of age. Surveillance data suggest that interruption of poliovirus transmission was probably achieved by the early 1980s. The last case of indigenous polio was reported in 1985. An additional five cases of vaccine-associated paralytic poliomyelitis were reported from 1986 to 1995 (figure 1) [12].

Because of the threat of wild poliovirus importation due to large-scale internal and external population movements beginning in 1991 [13] and the likely gap in population immunity among children resulting from recent problems in coverage and past problems with the cold chain, Albania conducted NIDs in April and May 1996. Approximately 350,000 children aged 2–59 months received two doses of OPV during the NIDs, for a reported coverage of 98% during each round. During the spring and early summer of 1996, an increasing number of suspected poliomyelitis cases were reported. In late August the Ministry of Health requested assistance from the WHO in the investigation of the outbreak.

Methods

Case ascertainment and investigation during the 1996 outbreak. Any case of acute flaccid paralysis without any other apparent cause was considered a suspected case of poliomyelitis. A confirmed case of paralytic poliomyelitis was defined as a case of suspected poliomyelitis meeting one or more of the following criteria: (1) poliovirus type 1 was isolated and characterized as wild, (2) residual paralysis was found at 60 days after onset of symptoms, or (3) the patient died or was lost to follow-up. In July 1996, the Institute of Public Health of the

Table 1. History of oral poliovirus vaccine (OPV) administration in Albania, by year, vaccine type, recommended schedule, and cold storage conditions, 1960–1996.

<table>
<thead>
<tr>
<th>Calendar years</th>
<th>Birth cohort age (y) in 1996</th>
<th>Vaccine type*</th>
<th>Total recommended doses of each vaccine</th>
<th>Routine schedule</th>
<th>Maximum interval (w) for OPV storage at peripheral level without refrigeration</th>
</tr>
</thead>
<tbody>
<tr>
<td>1960–70</td>
<td>26–36</td>
<td>MOPV 1, 2, 3</td>
<td>2†</td>
<td>. . .</td>
<td>1–12†</td>
</tr>
<tr>
<td>1971–77</td>
<td>19–25</td>
<td>MOPV 1, 2, 3</td>
<td>2‡</td>
<td>. . .</td>
<td>1–6‡</td>
</tr>
<tr>
<td>1978–81</td>
<td>16–18</td>
<td>TOPV</td>
<td>4</td>
<td>2, 4, 6, 18–24 mo</td>
<td>4</td>
</tr>
<tr>
<td>1982–85</td>
<td>11–14</td>
<td>TOPV</td>
<td>5</td>
<td>2, 4, 6, 18 mo; 5–6 y</td>
<td>4</td>
</tr>
<tr>
<td>1986–91</td>
<td>5–10</td>
<td>TOPV</td>
<td>5</td>
<td>2, 4, 6, 18 mo; 5–6 y</td>
<td>1</td>
</tr>
<tr>
<td>1992–96</td>
<td>0–4</td>
<td>TOPV</td>
<td>5</td>
<td>2, 4, 6, 18 mo; 5–6 y</td>
<td>≤1</td>
</tr>
</tbody>
</table>

* MOPV = monovalent oral poliovirus vaccine; TOPV = trivalent oral poliovirus vaccine.
† Campaign strategy: for children aged ≥2 months, MOPV 1, 3, and 2 were each given 4–6 weeks apart (MOPV 1 followed 4–6 weeks later by MOPV 3, and then 4–6 weeks later by MOPV 2). One year later, MOPV 1, 2, and 3 were given simultaneously.
‡ The interval may have varied by serotype of MOPV, based on the vaccine schedule noted above.
§ Campaign strategy: for children aged ≥2 months, MOPV 1, 2, and 3 were given 4–6 weeks apart (MOPV 1, followed 4–6 weeks later by MOPV 2 and MOPV 3). One year later, MOPV 1, MOPV 2, and MOPV 3 were given simultaneously.
¶ The interval may have varied by serotype of MOPV, based on the vaccine schedule noted above.
Ministry of Health convened a meeting in Tirana comprising district epidemiologists, infectious disease physicians, and pediatricians, and it instructed them to refer suspected poliomyelitis cases to the University Hospital, in Tirana. Hospital officials were advised to report all suspected poliomyelitis cases immediately to the Ministry of Health.

Clinical and epidemiological information on suspected cases was abstracted from medical records and/or obtained during interviews with case-patients; a standard case investigation form was used. To confirm the absence of cases in the year before the outbreak, hospital discharge data for 1995 and 1996 were reviewed to identify suspected cases in the neurology, infectious disease, and pediatric wards in the University Hospital, as well as in 11 (31%) of the 35 other district hospitals.

**Vaccination status.** Vaccination histories of patients with suspected poliomyelitis were obtained through review of vaccination registries, maintained since the beginning of the vaccination program, and/or vaccination cards, which have been provided to vaccinees since 1993. Patients were considered unvaccinated if no vaccinations were recorded on the local registry; vaccination history was considered unknown if the register could not be found. For patients <6 months of age, vaccination histories obtained from parents were considered valid.

**Laboratory methods.** Primary virus isolation and serotyping were performed by WHO-recommended standard methods [14]. Characterization of poliovirus isolates as vaccine-related or wild-type was conducted by ELISA with use of intratypespecific cross-adsorbed type-specific polyclonal antibodies [15]. Poliovirus characterization results were confirmed by partial genomic sequencing [16]. To determine the genotypic classification of poliovirus isolates, genomic sequences of the VP1/2A region were compared with a database of nucleotide sequences of contemporary wild polioviruses isolated in many different areas of the world [17].

**Results**

**Outbreak characteristics.** From April through November 1996, 143 cases of acute flaccid paralysis were reported in Albania, of which 138 (95%) met the definition of confirmed paralytic poliomyelitis. The first reported case of poliomyelitis occurred in a 12-month-old child with onset of paralysis on 17 April 1996, within 10 days after completion of the first round of the NIDs. In the second case, involving a 28-month-old child, onset was on 31 May. Onset of paralysis in the first two cases involving adults was on 26 May and 30 May, respectively.

An average of three cases of poliomyelitis per week occurred from the end of May until mid-August, when the number of cases increased to 7–9 per week. The epidemic peaked between 9 September and 13 October, with 13–15 cases reported weekly (figure 2). The last case involved a 32-year-old man, with onset of paralysis on 25 November. No additional cases of confirmed paralytic poliomyelitis prior to the first reported case (17 April) were identified through retrospective record review.

The first case was reported from the north-central district (Lac), with the next two cases, occurring within 3 days of one another, reported from nonadjacent northeast districts (Has and Dibra) bordering with Kosovo, Yugoslavia. Cases occurred in 27 (73%) of 37 districts, with the highest attack rates observed in the northeast and north-central districts (figure 3).

The median age of persons with paralytic poliomyelitis was 21 years (range, 1 month to 52 years); 107 (78%) of the 138 cases reported involved persons 11–36 years of age. The highest incidence (13 cases per 100,000 population) was reported among infants <1 year of age (figure 4). Among adults, the incidence was highest (10 per 100,000) for the 19–25 year age group (representing the 1971–1977 birth cohort). The incidence rates among the 11–14, 15–18, and 26–36 year age
groups were similar, ranging from 5.7 to 6.1 cases per 100,000. The lowest incidence rates were observed for the 37–51 year age group (1.3 per 100,000) and the 1–10 year age group (1.7 per 100,000) (figure 4).

Vaccination records were available for >80% of patients aged <18 years; among persons aged 19–36 years, vaccination histories were available for 30% (table 2). Among those aged 1–10 years and of known vaccination status, 82% had received three or more doses of OPV. Among those aged 11–18 years whose vaccination status was known, 93% had received three or more doses of OPV (table 2). None of the patients aged <1 year had received three or more doses of OPV. All of these patients were <6 months of age, and all but two had been born after completion of the second round of NIDs in May 1996.

**Virological investigation.** Isolation of wild poliovirus type 1 was first confirmed in a case of poliomyelitis on 16 September 1996, and by the end of the epidemic it had been isolated from a total of 69 (50%) of the 138 confirmed poliomyelitis cases. A vaccine-like poliovirus was isolated in the initial case. Genetic sequencing analysis of nine poliovirus isolates suggested that the wild poliovirus isolates responsible for the outbreak in Albania belonged to a genotype that originated in the Indian
subcontinent, although the sequence relationship did not prove conclusively that the virus had been imported directly from the subcontinent into Albania.

**Case fatality.** Sixteen (12%) of 138 patients with poliomyelitis died. The case-fatality ratio varied with age, with the highest risk of death observed in the 19–25 year age group. Seven (18%) of 33 patients aged 19–25 years and 5 (15%) of 33 aged 11–18 years died. In contrast, four (9%) of 44 patients aged >26 years died. No deaths were observed among those <10 years of age. Females were twice as likely to die as males; 7 (18%) of 40 females died, compared with 9 (9%) of 98 males. The median interval between onset of symptoms and hospitalization did not differ between fatal and nonfatal cases. More than two-thirds of the fatalities occurred during the first half of the outbreak. Among the first 69 consecutive cases, 11 (16%) were fatal, compared with 5 deaths (7%) among the subsequent 69 cases.

**Control efforts.** Two rounds of mass vaccination with OPV were conducted, during 7–14 October and 10–17 November 1996. A reported coverage of 81% and 88%, respectively, was achieved among persons aged 0–50 years. Twelve cases were reported from 14 October to 17 November, following the first round of the campaign, and only one case (involving a person not vaccinated in the mass campaign) was reported with an onset of 25 November, 8 days following the second round of the campaign.

**Discussion**

A large epidemic of paralytic poliomyelitis caused by wild poliovirus type 1 occurred in Albania from April through November 1996, >1 decade after the apparent interruption of indigenous wild poliovirus transmission. This epidemic was characterized by several unique features, including the following four. (1) There was a bimodal age distribution, with the highest incidence rates among infants <6 months of age and young adults. (2) Cases were reported in a majority of districts in the country and were not limited to a religious or ethnic subpopulation. (3) The overall case-fatality ratio was high (12%). (4) The outbreak started soon after NIDs that had targeted preschool-aged children. Epidemic transmission ceased abruptly following the OPV administration campaigns, which targeted the entire population <50 years of age and which achieved a coverage of >80% in the target population during each round.

The bimodal age distribution of reported poliomyelitis cases in this epidemic likely reflects historic deficiencies in the immunization program that resulted in widespread gaps in immunity among the young adult population. Children too young to be adequately vaccinated were also disproportionately affected. The variation in incidence among birth cohorts targeted by different vaccination strategies strongly suggests that certain strategies and differences in vaccine delivery led to differential gaps in immunity by birth cohort.

The highest incidence rates among non-infants were observed among persons aged 11–36 years (born 1960–1985), corresponding to the period when OPV, a thermolabile vaccine, may have been routinely stored at the peripheral level without refrigeration for up to 3 months. Within that period, the peak incidence among the 19–25 year age group may be due to birth at the time of (1) declining exposure to circulating wild poliovirus, (2) use of a two-dose monovalent OPV vaccination strategy, and (3) administration of OPV that was potentially exposed to ambient temperatures for prolonged periods.

The case-fatality ratio was high for an epidemic in the vaccine era, and is likely attributable to known greater severity of disease with increasing age at infection [18], as well as to difficulties in obtaining appropriate medical care.

The susceptibility gaps may be inferred from the age distribution of cases, but several serological studies provide direct evidence of prior high levels of poliovirus susceptibility among young Albanian adults. Serosurveys using a convenience sample of young adult Albanian immigrants found that 18% of those tested in Italy in 1991 [13] and 47% of those tested in

<table>
<thead>
<tr>
<th>Birth year</th>
<th>Age group in 1996 (y)</th>
<th>Total cases (n)</th>
<th>Valid vaccination histories: no. (%) of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1996</td>
<td>&lt;1</td>
<td>10</td>
<td>10 (100)</td>
</tr>
<tr>
<td>1992–95</td>
<td>1–4</td>
<td>5</td>
<td>4 (80)</td>
</tr>
<tr>
<td>1986–91</td>
<td>5–10</td>
<td>8</td>
<td>7 (87)</td>
</tr>
<tr>
<td>1982–85</td>
<td>11–14</td>
<td>19</td>
<td>17 (89)</td>
</tr>
<tr>
<td>1978–81</td>
<td>15–18</td>
<td>14</td>
<td>11 (78)</td>
</tr>
<tr>
<td>1971–77</td>
<td>19–25</td>
<td>38</td>
<td>14 (37)</td>
</tr>
<tr>
<td>1960–70</td>
<td>26–36</td>
<td>36</td>
<td>8 (22)</td>
</tr>
<tr>
<td>1945–59</td>
<td>37–51</td>
<td>8</td>
<td>1 (12.5)</td>
</tr>
</tbody>
</table>

NOTES: MOPV = monovalent oral poliovirus vaccine (OPV); TOPV = trivalent OPV.
* >30 days before onset of paralysis.
† Figures for years prior to 1978 represent percentage vaccinated with two doses of MOPV.
Greece in 1994 [19] lacked detectable antibodies to poliovirus type 1. Serosurveys conducted in Albania among persons born during the 1970s and early 1980s also provided evidence of 15%–17% levels of susceptibility to poliovirus type 1 (E. Diamanti, unpublished data).

A striking feature of this outbreak is that children aged 1–10 years were largely unaffected, in contrast to other recent outbreaks in the European region that have affected children, albeit primarily those unvaccinated or inadequately vaccinated [4, 6–8, 20]. Albanian children born from 1986 through 1991 (aged 5–10 years) appear to have been well protected by the routine vaccination program. The nearly 75% lower risk of poliomyelitis compared with that for the 11–18 year age group corresponds to a change in vaccine delivery: the period of OPV storage at peripheral levels without adequate refrigeration was reduced from 1 month to ~1 week. Other factors such as “catch-up” immunization may have provided additional protection to children in this age group. The few cases in the 1–4 year age group provide evidence of the effectiveness of NIDs targeted to children born during 1992–1995, a time of political transition during which the vaccine supply was interrupted.

The appearance of the first cases of the outbreak immediately after the NIDs, as well as the isolation of a vaccine-like poliovirus from the initial case, prompted confusion in the media as well as among some health care workers as to the etiology of this outbreak. Although excretion of vaccine virus by children or their household contacts following vaccination is expected, clusters of vaccine-associated paralytic poliomyelitis in association with OPV mass vaccination have not been reported [21]. The spread of this outbreak to neighboring countries, with poliomyelitis cases subsequently occurring in Greece and Yugoslavia (Kosovo region) [22], underscores the potential for rapid spread of poliovirus across political borders and emphasizes the need to maintain high immunity against poliovirus in all segments of the population. To allow timely, coordinated regional control efforts, suspected poliomyelitis cases need to be reported immediately.

Other outbreaks in Europe during the 1990s have occurred primarily among children because of (1) declining routine immunization coverage as a result of political and economic changes in eastern Europe [4, 20] or (2) low OPV coverage in ethnic subpopulations [6–8, 23] or among unvaccinated adults in religious groups whose members object to vaccination [24]. The outbreak in Albania represents an unusual convergence of several factors that created conditions for nationwide epidemic transmission of an imported wild poliovirus: (1) the accumulation of a large susceptible population due to problems with delivering potent vaccine during years with low or no wild poliovirus exposure; (2) limited internal and external population movement during this same time, which prevented introduction and circulation of wild poliovirus; and (3) following the opening of national borders in 1991, increased opportunities for poliovirus introductions from reservoirs in Asia and central Europe, into (4) a country with a poor sanitation infrastructure.

The poliomyelitis outbreak in Albania demonstrates that the absence of poliomyelitis cases for many years does not preclude the existence of substantial gaps in immunity. Although the combination of conditions precipitating the Albanian outbreak are unlikely to be present elsewhere, other countries in the region should evaluate available data to identify high-risk populations and determine the need for focused supplementary immunization. Furthermore, surveillance for wild poliovirus must be enhanced for rapid detection of suspected poliomyelitis cases following any importation of wild poliovirus, so that Europe may be certified as polio-free by the year 2000.

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References