In 1988 the World Health Organization (WHO) declared its commitment to the goal of global eradication of poliomyelitis by the year 2000, generating new enthusiasm in pursuing this objective worldwide. The nations involved are supported by a coalition of partners, including Rotary International, Centers for Disease Control and Prevention of Atlanta, Ga., UNICEF, and the WHO itself. Interventions in countries in which poliomyelitis is still endemic are also supported by the authorities of numerous countries free from this disease.

According to WHO data (29), 35,251 cases of poliomyelitis were reported around the world in 1988, 8,635 in 1994, and 6,197 in 1995, the last year for which complete data are available. The last figure demonstrates an 82% decrease of the number of cases since 1988. In 1994 the International Commission of Certification of Eradication of Poliomyelitis declared the Americas polio free (30), and in 1995 no case was reported in 150 countries (29). The vast majority of the cases reported were in developing countries in which only one of the paralytic forms that occur in reality. A WHO estimate put the true number of new cases of paralytic poliomyelitis at 80,000 in 1995. The incidence rates in east Mediterranean countries are among the highest, and in 1995 12% of all the cases reported worldwide were in these countries.

Before 1964, when the oral Sabin polio vaccine (OPV) became available, there were on average 3,000 cases of paralytic poliomyelitis in Italy each year (26, 27), with a mortality rate of around 10% (25). The permanent sequelae of this disorder account for an important number of paralyzed subjects in the present Italian population. Immediately after the introduction of the oral vaccine, the incidence of this terrible disease fell drastically, so the number of cases reported in the last decade can be counted on one hand (4, 16, 17). Despite this, poliomyelitis, unlike smallpox, still has not acquired the status of a historical viral disease.

In recent years, great alarm has been generated by outbreaks of paralytic poliomyelitis in vaccinated populations in which the levels of immunity against poliovirus are not adequate or not controlled. For example, epidemics were observed in Finland in 1984, Senegal and Brazil in 1986, and Israel and Oman in 1988, all countries in which vaccination is widely deployed. Four epidemics were reported between 1991 and 1992. The first, in 1991, was in Bulgaria, which uses oral vaccination. Forty-three subjects developed paralytic type 1 polio; 88% of them belonged to a nomad community and had not completed or even started a vaccination schedule (31). The second epidemic occurred in The Netherlands, where inactivated polio vaccine (IPV) is used, and involved 68 patients with type 3 poliovirus, members of the Amish community which refuses vaccination and which in the past (1978–1979) had already figured in a similar outbreak of polio type 1 (11, 32). The third epidemic was in Jordan, where in the winter of 1991–1992 flaccid paralysis was observed in 55 patients and confirmed as acute poliomyelitis type 1 in 32 (56%). All 55 were under 5 years of age, and half of them were still not immunized, although the health authorities estimated that 95% of children of that age had received at least two doses of vaccine following a national vaccination day (33). Poliovirus had presumably been imported by the numerous refugees arriving in Jordan from the area involved in the Gulf War. Lastly, in Malaysia—where OPV is used, vaccination coverage is over 90%, and no cases of poliomyelitis had been reported since 1985—three cases of paralytic poliomyelitis occurred in 1992 in a group of religious fundamentalists who refused any form of vaccination (34).

A series of seroepidemiological investigations have been performed, particularly in the countries where epidemics have occurred, to check the immune titer of the populations involved. The serological data obtained in different series indicate a gap in immunity against polioviruses, especially type 3 (10, 18, 28, 35). One particularly important finding was the wide antigenic variations detected in the wild poliovirus strains isolated in Israel and Finland with respect to the strains used in vaccines.

Other methods useful in monitoring the epidemiological situation, although less reliable than serology, consist of surveys of subclinical infections and detection of polioviruses in the environment. The presence of subclinical infections is determined by testing stools for the virus; this is not an easy investigation, because of the need for cell cultures and the practical difficulty of checking a significant number of samples.

The last cases recorded in Europe, apart from those in Bulgaria in 1991 and the Netherlands in 1992–1993, were epidemics in the Russian Federation in 1995 and Albania in 1996. The vaccination rate has fallen in both countries, for obvious political and economic reasons (36).

As already mentioned, in Italy the situation is excellent as regards paralytic poliomyelitis. For this reason and also because of the arrival of devastating new viral diseases, epidemiological research on polioviruses generates little interest and few or no funds. However, as wild polioviruses continue to circulate in populations with which our countries maintain numerous links (business, tourism, immigration), and because the recent epidemics suggest that it is better not to rest on one's laurels, the Milan University Institute of Virology decided to undertake new investigations in the field of polioviruses, with the partial support of the Lombardy region health authorities.

A serological study (7) on adolescents and young adults who had completed a regular poliomyelitis vaccination schedule demonstrated that 10 to 15 years after the end of the schedule the antibody titers could be considered good for poliovirus types 1 and 2 but not poliovirus type 3; antibodies to type 3 were not detected in 13 to 20% of the subjects examined (7). The problem of subjects who are seronegative years after vaccination is interesting and important. Two hypotheses can be formulated: a lack of take of the vaccine strains or a decline of...
antibody to undetectable levels in the first 10 years after vaccination. In the first case the subjects would be true negatives and would be susceptible to the strain against which antibodies were not demonstrated. In the second hypothesis, the subjects would be false negatives who might still be resistant to a paralytic form despite the absence of detectable serum antibodies. To test the above two hypotheses, a series of investigations were performed in which specific immunoglobulin M (IgM) antibodies were sought by indirect immunofluorescence after administration of a booster OPV dose to seronegative adolescents. The demonstration of IgM would indicate a primary response (true negative subjects before the booster); the absence of IgM would indicate a secondary response (false negatives before the booster). Table 1 lists the results of testing for specific IgM after a booster dose in all adolescents found to be seronegative in the above-mentioned investigation (7). Although these subjects came from two cohorts with a total of 188 subjects, the number of true negatives 10 years after vaccination was negligible for poliovirus types 1 and 2 and about 10% for poliovirus type 3. Further studies of larger series are needed. Viral excretion in stools was monitored in these subjects and on the basis of the results of some serological investigations are performed annually in Poland. The demonstration of low antibody prevalences led to the decision to administer additional boosters. The vaccination schedules have changed over time as follows: 1975 to 1980, three doses in the first year of life plus a fourth dose at the end of the second year; 1981 to 1989, a fifth dose at 6 to 7 years; since 1990, a sixth dose at 11 to 12 years. Also in Israel, following the previously mentioned epidemic of paralytic poliomyelitis (35) and on the basis of the results of some serological investigations (12), since 1989 it has been considered appropriate to administer booster doses of OPV at 6 to 7 years and 16 to 17 years (9). A similar schedule has also been adopted in the United States, starting in 1997 (5, 6).

As the strategies suggested by the WHO for the eradication of poliomyelitis (29) include surveillance of acute flaccid paralysis, in December 1996 our Institute of Virology set up a regional acute flaccid paralysis surveillance network, in accordance with the National Health Service’s desire to obtain the certification of “polio-free country” for Italy. A total of 13 neurology and 14 pediatric departments are involved, and each report of acute flaccid paralysis is followed by an accurate diagnostic ascertainment performed by our laboratories. In this way it is possible to study the cases of vaccine-associated paralytic poliomyelitis and to demonstrate any circulation of wild strains promptly.

In polio vaccination, the debate about inactivated versus live, attenuated vaccine has been going on for a long time. A few countries have opted for IPV, and others, the majority, have opted for OPV. The question of the safety, immunogenicity, herd immunity, cost, and practicality of the Sabin and the Salk vaccines was reviewed by Beale (4), who came to the conclusion that both vaccines present notable advantages and that neither was without problems and drawbacks. Referring to the study by McBean and Modlin (13), Beale (4) also considered the sequential use of the two vaccines with the aim of obtaining the advantages of the oral vaccine (especially immunity at the mucosal level) while avoiding the risk of paralysis associated with this formulation. Although the risk is minimal, it exists, and it appears to be related to the administration of the first dose of the vaccine (4). For this reason, in all the sequential schedules, IPV is always administered first. The new regulations on poliomyelitis vaccination in the United States

Other seroprevalence investigations have been performed on particular populations: drug addicts, including a human immunodeficiency virus (HIV)-positive subgroup, who had disturbingly high values of seronegativity (23); children 3 years after bone marrow transplantation, of whom 75% were seronegative for at least one poliovirus type and 30% were seronegative for all three types, suggesting yet again the usefulness of administering a booster dose (19); and children of HIV-positive mothers. The last population is increasing with the spread of HIV infection, and polio vaccination of such children represents a problem. Italy, like other countries including the United States, has decided to use Salk IPV. As information on the immunizing efficacy of this and of other vaccines in children infected with HIV was scanty, a study was performed to evaluate the antibody response after polio vaccination in children born to seropositive mothers (2). In this admittedly small series, HIV-infected children responded less well than those not infected to IPV, particularly type 3.

The importance of serological investigations on the immune status of populations with regard to polioviruses is illustrated well by Poland’s vaccination policy (37). In this country, which has used trivalent OPV since 1975, the last wild poliovirus was isolated in 1984, and therefore the eradication of poliomyelitis appears within sight. Despite the difficult economic situation, serological investigations are performed annually in Poland. The demonstration of low antibody prevalences led to the decision to administer additional boosters. The vaccination schedules have changed over time as follows: 1975 to 1980, three doses in the first year of life plus a fourth dose at the end of the second year; 1981 to 1989, a fifth dose at 6 to 7 years; since 1990, a sixth dose at 11 to 12 years. Also in Israel, following the previously mentioned epidemic of paralytic poliomyelitis (35) and on the basis of the results of some serological investigations (12), since 1989 it has been considered appropriate to administer booster doses of OPV at 6 to 7 years and 16 to 17 years (9). A similar schedule has also been adopted in the United States, starting in 1997 (5, 6).

### Table 1. Results of testing for specific IgM after a booster dose of OPV in subjects seronegative 10 years after completing a poliomyelitis vaccination schedule (8)

<table>
<thead>
<tr>
<th>Days since booster</th>
<th>No. of subjects positive for IgM/no. vaccinated</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Schedule 1&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Polio 1</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>0/3</td>
</tr>
<tr>
<td>30</td>
<td>0/2</td>
</tr>
<tr>
<td>Polio 2</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>1/3</td>
</tr>
<tr>
<td>30</td>
<td>1/3</td>
</tr>
<tr>
<td>Polio 3</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>5/11</td>
</tr>
<tr>
<td>30</td>
<td>4/10</td>
</tr>
</tbody>
</table>

<sup>a</sup> Monovalent vaccine doses plus two trivalent vaccine doses (used until 27 February 1972).
<sup>b</sup> Four balanced trivalent vaccine doses (used since 28 February 1972).
<sup>c</sup> Polio 1, 0; polio 2, 1; polio 3, 16.
(5, 6) involve three schedules. The one recommended is that in which two doses of IPV are administered at 2 and 4 months of age and two doses of OPV are administered at 12 to 18 months and 4 to 6 years (the third dose may be administered as early as 6 months of age); the primary aim is to reduce the number of cases of vaccine-associated flaccid paralysis.

In view of the current epidemiological situation, Italy should also consider the possibility of adopting a sequential vaccination schedule. This would reduce the possibility of postvaccination paralysis in immunized subjects while ensuring elevated antibody titers that would help maintain adequate long-term cover. The overall additional costs would not be high, considering the undeniable advantages in terms of disease avoided (15). With the aim of optimizing compliance with vaccination, it is important to minimize the side effects. The need for keeping the immune status of populations always under control, possibly with the use of additional booster doses, correlating these investigations with surveillance of the environmental spread of enteroviruses (24), must be emphasized.

REFERENCES


