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Persistence of poliovirus-neutralizing antibodies 2–16 years after immunization with live attenuated vaccine. A seroepidemiologic survey in the mainland of Venice.

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SUMMARY

A seroepidemiological survey was conducted on subjects who had received a full vaccination course with live attenuated poliovirus 2–16 years before. For strains 1 and 2 prevalence of seropositives and median values dropped gradually during the first 10 years; strain 3 showed a much earlier decline. Environmental displacement of wild poliovirus by the attenuated, less immunogenic strain might eventually induce a 'gap', should complacency hamper needed vaccination efforts.

INTRODUCTION

In developed countries the success of mass vaccination programs against poliomyelitis was marked by the virtual disappearance of paralytic disease and changes in the epidemiological distribution of the few remaining cases of poliomyelitis.

In the United States, during the pre-vaccine era, almost 90% of cases occurred in children under 5 years of age (Hopkins, Dismukes & Glick, 1969), probably because widespread circulation of the wild strain had induced an immune response in the majority of the general population. After extensive vaccination efforts, however, the distribution of cases of poliomyelitis shifted to older ages, and young adults became the group more affected, with about 50% of clinically ill patients (Moore *et al.* 1982).

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In Italy, however, with an equally successful vaccine the age distribution of paralytic cases did not change appreciably (Istituto Centrale di Statistica, 1976. 1980; Giannico, 1983). The most likely explanation for this difference lies in the poor sanitation in underprivileged communities where wild strains can continue to circulate because of incomplete vaccination coverage.

Since 1961, a small number of poliomyelitis cases has been ascribed to the attenuated 'Sabin' live poliovirus (OPV) (Hopkins, Dismukes & Glick, 1969). It has been estimated that one case of vaccine-induced paralytic poliomyelitis occurs for every five to ten million doses administered (Weekly Epidemiological Record, 1982; World Health Organization Committee on Poliomyelitis, 1976), and confirms the remarkable safety of the vaccine.

According to recent reports, vaccine-associated paralysis accounted for 50% of all poliomyelitis cases in the United States, while in Italy the corresponding percentage has been estimated as less than 10% (Campello, Dal Molin & Majori, 1985; Giannico, 1983).

Live attenuated poliovirus, excreted in the environment, has displaced the wild strains in many areas. As a consequence, the number of inadequately immune adults is going to increase, due to the lower immunogenicity of the attenuated vaccine strains.

Several studies (Melnick, Burkhardt & Taber, 1969; Rasmussen *et al.* 1973; Rousseau *et al.* 1973) have also reported that vaccine-induced humoral immunity declines substantially in the first 5 years following completion of a course of OPV. With time, therefore, adults might be at an increased risk, regardless of vaccination status.

In an unpublished study in Italy, Moschen *et al.* (1985) tested a group of 232 women of fertile age, living in the mainland adjacent to Venice for the presence of detectable serum antibodies at a titre of 4 against the three strains of poliovirus. Overall, unvaccinated subjects had a slightly higher prevalence of seropositivity as well as higher geometric mean titres than the women who had undergone a full vaccination course 15–20 years before. Particularly worrying was the lack of humoral protection against poliovirus 3, found in 23.0% of vaccinated and in 14.9% of unvaccinated study participants. This paper reports the results of two seroepidemiologic surveys on the sera of young persons taken 2–16 years after completion of a full vaccination course with live attenuated poliovirus vaccine. The purpose was to assess whether herd immunity was lacking in an area where good sanitation and widespread vaccination might have stopped the endemic circulation of wild poliovirus (Melnick, Durkhardt & Taber, 1969).

MATERIALS AND METHODS

Study population

Two different groups were studied. In 1976 a prospective study was started on a cohort of 276 children of both sexes, initially attending a public nursery on the mainland near Venice 2–4 years after completion of a full course of OPV. A serosurvey was done to assess the prevalence and titre of antibodies against the three strains of poliovirus. The survey was repeated on the same group in 1983: 197 (71.9%) youngsters were traced and participated in the second survey.

Table 1. *Percentage of subjects with neutralizing antibody titres < 4 against poliovirus strains 1, 2 and 3 at varying intervals after completion of a full vaccination course with live, attenuated vaccine*

	Time, in years, from vaccination				
Poliovirus strain	2	3	4	9–11	16
1	3.8	5.6	2.2	9.6	11.1
2	6.4	1.8	3.3	4.5	11.8
3	14.1	17.9	24.4	28.4	29.1

Table 2. *Median values of neutralizing antibodies (only those subjects with titres ⩾ 4) against poliovirus 1, 2 and 3 at varying intervals after completion of a full vaccination course with live attenuated vaccine*

	Time, in years, from vaccination				
Poliovirus strains	2	3	4	9–11	16
1	16	16	16	16	8
2	32	32	32	16	8
3	16	8	8	8	4

The second group consisted of 958 young males resident in the same area as the other subjects. They had undergone medical examinations in 1983 prior to compulsory military service. All had completed a full course of OPV 16 years earlier. (In Italy OPV vaccination became compulsory in 1964.)

Sera

Serum neutralization tests were employed according to the technique recommended by Hoskins (1969), utilizing 100 TCID50 from strains Brunhilde, MEF-1, and Saukett, for poliovirus strains 1, 2 and 3 respectively, in Hep-2 cells (Flow Labs, Scotland). Sera were serially diluted twofold from 1/4 to 1/512.

RESULTS

Table 1 shows the proportion of subjects without detectable antibodies (titre < 4) by type of poliovirus tested and by time, in years, from the completion of the full vaccination course. The results for antibodies to polioviruses 1 and 2 showed similar patterns, while titres against poliovirus 3 suggested either a lower primary immunogenic response or a faster decrease with time. Assuming the young draftees in the second group were part of the same cohort, the decrease in humoral immunity seems to continue after the first 10 years.

Median values from positive (> 4) titres (Table 2) confirmed the previous findings, with type 2 being the the most immunogenic and inducing higher titres while type 3 attenuated poliovirus appears to induce the lowest values, with a faster decrease in protective titres.

In the group of children followed prospectively, the second assessment 7–11 years after the completion of a full vaccination course showed a consistent

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(twofold or more) increase in titres in 21 cases (10.6%) for poliovirus 1, 13 (6.5%) for poliovirus 2 and 9 (4.5%) for poliovirus 3.

DISCUSSION

In epidemiological surveys of poliovirus antibodies, seropositivity rates in a population reflect the coverage by immunization programmes as well as the occurrence of chance environmental infection: the relative contribution of each variable depends therefore on local conditions and may be only empirically estimated.

As part of a study of marine pollution in the Gulf of Trieste, near Venice, a virological investigation of shellfish yielded only live attenuated strains of poliovirus (Majori, Campello & Cattaruzza, 1981); conversely, the small number of cases of poliomyelitis in South Italy is usually found, by virological assessment of the cases and environmental studies, to be due to wild strains.

Comparing the results of our study with those reported by Piazza *et al.* (1983) from the Naples area, the differences in seroepidemiologic status are clear. In the area of Venice in North Italy, there is good vaccination coverage of the infant population, and the children have high initial antibody titres against poliovirus. With time, these titres show a slow yet steady decline. The opposite seems to happen in South Italy, where seropositive adult cohorts have a higher median antibody level than younger ones. This is probably due to the booster effect of the wild poliovirus, which is still endemic in South Italy, coupled with less satisfactory vaccination rates in infants and young children.

Differences in antibody titres were particularly marked for poliovirus 3: for which the attenutated vaccine strain is the least immunogenic yet the most likely to revert to neurovirulence (*Weekly Epidemiological Record*, 1982).

From a public health viewpoint, sufficient herd immunity is provided by a 60% coverage with Sabin vaccine (Nightingale, 1977), compared with 80% with Salk vaccine (Bottiger *et al.* 1972), and therefore there should be no cause for immediate concern. However, it might now be time to reassess both the number and the schedules of vaccination. Clearly, a booster dose should be administered to young adults living in areas where wild poliovirus is not endemic and to travellers to the tropic (Melnick, 1982).

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