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Use of Killed Poliovirus Vaccine in a Routine Immunization Program in West Africa

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Combined diptheria-tetanus-pertussis (DTP)-killed poliovirus vaccine was used (along with bacille Calmette-Guérin, measles, yellow fever, and smallpox vaccines) in a routine immunization program in a rural area of Senegal. A control group in a neighboring region received DTP vaccine without poliovirus vaccine. All immunizations were given at two sessions six months apart by a small mobile health team led by a nurse. Six months after the second dose of DTP-polio vaccine, 97.4%, 97.7%, and 90% of subjects two to eight months old at the start had detectable antibody to poliovirus types 1, 2, and 3, respectively. In the control group, 50%, 38%, and 80% of such subjects had antibody to poliovirus types 1, 2, and 3, respectively, acquired by natural infection during the study year. An average of 3.9 cases of paralytic poliomyelitis (range, one to 13) were observed annually at one dispensary in the test region from 1966 through 1979. From 1980 through 1982, since the immunization program has been in effect, only one case has been observed (in a nonimmunized child).

The eight French-speaking countries of West Africa (Benin, Ivory Coast, Mali, Mauritania, Niger, Senegal, Upper Volta, and Togo) are implementing Expanded Programmes on Immunization (EPI) as defined by the World Health Organization (WHO). Some of these programs have been successfully established in urban areas that can provide fixed centers with adequate refrigeration equipment and well-qualified staff. Only 15%–20% of the population lives in such areas, however; 80%–85% of the population has no practical access to medical care. It is therefore important to develop effective immunization programs for large rural populations.

The West African countries, through their Organisation pour la Cooperation et la Coordination pour la lutte contre les Grandes Endémies (OCCGE), have given this goal a high priority and requested an evaluation of an immunization program that provides all EPI vaccinations in two field visits four to eight months apart. We placed particular emphasis on evaluating killed poliovirus vaccine, because reports from African countries [1–3], India [4], and Israel [5] have documented low efficacy of oral, live poliovirus vaccine when used in routine immunization programs in tropical and subtropical countries. This problem has been overcome in some areas by administering oral, live poliovirus vaccine in annual mass campaigns, but such campaigns are not practical in West Africa. We report here an evaluation of killed poliovirus vaccine used in a routine immunization program.

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Methods

A voluntary immunization program was begun in Kolda, a rural region of Senegal, in January 1980. The population of this area had not received vaccinations for some time. All children two months to four years old were initially included, although the target population for first immunizations in the routine program includes primarily infants two to eight months of age. The study reported here was carried out between April 1980, and April 1981.

Killed poliovirus vaccine was prepared by the Institut Mérieux (Lyon, France) in accordance with the methods of van Wezel [6]. This vaccine was standardized against a reference vaccine [7] to con-

Table 1. Immunization schedules in Kolda and Sedhiou, Senegal. The second immunization session occurred six months after the first.

Group	Age at first session (months)	Immunization	
		First session	Second session
Kolda	2–8	DTP–polio BCG	DTP–polio Measles Yellow fever Smallpox
	9–51	DTP–polio BCG Measles Yellow fever	DTP–polio Smallpox
Sedhiou	2–51	DTP BCG	DTP Smallpox

NOTE. Smallpox vaccine was initially used as a marker for completion of vaccination; this practice is no longer in effect. The control group received killed poliovirus, measles, and yellow fever vaccines at the end of the study year. Abbreviation: DTP = diphtheria-tetanus-pertussis.

tain 40, 4, and 16 D-antigen units of poliovirus types 1, 2, and 3, respectively. It was administered in the combination diphtheria-tetanus-pertussis (DTP)-polio vaccine.

The vaccination team consisted of four persons led by a qualified nurse working under the supervision of a physician in Kolda. Vaccines were kept refrigerated at 4 C in Kolda and carried to the field by the vaccination team using a vehicle equipped with a portable refrigerator. Temperature monitoring was carried out as part of a WHO cold-chain evaluation program. Vaccines were administered by jet injector, except for intradermal BCG injected by needle.

Table 2. Comparison of test group (Kolda) and control group (Sedhiou) at the beginning of the study.

Parameter	Test group	Control group
Age (months)		
2–8	120	116
9–15	115	116
16–24	119	108
25–51	120	106
Total	474	446
Sex		
Male	222	205
Female	252	241
Nutritional status*		
Satisfactory	67%	60%
Intermediate	28%	35%
Poor	5%	5%
Splenomegaly	16.5%	13.6%
Hepatitis B antigen–positive	9%	10%
Mortality data		
Live births per mother	4.1	3.8
Surviving children per mother	2.8	2.6
Child mortality†	30.5%	30.9%

* See Methods.

† Deaths of children younger than 10 years, as reported by mothers.

Table 3. Percentage of children in the test group (Kolda) and control group (Sedhiou) with detectable poliovirus antibody (titers, ≥1:4) at the beginning of the study.

Age (months)	Percentage with antibody to indicated poliovirus type					
	Type 1		Type 2		Type 3	
	Test	Control	Test	Control	Test	Control
2–8	27.6	35.5	35.7	27.9	39.8	33.3
9–15	25.2	35.9	21.4	24.6	32.9	47.4
1[illegible] 24	44.4	42.9	26.0	25.7	32.2	52.4
[illegible]–51	61.8	62.8	66.1	58.7	61.7	61.7

During the one-year study period, ~10,000 children received a full set of vaccinations. Among these, ~500 children were selected for detailed clinical and serologic studies. A control group consisting of ~500 children was selected from Sedhiou, a neighboring area where DTP was given but no polio vaccine. Immunization schedules for the different groups are shown in table 1. Blood was obtained at the time of initial vaccination and again 12 months later (six months after the second immunization session) from 474 children in the test group and 449 children in the control group. A physician examined these study subjects at the initial vaccination session to evaluate nutritional status and splenomegaly. Physical parameters (age, weight, height, skin-fold thickness) were compared with NCHS (National Center for Health Statistics, Rockville, Md., USA) norms [8]: poor nutritional status was defined as values <70% of the norm, intermediate nutritional status as values 70%–80% of the norm, and satisfactory nutritional status as >80% of the norm. Hepatitis B antigen was assayed in the initial serum sample. Titers of poliovirus antibody were determined by virus neutralization tests performed at the Rijks Instituut voor de Volksgezondheid using Vero cells in microtiter plates and starting with a 1:2 serum dilution.

Results

The test and control groups were comparable with regard to age, sex, nutritional status, malaria

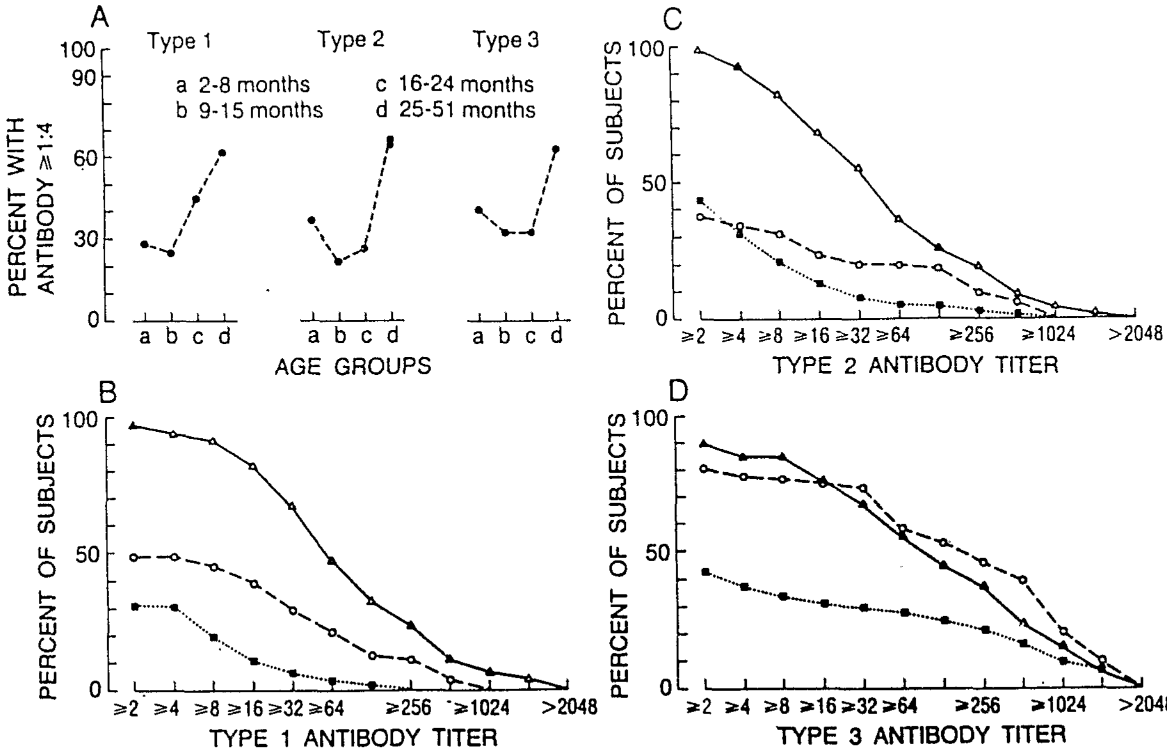

Figure 1. *A*, Percentage of children (by age groups) with titers of poliovirus antibody ≥1:4 at the start of the study (combined data from test and control groups). *B*, *C*, and *D*, Percentage of infants (two to eight months old at the start of the study) with the indicated titers of antibody to poliovirus types 1, 2, and 3, respectively. Antibody titers are shown as reciprocal of serum dilution; ■· · · · ·■ = test and control groups combined at start of study; O- - - - -O = nonvaccinated controls 12 months after start of study; Δ——Δ = vaccinated children 12 months after start of study (six months after second dose of killed poliovirus vaccine).

(splenomegaly), and exposure to hepatitis B (table 2). The general health of the two populations was equivalent, as indicated by mortality data. The initial titers of poliovirus antibody did not differ significantly between the test and control groups (table 3); these data are therefore combined in subsequent analyses on the initial bleeding.

The age distribution, among all subjects, of those with poliovirus antibodies (titers ≥1:4) at the start of the study is shown in figure 1A. Maternal antibody against each of the three poliovirus types is present in 30%–40% of two- to eight-month-old infants; these levels decline until after 16 months of age, when the effect of natural infection with circulating wild poliovirus becomes evident. Sixty percent of two to four year olds have antibody to at least one of the three poliovirus types, a finding that indicates a high incidence of natural poliovirus infection in the study areas before the start of the immunization program.

The distribution of antibody titers in vaccinated and control groups at the beginning and end of the study are shown in figures 1B, 1C, and 1D. Data for the two- to eight-month age group are shown here since that is the primary target population of the routine immunization program; similar responses were observed in all age groups. For both types 1 and 2, the distribution patterns are clearly different in the vaccinated and control groups. Among vaccinated children, 97.4% and 97.7%, respectively, still have detectable antibody against poliovirus types 1 and 2 six months after the second dose of vaccine. Among the nonvaccinated children, only 50% and 38% have detectable antibody to types 1 and 2, respectively, due to infection with wild poliovirus during the study year. There was widespread circulation of type 3 poliovirus in the control group during this period, a situation resulting in similar patterns of antibody distribution for the vaccinated and nonvaccinated children (figure 1D). It is uncertain how much of the type 3 antibody response in the vaccinated group is due to immunization and how much is due to natural infection; the temporal sequence of vaccination and possible infection is unknown.

During the first three years of this voluntary

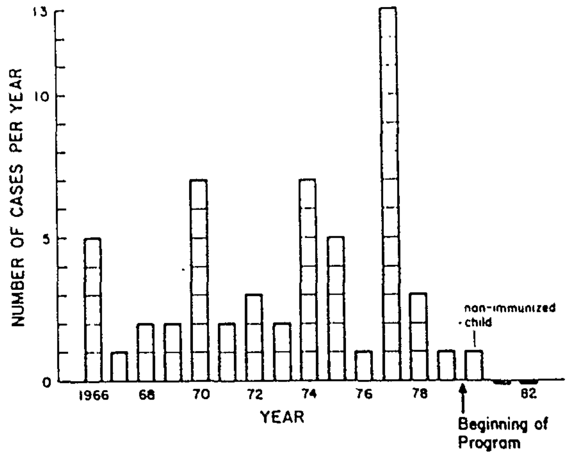

Figure 2. Number of cases of paralytic poliomyelitis seen at the Catholic Sisters Dispensary in Kolda, Senegal, 1966–1982.

program, involving two visits by a mobile health team four to eight months apart, ~26,000 children younger than four years of age were fully immunized. Surveys indicate that 75% of children three months to two years of age received at least one dose of poliovirus vaccine; 40% received two doses. The number of cases of paralytic poliomyelitis observed at the Catholic Sisters Dispensary in Kolda is recorded by one nurse-sister who has been in charge for more than 17 years (figure 2). From 1969 through 1979, there was an average of 3.9 cases annually; after 1980 the effect of the immunization program is apparent.

Discussion

This study of killed poliovirus vaccine used in a routine immunization program reveals that almost all children show persistence of detectable antibody six months after two doses of vaccine administered six months apart. The vaccine used in this study contained 40, 4, and 16 D-antigen units of poliovirus types 1, 2, and 3, respectively. Since 1981, the program has used a 40-8-32 D-antigen poliovirus vaccine that is expected to be effective against all three poliovirus types with a single dose [7].

In the Kolda region, there has been a marked decrease in the incidence of paralytic poliomyelitis observed at the only fixed health-care facility. Lameness surveys will be conducted for analyzing vaccine efficacy more thoroughly.

Killed poliovirus vaccine has proven to be particularly useful in a routine immunization program in West Africa for several reasons. It induces prompt, reliable production of antibody, which is important in areas where wild poliovirus circulates freely and infections occur early in life. Killed poliovirus vaccine can be combined with other antigens, such as DTP, a practice that simplifies vaccine administration. Killed poliovirus vaccine requires normal refrigeration (4–8 C) rather than freezing. Potency of killed poliovirus vaccine can be adjusted to yield any desired response; studies are currently underway to determine the antigen content necessary to induce immunity with a single dose administered within the first few days of life.

It is possible to reach a large rural population with a small mobile health team led by a nurse, using a vaccination schedule that involves only two visits per year for immunization against all the recommended EPI diseases: diphtheria, pertussis, tetanus, poliomyelitis, tuberculosis, measles, and yellow fever. Serologic studies of the vaccines for diseases other than poliomyelitis are underway. The program in Senegal is being expanded and similar two-dose immunization programs are being implemented in Mali and Upper Volta.

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