Combined Administration of Measles, Mumps, Rubella, and Trivalent Oral Poliovirus Vaccines

Combined vaccine studies

RECOMMENDATIONS ON THE USE of live virus vaccines call for the administration of measles, mumps, rubella, and poliomyelitis vaccines during the second year of life. Initially, it was recommended that these vaccines be given separately with at least 1 month between doses. Often, however, simultaneous administration of the vaccines would be advantageous; for example, when medical personnel or funds for immunization programs are in short supply or when continuity of medical care over the time required for separate administration of the vaccines cannot be guaranteed. Data from previous studies have shown the efficacy of various combinations of live virus vaccines administered in one injection (*1,2*) or simultaneously but at separate sites (*3*). To gain further information about the effectiveness of vaccines used together, a study was undertaken of the simultaneous administration of a combined measles-mumps-rubella vaccine and a trivalent live oral poliovirus vaccine.

Methods

Children 1–4 years of age receiving routine well-child care at public health clinics in Houston, Tex., and in the territory of Guam were the subjects of the study. Children with febrile illnesses, diarrhea, or other contraindications to vaccine administration were excluded.

The immunizing preparations used were licensed, commercially available lots of monovalent measles, mumps, and rubella virus vaccines and trivalent oral poliovirus vaccine. All vaccine lots were tested for potency before, during, and after the study. One lot of measles vaccine and one lot of mumps vaccine, both frozen liquid, lost 99 percent of their potency during shipment to Guam. All lots of the lyophilized measles, mumps, and rubella vaccines (two each) and one lot of liquid rubella virus vaccine, as well as all four lots of the trivalent oral poliovirus vaccine, retained their potency throughout the study under the same conditions of storage and handling. Data for the children who received vaccine from the two impotent lots were omitted from the final results.

The vaccines were reconstituted or thawed and the measles, mumps, and rubella vaccines were combined in a single syringe just before they were administered. Three groups of children were studied. One group (Guam and Houston) received only the combined measles-mumps-rubella vaccine; the second group (Guam only) received only the trivalent oral poliovirus vaccine; and the third (Guam and Houston) received both the measles-mumps-rubella vaccine and the poliovirus vaccine. The measles-mumps-rubella vaccine (1.5 ml) was given subcutaneously in the deltoid region, and a single dose of the poliovirus vaccine was given orally.

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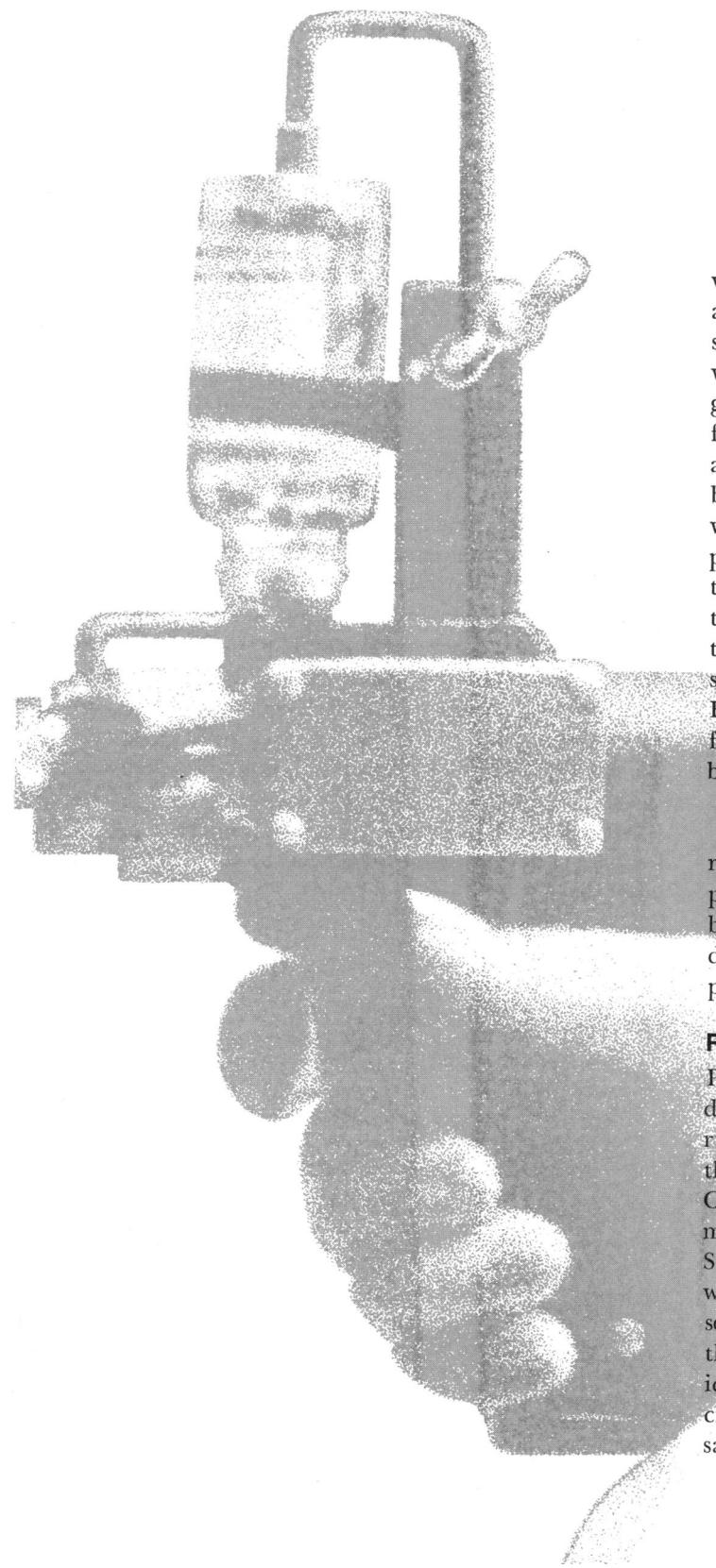

Approximately 10 ml of blood was obtained by venipuncture before administration of the vaccine and approximately 8 weeks afterward. Serum was separated within 6 to 24 hours after collection and was stored at −20°C. Measles and rubella hemagglutination-inhibition antibody titrations were performed by methods previously described (*4,5*), with an initial serum dilution of 1 : 8. Neutralizing antibodies to mumps and the three types of poliovirus were assayed by means of microneutralization test procedure (*6*). Initial serum dilutions were 1 : 2 for the mumps and poliovirus antibody tests done at the Bureau of Biologics, Food and Drug Administration, and 1 : 5 for the Houston series. The serum samples obtained in Houston were tested by the Houston City Health Department and the Center for Disease Control. Those from Guam were tested by the Bureau of Biologics.

The childrens' parents were asked to report any reactions to the vaccination during the 8-week study period to the physician at the time the convalescent blood specimen was collected. Seroconversion was defined as a fourfold increase in antibody from a previously undetectable level.

Results

Paired serum samples were obtained from 175 children who received the combined measles-mumps-rubella vaccine alone and 121 children who received that vaccine plus the poliovirus vaccine (table 1). Only children initially seronegative to measles, mumps, and rubella are included in these groups. Samples from two children in the latter group were not of sufficient quantity for testing. The seroconversion rates for the children receiving only the measles-mumps-rubella vaccine were not significantly different from the rates induced by this vaccine when the poliovirus vaccine was given at the same time.

Table 1. Seroconversion rates of seronegative children to measles-mumps-rubella vaccine given alone or simultaneously with trivalent oral poliovirus vaccine

Study area and vaccine administered	Number vaccinated	Seroconversion rate (percent)		
		Measles	Mumps	Rubella
Guam				
Measles-mumps-rubella	95	100	85	99
Measles-mumps-rubella plus poliovirus	41	100	95	98
Houston, Tex.				
Measles-mumps-rubella	80	91	95	89
Measles-mumps-rubella plus poliovirus	78	97	94	91
Both areas				
Measles-mumps-rubella	175	96	90	94
Measles-mumps-rubella plus poliovirus	[1] 119	98	94	93

[1] Serum samples from 2 children not sufficient for testing.

The effect of the measles-mumps-rubella combination on the response to the poliovirus vaccine is shown in table 2. Serum samples from 121 children who received both vaccines and from 88 children who received only the poliovirus vaccine were tested. The latter group had received various numbers of doses of poliovirus vaccine during the first year of life. The percentages of children developing antibodies to the three types of poliovirus were about the same for the two groups.

No adverse effects were noted at the time of immunization, nor did the parents report any unusual reactions during the 8 weeks after. No cases of natural measles, mumps, rubella, or poliomyelitis were reported in any of the children vaccinated or in their contacts during the study; thus, there was no evidence that natural infection caused the observed changes in antibody titers. Since testing was performed in three laboratories, no effort was made to compare the geometric mean titers of the three groups.

Table 2. Percentage of children in both study areas with antibodies to poliovirus before and after receiving a reinforcing dose of trivalent oral poliovirus vaccine alone or with a measles-mumps-rubella vaccine

Vaccine status	Number of children	Children with antibodies poliovirus (percent)		
		Type 1	Type 2	Type 3
Poliovirus alone:				
Before reinforcing dose	88	69	88	78
After reinforcing dose	88	85	97	89
Poliovirus plus measles-mumps-rubella:				
Before reinforcing dose	121	77	93	77
After reinforcing dose	121	93	98	88

Discussion

The results of this study support the recommendation of the American Academy of Pediatrics (*7*) and of the Public Health Service Advisory Committee on Immunization Practices (*3*) that, when considered advantageous for the health of the public or of an individual child, measles, mumps, rubella, and poliovirus vaccines can be given simultaneously with no loss of immunogenicity. Although the children studied were not professionally observed for fever or other reactions, the parents reported no reactions in any of the children.

In the effort to raise the immunization levels of children in this country, many States have enacted legislation requiring proof that immunizations are up to date before a child enters school. These laws are intended to insure that children are adequately protected so as to decrease the likelihood of epidemics of these potentially preventable diseases.

Although school children are a captive population and presumably could be given measles, mumps, rubella, and poliovirus vaccines at separate times, the simultaneous administration of the vaccines has the advantage of reducing the cost. This approach may also be advantageous to obtain quick protection in such poorly immunized or hard-to-reach groups as migrant children or Eskimos. Finally, a reduction in the number of well-child care visits during the second year of life, with a concomitant decrease in costs to the consumer, might be possible with this approach.

References

1. Weibel, R. E., Buynak, E. B., Stokes, J., Jr., and Hilleman, M. R.: Persistence of immunity following monovalent and combined live measles, mumps, and rubella virus vaccines. Pediatrics 51: 467–475, March 1973.
2. Landrigan, P. J., et al.: Combined measles-rubella vaccines. Virus dose and serologic response. Am J Dis Child 125: 65–67, January 1973.
3. Center for Disease Control: Recommendation of the Advisory Committee on Immunization Practices. Morbidity—Mortality Weekly Rep 21: 402–403, Dec. 1, 1972.
4. Rosen, L:. Hemagglutination and hemagglutination-inhibition with measles virus. Virology 13: 139–141, January 1961.
5. Stewart, G. L., et al.: Rubella-virus hemagglutination-inhibition test. N Engl J Med 276: 554–557, Mar. 9, 1967.
6. Mayner, R. E., et al.: Automated microtransfer technique for the assay of poliovirus and mumps virus neutralizing antibodies. Appl Microbiol 28: 968–971, December 1974.
7. American Academy of Pediatrics: Report of the Committee on Infectious Diseases. Ed. 17. Evanston, Ill., 1974.