Scientific evidence indicates that immunization schedules and doses can be varied to fit the conditions of agricultural migrants and other special groups without impairing effectiveness.

Adapting Immunization Programs to Special Groups

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IMMUNIZATION programs generally follow fixed routines. These fit the convenience of physician and patient and conform to desirable patterns of well-child supervision under ordinary circumstances. For people on the move and for people living in areas remote from health services, conventional patterns may not be applicable. Health workers who attempt to follow them may earn only frustration for their effort.

What flexibility in immunization schedules is permissible under special circumstances? To what extent can time intervals between injections or size of doses be varied without endangering program effectiveness?

This article looks at the problem from the specific point of view of the need for adapting immunization programs to fit the special conditions of agricultural migrants. It reviews recent information regarding the immunization status of the general population, as well as that of migrants. It also summarizes recent evidence of the possibilities of varying immunization procedures to fit special circumstances. Although the article was prepared primarily with the needs of agricultural migrants in mind, the possibilities of varying schedules obviously have wider application if circumstances warrant.

Agricultural migrants in the United States number about three-quarters of a million persons, including both workers and dependents who accompany them. Each year, they move from one area to another to help produce and harvest the Nation's crops. An area may depend on them for its economic existence. Yet local communities may reject them, in part because of the fear that they may be disease carriers.

The mobility of migrant workers in agriculture and their brief convergence on areas that may be far removed from population centers are among the factors that make it difficult for health workers to extend services to these people. Services provided in the usual places and ways and at the usual hours are likely not to reach them.

Temporary arrangements for provision of health services at times and places convenient

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Important contributions to this paper, especially concerning diphtheria, were made by Dr. Alexander Langmuir and Dr. Helen Moore, Communicable Disease Center, Public Health Service, Atlanta.

to both the workers and their employers may sometimes be possible. Immunization services, however, differ from most others in that there is a general belief that fixed time schedules must be followed if immunization is to be effective. Many health workers hesitate to initiate a series of primary injections unless they are sure that they can complete the series in accordance with the customary time schedule.

The frequently severe reactions among adults to the usual doses of antigens also deter immunization programs among migrants. The reactions in adults may cause great discomfort and even loss of time from work at a period which is crucial for both workers and employers. Such problems, of course, are not peculiar to the agricultural migrant population.

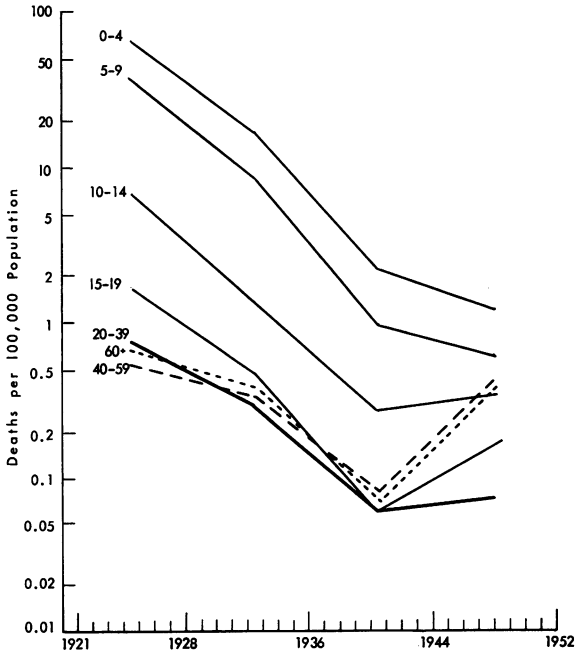
Immunization Status

The available information concerning the immunization status of the population is chiefly in terms of the continued occurrence of diseases for which effective control techniques have long been known. Diphtheria, for example, has long been subject to control by immunization. Yet data compiled by the Communicable Disease Center, Public Health Service, show that more than 2,000 cases of diphtheria occur each year over the Nation as a whole.

Special studies seem to indicate a shift in the importance of diphtheria from the younger to the older age groups. A long-term study of age-specific mortality rates in Massachusetts shows that diphtheria mortality rates among children under 10 years of age have declined throughout the period 1921–53. In other age groups, however, the long-term decline was interrupted in the early 1940's, as shown in figure 1 (*1*). More than half the cases of diphtheria in California during the period 1950–54 were among persons over 19 years of age, according to Communicable Disease Center data. In the southern States, the shift in the importance of diphtheria from younger to older age groups is much less prominent, although this region, too, shows some increase in the proportion of cases in age groups over 19 years.

Some of the southern States, including Texas, have reported more cases and a greater number of diphtheria outbreaks than other parts of the

Figure 1. Diphtheria trends in age-specific mortality in 8-year periods, Massachusetts, 1921 through 1952.



SOURCE: Reference 1.

country in recent years. Data for these States show that diphtheria among the nonwhite population is on the increase. These same States supply a large segment of the labor force that annually moves northward from one crop harvest to another.

To a somewhat lesser extent than diphtheria, tetanus continues to be an important problem. The proportion of cases among children and young adults has decreased in recent years. These are the groups most extensively reached through immunization programs for young children and for military personnel. The proportion of cases among older adults, however, has been gradually increasing. According to a Massachusetts study in 1954, more than one-half of the persons over 20 years of age had antibody levels of less than 0.01 units of antitoxin. Women had significantly lower antibody levels than men, as shown in figure 2 (*1*).

How much the situation among agricultural migrants may deviate from that in the general population is not known. In the opinion of public health workers and others familiar with the situation, however, migrants' lack of protection through immunization and the pos-

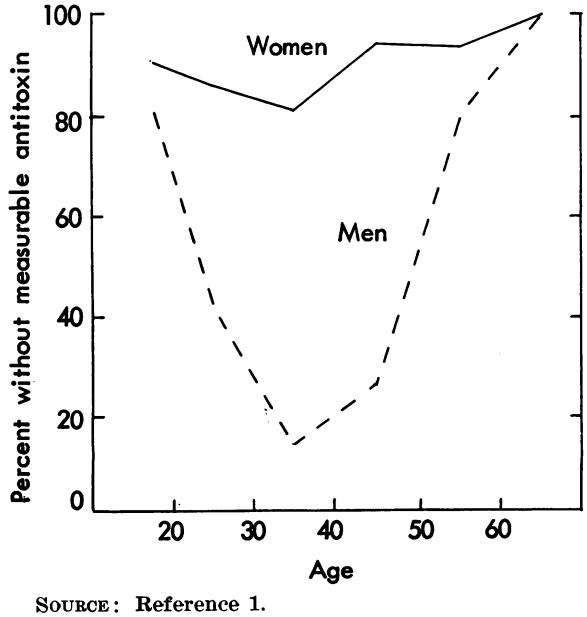
sibility that they may contract and carry disease from one place to another are matters of concern.

Two outbreaks of diphtheria were reported among people living in migrant labor housing during the first 6 months of 1956 (*2*). During 1955, an outbreak of chickenpox among migrant workers in Lee County, Ill., led to an investigation by the Illinois Department of Public Health. A report from the county states: "A minority of the entire personnel showed evidence of previous smallpox vaccination, and only a few of the children had ever received immunization against diphtheria, pertussis, or tetanus" (*3*).

A Colorado study based on interviews of 260 migrant families, including 1,153 adults and children, during 1950 indicates that only 42 percent had had smallpox vaccination and probably only 1 out of 5 or fewer were immunized against diphtheria, whooping cough, or tetanus (*4*). Informal reports from several Colorado nurses who are working with agricultural migrants are in accord with these findings. Health workers in other areas have made similar reports.

In some of the labor camps and fringe areas of population centers where agricultural migrants live for brief periods, living conditions are primitive. Occasional outbreaks of typhoid fever occur. This situation is believed to warrant consideration of immunization against typhoid fever for agricultural migrants even though this is not advocated for the general population under ordinary conditions.

Figure 2. Tetanus immunity among adults, Massachusetts, 1954.



SOURCE: Reference 1.

State Immunization Policies

The Committee on the Control of Infectious Diseases of the American Academy of Pediatrics recommends that combined immunizations against diphtheria, pertussis, and tetanus be given "at intervals of not less than 1 month and preferably not more than 3 months" (*5*). The States and Territories are using this standard to an increasing extent in setting policies for their immunization programs. States continue to vary, however, in their policies and in the standards to which they refer.

This State-to-State variation in itself suggests that flexibility in immunization programs is possible. However, the policies in each State, whether or not set by law, have frequently been translated into long-standing practices that are strictly adhered to in immunization programs whether the programs are carried out in the offices of private physicians or in public clinics.

In comparing State immunization policies, Eliot noted that 22 States and 1 Territory set the maximum permissible time interval between injections in the primary DPT series at 1 month. No flexibility is permitted in this time interval. Two States and two Territories permit an interval of 3 months between primary injections, and 3 States permit a 4-month interval. Eight States and one Territory, on the other hand, permit an interval of 6 months between injections without requiring that the series be restarted (*6*).

Effect of Lengthened Time Interval

Opinions differ as to the levels of antitoxin in the blood serum necessary to confer immunity against diphtheria and tetanus. The evidence available, however, points to as high or higher levels of antibody response when the interval between doses is prolonged as when the interval is the length usually recommended for primary immunization. Jones pointed out

that by increasing the interval between injections for immunization against diphtheria, a higher antibody response is seen (*7*). Similar findings of higher antibody levels with longer intervals between tetanus immunizations have been reported by Bigler and Werner (*8*), Bigler (*9*), and Deamer and associates (*10*).

In a controlled study in which an interval of 6 months or more between first and second primary diphtheria and tetanus immunizations was compared with a 2-month interval (figs. 3 and 4), Bigler and Werner found that the immediate antibody response averaged 4 times higher for the longer interval than for the shorter (*8*).

In a group of children receiving primary tetanus injections at intervals of from 6 to 51 months, Bigler noted that 6 months after the final injection the titers were in the same range as those present in children receiving primary injections at intervals of from 1 to 3 months (*9*). Deamer and his co-workers confirmed the findings of a higher tetanus antitoxin response in infants when the interval between injections was lengthened (*10*).

Ipsen noted a satisfactory antibody response in the tetanus antitoxin titer in previously unimmunized adult men who were given small doses of toxoid (5 Lf) at an interval of 28 weeks between the first and second primary injections (*1*). Edsall and his associates demonstrated diphtheria antibody titers greater than 0.03 units per milliliter in 250 of 252 patients given 1-Lf doses of adsorbed diphtheria toxoid with a 5–month interval between the second and third doses (*11*).

According to Dr. J. H. Lapin, attending pediatrician, Bronx Hospital, New York City, other investigators report that antibody levels for diphtheria, tetanus, and pertussis following

Figure 3. Comparison of 6-month interval and 2-month interval between first and second injections of combined alum precipitated diphtheria and tetanus toxoid as to titers of diphtheria antitoxin.

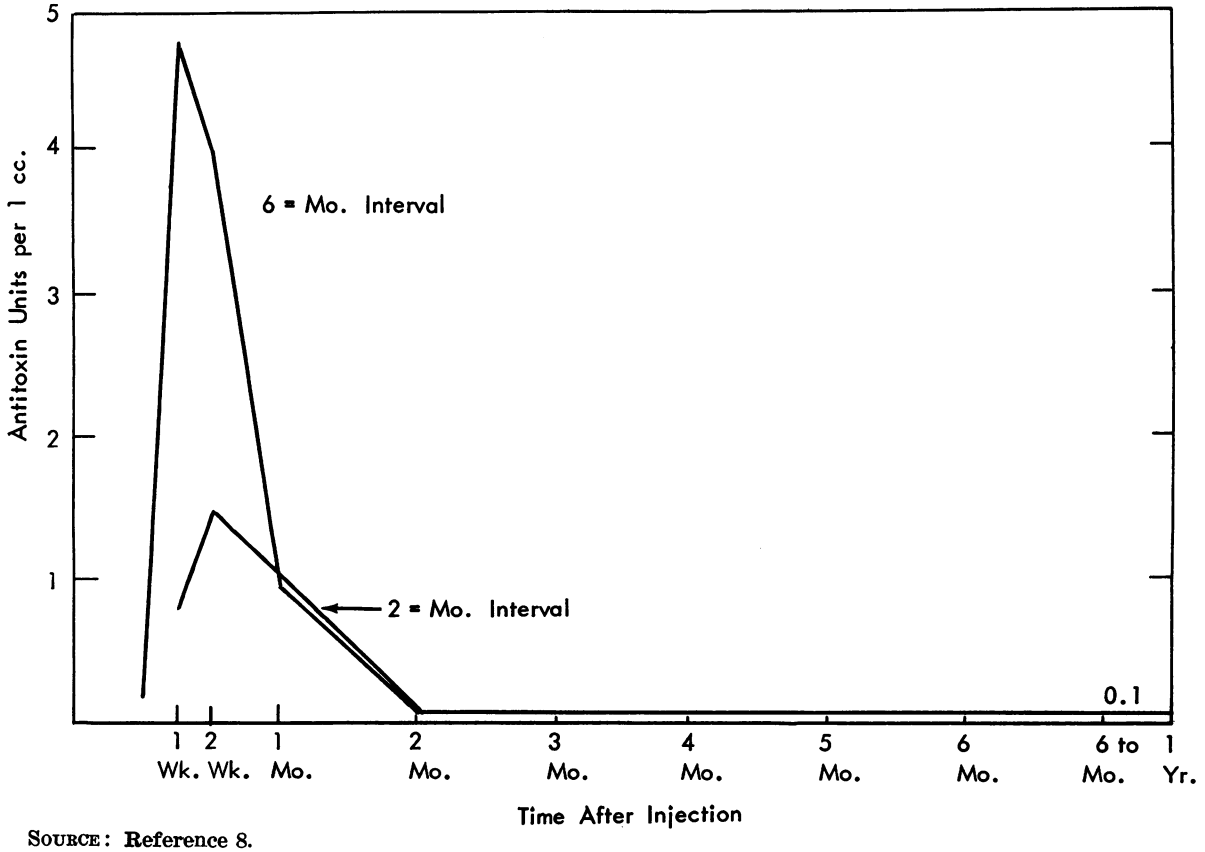


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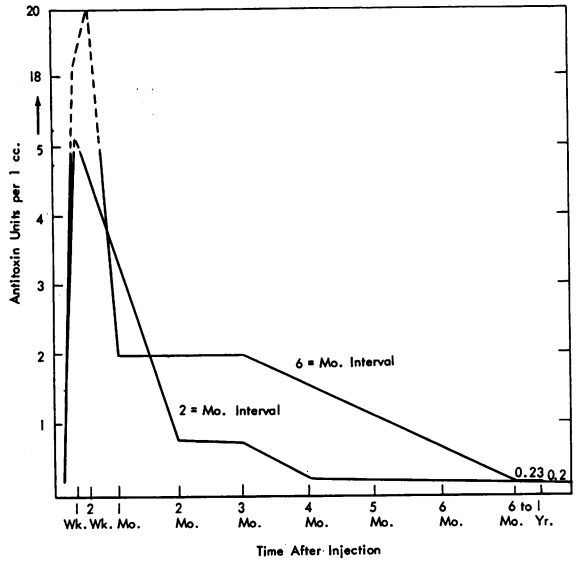
Figure 4. Comparison of 6-month interval and 2-month interval between first and second injections of combined alum precipitated diphtheria and tetanus toxoid as to titers of tetanus antitoxin.



SOURCE: Reference 8.

the use of triple antigens with injections from 6 to 12 months apart are at least as good as the levels obtained when the antigens are given at intervals of from 1 to 4 weeks.

There is also evidence that when the time interval between primary injections is increased, a higher immediate antibody level is produced by a stimulating, or secondary, injection given 3 months to 7 years later (*8*, *9*).

In infants studied, there was no relationship between a poor initial response and the recall response obtained years later with diphtheria and tetanus toxoids. It appears that adequate recall response can be expected in most cases in spite of poor initial response (*10*). The majority of adults will show protective antibody levels within 6 days after a recall dose of tetanus toxoid as long as 10 years after primary immunization (*1*, *12*, *13*).

Taken together, these data suggest that the usual telescoping of injection schedules has value chiefly for the convenience of physicians and patients, for emergency situations (*1*), or for producing immunity in infants as rapidly as feasible at a time when the hazards are likely to be the greatest for the infant. Many immunologists believe that ineffective immunization is more likely to result from relatively short intervals between doses than from long intervals.

Methods of Reducing Untoward Reactions

Three methods of decreasing severe reactions to diphtheria toxoid among adults are to immunize only susceptibles as determined by the Schick test, to use purified toxoids, or to decrease the dose of toxoid. The first, of course, might not be feasible for a seasonal farm worker since he might be on his way to another work location by the time the results of the test were known. The second decreases the incidence of reactions only in age groups under 30 years (*14*).

On the basis of present evidence, the most effective means of decreasing untoward reactions in diphtheria immunization is by decreasing the dose of toxoid. Small doses of diphtheria toxoid (in the range of 1 Lf per dose) can be used to immunize adults successfully without regard to selection of Schick positive individuals (*11*). Only occasional reactions are encountered with 1-Lf doses (table 1).

Table 1. Reactions to 1-Lf diphtheria toxoid

Degree of reaction	Number of subjects			
	Local reaction		General reaction	
	FTT [1]	APT [2]	FTT [1]	APT [2]
None	5	39	42	71
Mild	27	31	8	2
Moderate	14	4	5	0
Severe	10	1	1	2
Total	56	75	-------	-------

[1] FTT=fluid toxoid, in tetanus toxoid.
[2] APT=$AlPO_4$—adsorbed toxoid.

SOURCE: Reference 11.

In studies conducted by the Commission on Immunization of the Armed Forces Epidemiological Board with doses of 1 Lf (in 0.5 cc.), less than 5 percent of the patients had systemic reactions. (The vaccine usually used in immunizing children contains 20–25 Lf/cc.) Although there has been some question as to the

Table 2. Diphtheria antitoxin titer in adult men before and 1 week and 3 weeks after one injection of 1-Lf diphtheria toxoid

Titer before booster	Alum-toxoid antitoxin titer			Fluid-toxoid antitoxin titer		
	Number patients	At 1 week	At 3 weeks	Number patients	At 1 week	At 3 weeks
0.001	1	0. 10	3. 2	0		
0.001–0.01	3	. 32	2. 1	4	0. 10	1. 3
0.01–0.1	8	. 56	4. 2	8	. 49	10. 0
0.1–1.0	19	. 84	4. 8	25	1. 9	11. 0
1.0	6	3. 20	4. 7	3	3. 2	15. 0
Total	37			40		
Average		. 84	4. 3		1. 06	9. 0

SOURCE: Reference 1.

effectiveness of these small doses as a primary antigenic stimulus, they are known to be effective as a recall dose for maintaining a satisfactory immunity level (*1*, *11*, *15*). Results obtained with 1-Lf doses in two studies are given in table 2 and figure 5.

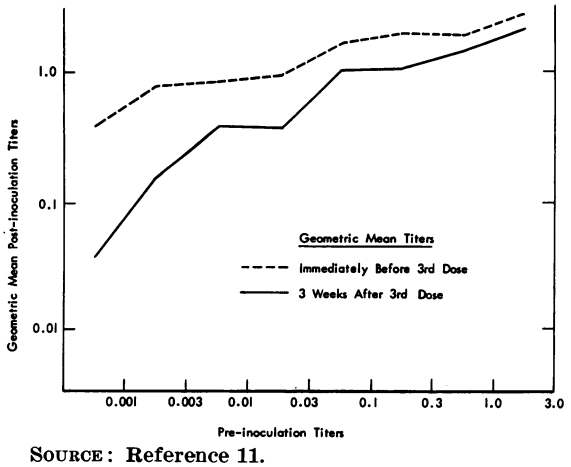
In immunization against typhoid fever, systemic reactions can be reduced considerably and protective levels of antibodies can be achieved by intracutaneous administration of typhoid-paratyphoid vaccine (*16–18*).

Combined Antigens

For the past 5 years, the Canadian Armed Forces have used a vaccine containing typhoid, paratyphoid, tetanus (8 Lf), and diphtheria (4 Lf) antigens. The results of studies of this vaccine compare favorably with data relating to children who have received 3 doses of fluid toxoid (*19*). The vaccine proved effective both as a primary stimulus and as a secondary stimulus and provided antibody levels as high as 3 doses of plain toxoid.

Use of such a combined vaccine would greatly simplify immunization procedures among adults in the agricultural migrant population since it would decrease the number of injections by about one-third. In addition, as indicated by the preceding information concerning lengthened time interval, the interval between injections may be increased far beyond the conventional limits with satisfactory results.

Figure 5. Relationship of postinoculation titers to preinoculation titers following two and three 1-Lf doses of adsorbed diphtheria toxoid.



SOURCE: Reference 11.

Summary

Agricultural migrants and other mobile or isolated population groups have long frustrated health workers' efforts to fit them into conventional immunization programs. All too frequently, the belief that any deviation from standard procedures would preclude an adequate immune response has led health workers to avoid attempting to initiate immunization procedures when conditions would not permit following the usual patterns.

This paper reviews evidence which refutes the frequently held view that if the doses of antigens cannot be given at the usual time intervals, or if one injection is omitted, the entire series of primary injections must be restarted and completed in the usual sequence in order to attain effective immunization levels. It also

summarizes evidence that the use of small doses of antigens is effective in minimizing untoward reactions; at the same time, these small doses produce adequate antibody response. The small doses also lend themselves to use in a combined vaccine, thus decreasing the number of injections required.

If the usual patterns followed in immunization programs can be conveniently fitted to any group, including agricultural migrants, no change in these patterns is suggested. However, permissible variations, such as those reviewed in this paper, need to be considered in order to tailor programs to groups which are difficult to reach by conventional means.

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