Diphtheria Immunization

Effect Upon Carriers and the Control of Outbreaks

Louis W. Miller, MD; J. Justin Older, MD; James Drake; and Sherwood Zimmerman, Austin, Tex

A diphtheria epidemic in a small central Texas community centered in the elementary school. Epidemiological investigation at the school included throat cultures and immunization histories of 306 of the 310 students and staff. Of these, 104 (34%) had culture-proven diphtheria infections; 15 were symptomatic cases and 89 were carriers. There was no statistical difference in the risk of diphtheria infection among those with full, lapsed, inadequate, or no previous diphtheria immunizations. However, the risk of symptomatic diphtheria was 30 times as great for those with none, and 11.5 times as great for those with inadequate immunizations as for those fully immunized. Diphtheria toxoid helps prevent symptomatic disease but does not prevent the carrier state nor stop the spread of infection. Identifying, isolating, and treating carriers are very important aspects in the control of diphtheria outbreaks.

With the increase in the number of cases of diphtheria in the United States during the past few years, the effect of immunization on the control of outbreaks has become an important question. In the Austin, Tex, diphtheria epidemic of 1967-1969[1] cases continued to occur despite the administration of 155,200 doses of diphtheria toxoid and the concomitant rise in immunization levels of school age children from 68% to 89%. Data from the Austin outbreak suggested that a large reservoir of carriers was important in the continued transmission of *Corynebacterium diphtheriae*. Other diphtheria outbreaks have shown that epidemics occur in populations with high immunization levels.[2-4] A diphtheria outbreak in an elementary school in Elgin, Tex, in the spring of 1970 provided an opportunity to study the effects of immunization on carriers and on the control of an epidemic situation.

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From the Epidemiology Program Center for Disease Control, Atlanta (Drs. Miller, Older, Drake, and Zimmerman); the Communicable Disease Services, Texas State Department of Health, Austin (Drs. Miller, Older, Drake, and Zimmerman); and the Department of Preventive Medicine, University of Maryland School of Medicine, Baltimore (Dr. Miller).

Reprint requests to Epidemiology Program, Center for Disease Control, Atlanta 30333.

Table 1.—Definitions of Immunization Status*

Status	Definition
Full	Primary series (three or more injections), or a primary series plus a booster, completed within ten years.
Lapsed	Primary series, or a primary series plus booster, completed more than ten years ago.
Inadequate	Uncompleted primary series (less than three injections) at any time.
None	No diphtheria toxoid ever received.

* Adapted from the Center for Disease Control.[6]

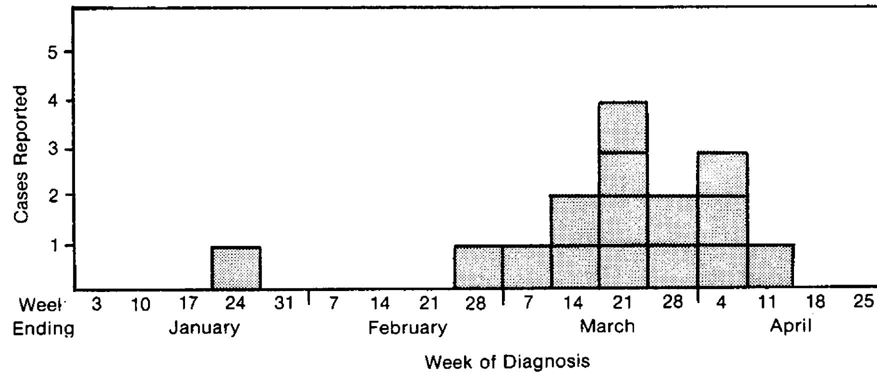
Materials and Methods

When it became obvious in the Elgin diphtheria epidemic (Older JJ et al, unpublished data) that cases were clustered in the elementary school, a special throat culture and immunization survey was begun there. Throat cultures were obtained from and immunization status was determined for 306 of 310 students and staff. Throat swabs were taken on three separate occasions from each person: April 7, April 17, and May 4. These were streaked on Loeffler blood serum or Pai medium and incubated overnight. Cystine tellurite blood agar and Tinsdale medium were used for isolation, Elek-King agar diffusion plates were used for toxigenicity determination.

Immunization status information was

obtained by personal interview and review of available school and medical records. The status of each person classified as "adequate," "lapsed," "inadequate," and "none," according to the definitions of the Center for Disease Control[5] (Table 1).

Any person with a sore throat or other symptoms compatible with diphtheria and a positive culture for *C diphtheriae* organisms was classified as a "case." A person without symptoms but who had a positive throat culture for *C diphtheriae* organisms was classified as a "carrier." The term "infection" applied to anyone with a positive culture regardless of his clinical state and, therefore, included both cases and carriers.



Diphtheria cases in Elgin, Tex, elementary school, spring 1970.

Results

When diphtheria was first diagnosed in the elementary school, 67% of the children and staff were already fully immunized, and 97% had had at least one dose of diphtheria toxoid. The first case in the elementary school population was diagnosed in late February 1970, and by April 8, 15 cases had occurred (Figure).

Throat cultures were done on 306 children and staff; toxigenic *C diphtheriae*, gravis type, was isolated from 104 (34%). Fifteen of these (14%) were cases, and 89 (86%) were carriers. There was *no* statistical difference in the risk of diphtheria infection among those with full, lapsed, inadequate, or no previous diphtheria immunization (Table 2). However, the risk of becoming a case was 30 times as great for those with no immunization and 11.5 times as great for those with inadequate immunizations as for those with full diphtheria immunization (Table 3). Among the 104 infected with *C diphtheriae*, the risk of being symptomatic was 13.3 times as great for those inadequately immunized and 37.0 times as great for those with no previous immunizations as for those who were fully immunized (Table 4).

Comment

The importance of carriers in the spread of diphtheria was well documented by Doull and Lara[6] in the

Table 2.—Immunization and Culture Status of Students and Staff, Elgin, Tex, Elementary School, Spring 1970

	Culture Status			Diphtheria Infection
Immunization Status	Positive	Negative	Total	Attack Rate (per 100)
Full	73	132	205	35.6
Lapsed	0	4	4	0
Inadequate	28	59	87	32.4
None	3	7	10	30.0
Total	104	202	306	34.0

Table 3.—Immunization Status of Diphtheria Cases, Elgin, Tex, Elementary School, Spring 1970

Immunization Status	Cases	No. at Risk	Diphtheria Case Attack Rate (per 100)
Full	2	205	1.0
Lapsed	0	4	0
Inadequate	10	87	11.5
None	3	10	30.0
Total	15	306	4.9

Table 4.—Risk of Symptoms and Immunization Status of Students and Staff With Positive Diphtheria Cultures, Elgin, Tex, Elementary School, Spring 1970

Immunization	Symptomatic Cases	Asymptomatic Carriers	Total Infected	Symptom Attack Rate (per 100 Positive Cultures)	Relative Risk
Full	2	71	73	2.7	...
Inadequate	10	18	28	35.8	13.3
None	3	0	3	100.0	37.0
Total	15	89	104	14.4	...

early 1920s. In very thorough investigations, only about 20% of diagnosed diphtheria cases could be traced to another suspected case, and the remaining 80% of the cases were attributed to asymptomatic carriers in the population. Recent epidemics in Austin[1] and Elgin,[5] Tex, provided ample evidence that carriers continue to play a very important role in the transmission of diphtheria.

When diphtheria toxoid became available, it was generally believed that it induced immunity that protected individuals from symptomatic illness but not from asymptomatic infection. This was based on the observation that immunity is related to the neutralization of toxin elaborated by *C diphtheriae* and not interference with diphtheria infection.

In 1936, Frost et al[7] alluded to a paucity of observations on record concerning antitoxic immunity and the carrier state. Nonetheless, he stated that the limited data suggested that there is little, if any, difference between those individuals with and those without antitoxic immunity in their risk of becoming infected.

More recently, Tasman and Lansberg[8] put forth the hypothesis that toxoid use reduces the number of carriers. This is based on surveys that showed a steady decline in the prevalence of carriers. Since toxoid immunization does prevent cases and since cases are more contagious than carriers,[6] the decline in carriers could be due to the decrease in contagious cases rather than to the direct effects of immunization.

The findings in Elgin corroborate the assumptions of Frost et al[7] and show that there is no difference in the risk of diphtheria acquisition among those with full, lapsed, inadequate, and no immunizations. However, they also demonstrate the value of immunization in reducing the risk of disease and show that the protection against symptomatic illness afforded those infected with *C diphtheriae* is directly related to their immunization status.

Some authors[9] have estimated that if 70% or 80% of the population were adequately immunized against diphtheria, spread of diphtheria would be prevented. However, diphtheria outbreaks have been described in populations with as much as 94% of the people being previously immunized.[2-4] These outbreaks, the known importance of carriers in the spread of diphtheria, and the demonstrated failure of toxoid to prevent the carrier state lead us to conclude that the concept of herd immunity is not applicable in the prevention of diphtheria. A high level of community immunization will not stop the transmission of diphtheria, but it will limit the number of contagious cases. At the first appearance of a diphtheria case, control activities should be directed toward identifying, isolating, and treating carriers, as well as toward immunizing persons with less than full immunization status. This dual approach will reduce or eliminate the spread of infection by reducing the number of carriers, and it will reduce the number of cases by improving the immunization status of exposed individuals.

Roy Morris, MD, Elgin city health officer, treated the majority of cases and arranged for treatment of carriers; Milton Saxon, Elgin school superintendent, and Eva C. Danklefs, Elgin school nurse helped arrange culture surveys; M.S. Dickerson, MD, coordinated federal, state, and local assistance and support; Will Callihan assisted in culture surveys, interviews, and immunization of patients; Jesse V. Irons, ScD, and Carl D. Heather, DVM, coordinated state laboratory assistance; H.D. Bredthauer and Lucie M. Hickman, Texas State Department of Health, processed bacteriological specimens; and Wallis Jones, PhD, Susan Bickham, Geraldine Wiggins, and Jane McLaughlin, Laboratory Division, Center for Disease Control, Atlanta, processed specimens and performed all typing of *C diphtheriae* organisms. All isolates from the initial throat cultures were typed by the Bacteria Immunology Unit, Center for Disease Control.

References

1. Zalma VM, Older JJ, Brooks GF: The Austin, Texas, diphtheria outbreak. *JAMA* **211**:2125-2129, 1970.

2. Murphy WF, Maley VH, Dick L: Continued high incidence of diphtheria in a well immunized community. *Public Health Rep* **71**:481-486, 1956.

3. Fanning J: An outbreak of diphtheria in a highly immunized community. *Brit Med J* **1**:371-373, 1947.

4. Corothers TE, Zatlin GS: An outbreak of diphtheria: A story of investigation and control. *Clin Pediat* **5**:29-33, 1966.

5. *Diphtheria Surveillance Report No. 9.* Atlanta, National Communicable Disease Center, 1969.

6. Doull JA, Lara H: The epidemiologic importance of diphtheria carriers. *Amer J Hyg* **5**:508-529, 1925.

7. Frost WH, Frobisher M Jr, VonVolkenburgh VA, et al: Diphtheria in Baltimore: A comparative study of morbidity, carrier prevalence and antitoxic immunity in 1921-1924 and 1933-1936. *Amer J Hyg* **24**:568-586, 1936.

8. Tasman A, Lansberg HP: Problems concerning the prophylaxis, pathogenesis and therapy of diphtheria. *Bull WHO* **16**:939-973, 1957.

9. Wilson GS, Miles AA: *Topley and Wilson's Principles of Bacteriology and Immunity*. Baltimore, Williams & Wilkins Co, 1957, pp 1587-1588.