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## Foreign and Domestic Trends in Diphtheria\*

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EVER since the advent of diphtheria immunization there has been constant speculation as to whether the decline in the incidence of diphtheria could be attributed to immunization or was a coincidental but not related phenomenon and, if so related, whether or not the prevailing low levels of incidence could be maintained. Those who were most doubtful as to the effect of community immunization pointed out correctly that diphtheria had decreased in many non-immunized communities at the same rate as in the immunized. Subsequent experience has shown, however, that in the former the decrease has not been maintained. Although it is agreed that there are many factors other than mere extent of immunization that have influenced this decline, I believe that most observers in this country are in agreement that immunization has been a force that has not only directly reduced the incidence but may also have so

shifted the balance of other factors as to effect a further reduction.

It has been logical to speculate, however, as to the permanence of this effect. Diphtheria occurs in definite though possibly irregular cycles of altered prevalence and virulence. Is there reason to believe that immunization may have been effective when it coincided with the downswing of a cycle but would be less effective on the upswing? May protection be adequate so long as the prevailing form of the infection is relatively mild but be inadequate at a future date when more virulent strains of organisms reappear and become dominant? These are questions that cannot be answered at this time, but on which some gleam of light may be shed by examination of recent trends in the prevalence of diphtheria in this country and abroad.

The war period has been marked by an upsurge in the incidence of diphtheria throughout the world, an increase noted on all continents to a varying degree. In Europe this increase was most pronounced in the northwestern section

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where the disease rebounded to equal the high morbidity rates of the last century. Southern and southeastern Europe was mercifully spared these wartime increases, possibly due in part to the fact that it was recovering from high rates during the previous decade when northwestern Europe had been enjoying a moderate decline unattributable to immunization.

The pre-war years had, however, been marked by several features which held an ominous foreboding for the diphtheria situation. The first of these was the obvious prevalence in Europe of a form of diphtheria appreciably more malignant than that which prevailed in the United States. This form had been repeatedly described in England and Germany as well as in other countries. In Germany there had been much speculation about its relationship to coincidental streptococcal infection and even doubts as to the adequacy of diphtheria antitoxin in treatment. The English studies of strains of diphtheria bacilli, distinguishing *gravis*, *mitis* and *intermedius strains*, gave hope of an explanation of the enhanced virulence of the prevailing infections. Although most bacteriologists in this country currently doubt the significance of this differentiation of strains, certain English investigators still attribute significance to it. Regardless of the explanation, there was doubtless a more malignant form of diphtheria in Europe, and one might logically wonder as to the efficacy of immunization in the United States if the more malignant strains were to be introduced.

A second factor that added to the gravity of the pre-war situation in Europe was the lack of immunization. Exact data as to extent of immunization are not available. It is obvious, however, that the procedure had not become an accepted part of the public health program to the same extent as in the United States and Canada, and that

even in those countries such as Denmark, France, and Hungary where it has been used extensively, only a very small segment of the population had been reached. England had hardly been touched whereas Norway was almost completely non-immunized, the only children who had been protected being the rare child immunized by a private physician. The number of these was so small that the Norwegian authorities themselves described the country as completely non-immunized. The low incidence rates, rivalling the lowest state rate in the United States, were attributed to the efficacy of conventional restrictive measures or to other factors that had made control possible without resort to immunization.

A third element of concern was the fact that at the outset of the war, diphtheria prevailed in some parts of central Europe at a higher rate than had been experienced in this country since the preimmunization period. Exact morbidity rates are hard to determine owing to inadequacies of reporting, unknown differences in case fatality rates, and uncertainties as to population, but the data in Table 1 represent adequate approximations. The data show a high rate in central Europe and England, more moderate rates in northwestern Europe, and remarkably low rates in

TABLE 1  
*Diphtheria Morbidity Rates — 1939*  
(Per 100,000 Population)

Country	Population *	Cases	Rate
Austria	6,694,782	19,137	285
Denmark	3,835,000	1,106	29
Eire	2,980,000	2,087	70
England and Wales	41,400,000	47,698	115
France	42,000,000	14,019	33
Germany	69,485,732	143,585	207
Hungary	10,817,286	6,397	59
Netherlands	8,815,000	1,273	14
Norway	2,920,000	71	2.4
Sweden	6,340,000	188	3.0
Switzerland	4,230,000	751	18
United States	130,800,000	24,391	19

\* All populations estimated except for those of Austria, Germany, and Hungary in which a census was taken in 1939.

TABLE 2  
*Diphtheria Incidence\**

	<i>Austria</i>	<i>Denmark</i>	<i>France</i>	<i>Germany</i>	<i>Hungary</i>	<i>Netherlands</i>	<i>Norway</i>	<i>Roumania</i>	<i>Sweden</i>
1937	19,494	1,348	19,187	146,733	8,148	1,068	417	3,242	299
1938	16,800	870	16,800	149,490	6,266	1,272	190	2,272	107
1939	19,137	1,106	14,019	143,585	6,397	1,273	71	2,279	188
1940	15,910	860	13,563	138,397	4,927	1,730	149	1,839	290
1941	14,255	917	20,018	173,161	5,049	5,501	2,609	1,103	252
1942	15,534	1,661	31,466	237,037	6,676	19,527	8,349	1,612	1,285
1943	22,444	2,527	46,539	238,409	8,259	56,603	22,787	1,879	2,496
1944	....	3,333	40,230	....	....	....	....	....	4,520

\* Source of data. *Epidemiological Information Bulletin*, United Nations Relief and Rehabilitation Administration. 1:241-246 (Mar. 15), 1945.

Norway and Sweden. As many of these lower rates had been achieved without resort to immunization, the population represented veritable tinder in which a conflagration might develop if the spark should spread from central Europe.

Such was the situation preceding the wartime explosion of diphtheria in northwestern Europe—a highly susceptible population already threatened on the East by a high incidence of diphtheria, much of which was of a virulent form. England alone adopted an energetic and highly successful control program through extensive immunization as a part of its civilian defense program. In 1939 France had ordered universal childhood immunization effective June 1, 1940, but France's defeat that spring had precluded enforcement of the program. Nazi conquest of Norway, Denmark, Belgium, and the Netherlands not only precluded active control measures but may even have precipitated the diphtheria outbreak through enforced malnutrition, crowding, and lack of medical supplies and services. The extent of the outbreak of diphtheria is shown in Table 2. It will be noted that Norway and the Netherlands, countries which felt the weight of the oppressor's yoke most severely, suffered the most. The disease began to increase rapidly during 1941, reaching its peak during the winter of 1943-1944. During the spring of 1944 the weekly incidence in the Netherlands was almost twice the pre-war yearly incidence. Denmark, which was possibly the best

immunized country of this area, felt the increase somewhat later than its neighbors and never suffered to the same degree. In Sweden the increase began in 1942 and was of somewhat less serious proportions. Accurate data for many of these countries for 1944 will probably never be available. In 1945 and 1946 the disease has continued throughout northwestern Europe at a high rate but very much below the 1943-1944 peak. Table 3 shows sample comparative data.

TABLE 3  
*Diphtheria Incidence*

	<i>Oct.</i>	<i>Dec.</i>	<i>Feb.</i>
<i>Denmark</i>			
1943-4	223	390	428
1944-5	306	397	367
1945-6	153	150	116
<i>France</i>			
1943-4	4,280	5,842	4,768
1944-5	3,266	4,329	4,125
1945-6	4,259	4,164	2,765
<i>Norway</i>			
1943-4	2,982	2,519	1,505
1944-5	1,031	946	758
1945-6	570	553	291

The wartime data of the British Isles present an interesting contrast to the continental experience. Table 4 shows the incidence in war-congested England and Wales on the one hand, and in neutral Eire on the other. The former, facing the obvious risk of increasing diphtheria—a risk accentuated by displacement of the population and crowding in air-raid shelters—provided for extensive immunization; the latter did little to protect itself against an in-

crease. Whereas Eire experienced an increase from less than 2,000 cases in 1941 to over 5,000 in 1944, England and Wales enjoyed a decline to the lowest level ever recorded, a rate of decline comparable in magnitude with that of the United States during the same period (Table 4). The English data are of special significance, for this county was the only part of northwestern Europe that weathered the storm with a significant decrease in diphtheria. May it not have been more than mere coincidence that it was also the only country that increased its immunization program to a point comparable with that of the United States and Canada? The data strongly suggest that immunization is actually effective in guarding against whatever strains of infection may have been operative in Europe during the war period.

TABLE 4

*Diphtheria Incidence \**

	<i>Eire</i>	<i>England and Wales</i>		<i>United States</i>
		<i>England</i>	<i>Wales</i>	
1937	2,511	61,341	28,536	28,536
1938	2,983	65,008	30,508	30,508
1939	2,087	47,698	24,391	24,391
1940	1,891	47,683	15,618	15,618
1941	1,447	51,091	17,310	17,310
1942	2,949	42,318	16,421	16,421
1943	4,650	35,944	14,943	14,943
1944	5,168	29,446	14,103	14,103

\* Source of data: *Epidemiological Information Bulletin*, United Nations Relief and Rehabilitation Administration. 1:241-246 (Mar. 15), 1945.

The explanation for the dramatic outbreak in northwestern Europe is not clear. Some persons have talked freely of strains of diphtheria bacilli of increased virulence. Unfortunately for this hypothesis, no one has demonstrated strains that differ in virulence from those that prevailed in this area before the war. The usual number of *gravis* strains are still being reported in England but their significance is still problematical. Furthermore, the disease as it was seen in Norway and the Netherlands was not more severe than in for-

mer years; on the contrary, the only comforting aspect of the outbreak was the fact that the prevailing form was relatively mild even though there was a shift upward in the age distribution. It is my personal belief that the most probable explanation is to be found in factors of crowding, impaired nutrition, and lack of immunization and medical care. If the level of resistance may be depressed by faulty nutrition, persons who might normally have resisted infection or become mere carriers would have developed clinically recognizable or subclinical attacks. Doull and Lara some years ago showed that, given equal opportunities for exposing other persons, cases have an infection potential some ten times that of the carrier. A slight shift in the balance of community resistance might thus precipitate a wave of infection and this wave be augmented by increased opportunities for exposure of others owing to the overcrowding incidental to wartime conditions. I cannot escape the suspicion that these demonstrable secondary factors were of greater significance than the presence of some hypothetical and still undemonstrated enhanced virulence of the prevailing strain of infection. If this be the explanation, there is little reason to fear that other countries will be menaced by this diphtheria wave. So far, at least, we have seen no evidence of such menace, and if the experience of England is any guide, we have seen evidence that immunization in its present form is an adequate measure of protection.

Coincident with these significant phenomena in western Europe there has been an equally interesting shift in the diphtheria trend in the United States and Canada. Both countries had experienced a pre-war decline in diphtheria far greater than had been observed in any other part of the world. Beginning in 1923 the United States had enjoyed an almost precipitous drop

to previously unachieved minima. Except for slight variations and momentary upsurges, this had been a constant decline, paralleling the increasing acceptance of immunization. The drop was most marked in the northern half of the country which had formerly experienced higher rates than had the South. Today by way of contrast the diphtheria rate is very significantly higher in the South, whereas the north-eastern section of the country, which for years had experienced the highest rates, has today the lowest. It is hard for me to escape the belief that this difference is not significantly related to the extent of immunization.

During the last few years, however, there has been in some places an upsurge in diphtheria that has caused some concern and even precipitated fears lest military forces returning from Europe might be introducing more virulent strains of infection. One of the earliest and most disconcerting evidences of a rise in the western hemisphere was the outbreak in Halifax in 1940-1943. While it is true that *gravis* strains were isolated here, that the age distribution tended toward older age groups, and that many of the cases were quite

severe, yet there was nothing to cast serious doubt on the efficacy of immunization or to suggest that the apparent severity of the infection was associated with the introduction of more virulent strains than already existed in North America.

In the United States the increase has not been marked by particular episodes like that in Halifax. On the contrary it has been more general over certain areas. Table 5 based on data for 52 weeks as published in the *Public Health Reports*, shows the changes in incidence over the past few years. The year 1943 represented a minimum after which there was a sharp rise in 1944 and 1945. During the first half of 1946, the incidence was higher than for the corresponding period of any of the previous three years, but during the summer the trend shifted and the weekly rates for the current fall are strikingly below those of a year ago (Table 6). The rise in 1944 and 1945 was due principally to marked increases in incidence in the South and Southwest. The present decline is marked by an incidence below that which prevailed prior to the 1944 and 1945 rise in those areas. At the same time, however, we

TABLE 5  
*Diphtheria Cases in United States*  
*Cumulative Totals by Years*

	1941	1942	1943	1944	1945	1946
13 weeks	3,826	4,037	3,769	3,212	4,020	4,938
26 weeks	6,399	6,304	6,126	5,555	6,738	8,421
39 weeks	9,879	9,374	9,063	8,406	10,749	11,436
52 weeks	17,008	15,559	13,744	14,103	18,541	....

TABLE 6  
*Current Prevalence of Diphtheria*  
*United States by Weeks*

Week	1940	1941	1942	1943	1944	1945	1946
35	185	360	248	198	205	284	193
36	227	310	321	314	239	410	221
37	249	393	349	302	301	446	273
38	336	444	385	326	325	467	295
39	307	599	448	425	352	532	313
40	432	517	550	387	409	514	351

are seeing a slight increase in rates in the North, a rise that is more than offset by the decline in the South.

These changes in incidence do not suggest changes in the character of diphtheria, nor are they suggestive of the introduction of strains of enhanced virulence. On the contrary, they probably represent the normal fluctuation in the incidence of the residual diphtheria. We have enjoyed declines in rates for so long that many persons seem to have forgotten that in the preimmunization era, diphtheria showed periodic fluctuations in incidence, with peaks spaced three to five years apart. Careful study of the declining morbidity rates reveals that the rate of decline was not constant; on the contrary it showed variations comparable to the previous periodic changes in incidence. These fluctuations were not constant throughout the nation. It is logical to believe, therefore, that the episodes of the past three years do not imply any profound or even significant change in the diphtheria problem, but rather that they represent the normal fluctuations in incidence that were formerly masked by the precipitous decline of the disease. There is no evidence that they are due to defects in immunization. On the contrary, the increases were greatest in those areas where diphtheria was already highest. The best immunized communities with the lowest rates experienced the smallest rise in incidence. Furthermore, so far as I am aware,

nowhere has there been a sharp upsurge attended by enhanced severity of the infection and isolation of an especially virulent strain of organisms.

#### SUMMARY

From the foregoing it is apparent that the past five years have witnessed an actual increase in the incidence of diphtheria. Although occurring throughout the world, the only significant episode has been that of northwestern Europe where an amazingly high rate occurred in certain occupied areas, with appreciably smaller increases in neutral countries. There is reason to believe that this was attributable to secondary epidemiological factors rather than the appearance of new virulent strains, and that it was controllable by vigorous programs of immunization. The rise in the United States during the past two years is probably an expression of the normal periodic fluctuations in incidence, fluctuations that have heretofore been largely obscured by the rapid increase in the proportion of the population that was being immunized. That this is nothing more than a transient rise is suggested by the fact that the disease is again declining rapidly in those parts of the country chiefly responsible for the rise.

There is no evidence that especially virulent strains have been introduced from Europe or that immunization is not effective against all prevailing strains.