A NOTE ON DIPHTHERIA INCIDENCE IN CERTAIN EUROPEAN COUNTRIES

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England and Wales

In England and Wales diphtheria morbidity and mortality have alike shown a spectacular decline within recent years. The year 1944 provided the lowest incidence and mortality ever recorded; and this gratifying state of affairs is to be traced to mass immunization of children against diphtheria, which, begun in 1940, has since continued without interruption. Between 1940 and 1943 no fewer than 4,829,115 children under 15 years of age had been immunized—the estimated population of those ages in 1943 having been 8,583,000. Analysis of the returns made for 1943 shows the following rates:

Annual rates of incidence per 1,000 child-years:			
(a) In immunized children	..	..	1.16
(b) In non-immunized children	..	..	4.06
Annual rates of death per 1,000 child-years:			
(a) In immunized children	..	..	0.0104
(b) In non-immunized children	..	..	0.260

The estimated death rate in 1943 from diphtheria was about 25 times as great among the non-immunized as among the immunized. In the two years 1942 and 1943 the ratio was about 23 to 1.

But England's experience in this respect has not been paralleled by that of many other European countries, certainly not in France, Germany, Belgium, the Netherlands, and Norway. Of all the communicable diseases, diphtheria has shown in those countries by far the greatest increase during the war period; and this increase has been greatest in countries—e.g., the Netherlands and Norway—where the disease had in pre-war years reached the lowest level and where in consequence the proportion of susceptible individuals was highest.

France

In France, despite the proportion of children of school age inoculated against diphtheria with Ramon's diphtheria toxoid, a very considerable incidence was observed each year—an incidence which has become significant since 1941. Thus, whereas the average annual incidence during the 11-year period 1928–38 was 19,371 cases (maximum 23,714 in 1930 and minimum 16,264 in 1936) and the median for the same period was 19,893, the number of cases, which had dropped to 14,019 in 1939 and to 13,568 in 1940, rose steeply to reach 46,539 in 1943—i.e., an increase in the morbidity rate per 100,000 from 32.3 (in 1940) to 110 (in 1943). The first half of 1944 provided 22,179 cases, as against 22,957 in the corresponding 6 months of 1943; thus showing little reduction from the abnormal increase of 1943. During 3 months of the latter half of 1944—from August to October—the number of cases fell to 6,030, as against 10,025 in the same period of 1943. Thus 9 months of 1944 yielded 28,209 cases, as compared with 32,982 in the corresponding 9 months of 1943, and with the median figure of 14,083 for the same period. The 1944 incidence in France has therefore been twice as great as in ordinary years, and the morbidity rate per 100,000 has been 90, as against 110 in 1943 and 32 in 1940.

As regards mortality, the proportion of deaths to cases would appear to have remained unaltered. In this connexion the mortality rates per 100,000 inhabitants of certain French towns during 1938 are of interest:

Town	Mortality Rate per 100,000	Town	Mortality Rate per 100,000
Bordeaux ..	1.9	Montpellier ..	3.3
Dijon ..	2.1	Nancy ..	3.6
Lille ..	6.5	Nantes ..	1.0
Lyons ..	3.2	Paris ..	2.5
Marseilles ..	4.7	Saint-Etienne ..	10.0

Greater Germany

In Greater Germany the number of cases in the first 40 weeks of 1944 is stated to have been 204,361, as against 197,831 in the corresponding period of 1943. This increase proves that the incidence, which has been progressively rising since 1939, is

continuing on a still higher level. In the 11-year period 1928–38 the annual median was 78,452 for the Altreich, but epidemic peaks had been observed in 1928–9 and in 1935–7. The occurrence in the Altreich of 446,333 cases in the 3-year period 1936–8 had already placed diphtheria among Germany's major public health problems, but the position in the succeeding 5 years was aggravated in the territory by a rise from 143,584 in 1939 to 238,409 in 1943. In Greater Germany between 1939 and 1943 the incidence rose from 174,891 to 196,568 cases. As in other countries, distribution has been unequal; thus whereas the incidence was relatively low in Hamburg, Oldenburg, Bremen, Brandenburg, Württemberg, and Baden, it was high in East Prussia, Saxony, Silesia, Anhalt, Westphalia, and Bavaria.

As regards case mortality, the percentage fatality between 1934 and 1938 was respectively 4.6, 4.7, 3.8, 3.7, and 3.5. In 1939 it was 5%. In 1944 the case mortality rose to over 6%—thus showing an increase of 70% between 1938 and 1944; and it may be confidently asserted that, in view of the very large number of cases under consideration, the increase can scarcely be regarded as accidental.

In the Altreich, morbidity rates have risen during the past 5 years from 180 in 1939 and 174 per 100,000 in 1940 to over 300 in 1943 and 1944; while in Greater Germany the corresponding rates have been respectively 184, 179, and 315 per 100,000.

The severity of the type of diphtheria in Germany is further reflected in the fatality rates per 100,000: (a) in the Altreich between 1936 and 1939, and (b) in the Grossreich between 1940 and 1944.

Mortality Rates per 100,000 between 1936 and 1944

Altreich		Grossreich	
Year.	Rate per 100,000	Year	Rate per 100,000
1936	9.3	1940	9.0
1937	8.4	1941	11.0
1938	8.4	1942	15.5
1939	9.3	1944	18.0

The reason underlying the high morbidity in Germany and its incorporated territories is largely determined by the absence of any nation-wide policy of immunization comparable to that so successfully applied in Great Britain. On the other hand, a large-scale campaign was introduced in the pre-war period in Western Germany, while an increase in diphtheria morbidity and mortality has since led the Reich and Prussian Ministry of the Interior to approve immunization in those parts of Germany particularly affected. Moreover, immunization is compulsory for all youths at the beginning of their Landjahr—i.e., their year of agricultural service.

Belgium

In Belgium, incidence—which had risen alarmingly from 2,419 cases in 1939 (and a yearly median of 2,089 cases) to 16,072 cases in 1943—showed a decline after the first quarter of 1944. As a result the total incidence in the first 11 months of 1944 was but 6,112 cases, as compared with 13,681 in the corresponding period of 1943. The following tabular statement provides figures to illustrate the trend quarter by quarter in 1943 and 1944.

Diphtheria Incidence in Belgium by Quarters, 1943–4

Year	1st Quarter	2nd Quarter	3rd Quarter	4th Quarter (2 months)	Jan. to Nov.
1943 ..	3,085	2,885	3,621	4,090	13,681
1944 ..	3,373	1,398	647	694	6,112

The importance of the diphtheria impact on Belgium will be appreciated from the fact that between 1928 and 1938 the average number of cases annually reported was 2,111; while the average number of deaths from diphtheria was no less than 446 yearly during the same period. The subjoined table shows for the period 1930–8 the number of cases and deaths, morbidity and mortality rates per 100,000 inhabitants, and the percentage of case mortality. Morbidity and mortality rates have been calculated on a population increasing from 8,092,000 in 1930 to 8,386,000 in 1938.

Diphtheria in Belgium, 1930-8

Year	No. of Cases	Morbidity Rate per 100,000	No. of Deaths	Percentage Case Mortality	Mortality Rate per 100,000
1930	2,848	35.2	505	17.7	6.2
1931	2,016	25.0	455	22.0	5.6
1932	2,265	28.0	464	20.4	5.8
1933	2,169	26.2	470	21.2	5.8
1934	2,339	28.2	382	16.3	5.7
1935	1,780	21.4	384	21.5	4.6
1936	1,916	22.8	377	19.6	4.5
1937	2,090	24.8	476	22.8	5.7
1938	2,572	30.7	499	19.4	5.9

In 1940 the incidence rose considerably; in 1941 it was already twice the average (with 4,271 cases); and 1942, with the still higher incidence of 5,464 cases, paved the way for the explosive outburst of 1943, which provided 16,072 cases—an incidence nearly 8 times the average. The year 1944 saw a continuation of epidemic prevalence only until March, since when the curve of the incidence has fallen rapidly. November, with 447 cases, showed an incidence about one-fifth that of Nov., 1943, but one still nearly twice the normal.

It is of interest to compare the mortality of 1921 with that obtaining within recent years; in 1921 there were 884 fatal cases—representing a mortality rate of 11 per 100,000, as against the 6 reported to-day. It is stated that the mortality rate for children between the ages of 1 and 15 years was 34.6 per 100,000 in 1910, as against 20.3 between 1929 and 1931 and as compared with 15.0 in the Netherlands. In this connexion also the 476 diphtheria deaths in 1937, which represent an overall mortality rate of 5.7 per 100,000, have to be contrasted with the Netherlands rate of 1.4 in the same year.

As regards prophylaxis, immunization with Ramon's antitoxin has been fairly widely attempted, but is not compulsory.

The Netherlands

Caught up in the epidemic wave which swept over Western and Central Europe during 1942 was also Holland, from which country the wave shows even now little sign of receding. In a country where incidence during the 11-year period 1928-38 averaged 3,700 cases annually and deaths from diphtheria 210, the number of cases, which in 1939 had reached the low figure of 1,273 (14.7 per 100,000 inhabitants), totalled 5,501 in 1941, 19,527 in 1942, and 56,603 in 1943—representing morbidity rates per 100,000 of 63.6, 226, and 655. The 1943 incidence was thus 44.5 times greater than that of 1939 and 15 times the 1928-38 annual average. It is somewhat difficult to estimate the 1944 trend of the disease, as statistics are far from complete. The occurrence of 20,669 cases in the first quarter alone, however, showed that the epidemic had reached new heights, the incidence having been nearly twice that of the corresponding quarter of 1943. Moreover, that the incidence continued on this unprecedented high level during the second quarter is proved by the following returns: April (3 weeks), 3,938 cases; May (2 weeks), 2,262 cases; and June (complete), 4,293 cases. It would be safe to assume that the second quarter yielded, therefore, about 14,068 cases, making the first half-year's total 34,737, as against 19,627 in the corresponding half of 1943. July provided 3,674 cases and August (3 weeks) 3,182, as against 2,658 and 3,466 in the complete months of July and August in 1943.

Although figures have not been made available since Aug. 20 it is evident that 1944 has provided an even greater diphtheria problem than did 1943. With some 43,654 cases in the first 8 months and incidence during the remaining 4 reported as being not less than in 1943, it would appear that 1944 constituted the peak year of the war period.

In explanation of the ravages made by diphtheria in the Netherlands it has been advanced that the immunization programme, which in respect of school-children was formerly widespread but not universal, was not carried out during the war years. Thus two-thirds of the children from 6 months to 12 years of age in the liberated areas of Holland have not been immunized against diphtheria. (A new immunization campaign, however, has now been started.)

During the epidemic years it is noteworthy that the case fatality rate has not increased—remaining, as in non-epidemic

times, somewhere between 4.5 and 6.9%. Thus the case mortality rate in Holland is similar to that in Germany, but much lower than that in Belgium.

The following table shows the distribution of diphtheria in the four provinces of Limburg, Zeeland, Noord Brabant, and Gelderland during the years of occupation.

Diphtheria in Holland, 1940-4

Province	Population	Number of Cases				
		1940	1941	1942	1943	1944
Limburg	653,000	681	2,322	3,699	4,311	1,793*
Zeeland	254,000	9	35	333	965	493†
Noord Brabant ..	1,103,105	436	1,308	2,872	2,798	1,612†
Gelderland ..	993,000	139	515	2,434	5,676	3,578*

* To September. † To August.

In the year 1943, in respect of which complete returns are available, the morbidity rates per 100,000 are thus shown to have varied widely, but in all cases to have been extremely high—viz., Limburg, 660; Gelderland, 572; Zeeland, 380; Noord Brabant, 254.

Norway

Norway in 1939 had but 54 diphtheria cases; in 1943 it had 22,787. Thus with a morbidity rate per 100,000 mounting within 5 years from 1.8 to 760, Norway has earned the unenviable distinction of being the most intensely infected country during the worst diphtheria wave Europe has experienced in 50 years. Now, diphtheria incidence in Norway had been decreasing regularly during the decade immediately before the outbreak of World War II; and, because it was not considered necessary, immunization had not been carried out. But after the German occupation of the country the whole picture changed dramatically, apart from the fact that clinically the disease would not appear to have been more malignant than before, the case mortality still varying between 3.4 and 6.9%. In the autumn of 1941 diphtheria broke out in epidemic form, with the result that by the end of that year 2,611 cases had been reported, as compared with 138 in 1940. In 1942 the disease took heavy toll of the susceptible population, and 8,349 cases were notified—the incidence having been some three times higher in the towns than in the rural areas, and especially high in Stavanger. During this period the extension of diphtheria was mainly from the ports towards the interior and from the south northward. In 1943, when with 22,787 cases the overall morbidity rate of 760 per 100,000 had been reached, the incidence was no less than 3,400 per 100,000 of children under 15 years of age—the highest recorded in Europe during the war. Indeed, the only comparable attack on child life experienced in this war epidemic was in the Netherlands, where during the 3 years between April, 1941, and March, 1944, 102,726 diphtheria cases were reported among a population of 8,640,000, of which about 2,500,000 were under the age of 15 years. From this it emerges that during the 3 years under review as many as 4% of the child population in Holland between 1 and 15 years fell victim to the attack. In Germany the incidence among children under 15 years of age during 1943 was one-half that encountered in Norway in the same year.

After incidence began to rise in so alarming a fashion, active immunization is stated to have been made compulsory for school-children in Oslo and in many other cities, yet in 1942 only 15,000 were reported to have been thus protected. The temporary lack of toxoid was the reason assigned for so unsatisfactory a result of the immunization campaign. In any case, the campaign was launched too late to arrest the outbreak in its early stages.

As regards 1944, statistical data are incomplete. The disease would, however, appear to have declined somewhat, although in the first quarter of the year 4,884 cases were reported, as against 4,391 in the corresponding quarter of 1943. In the second quarter 1944 produced 3,215 cases; 1943 in the same period had 4,017; while the combined incidence of July and August in 1944 totalled but 1,321 cases, as against 3,410 in the corresponding 2 months of 1943. Thus in 1944 between January and August there were 9,440 cases, as compared with 11,908 in the same 8 months of 1943; the incidence, therefore, was still 18 times higher than the median (521).

Observations

From 1941 there has been in Northern and Central Europe an increase in diphtheria incidence unparalleled since control of the disease became possible.

Diphtheria has proved to be the leading epidemic war disease on the European continent, both in morbidity and in mortality.

Only in such countries as have pursued a vigorous immunization campaign over a period of years has a reduced incidence been observed.

The continued high incidence, with a proportionate increase in the number of carriers, places diphtheria high on the list of post-war problems in Germany and the liberated countries of the north and west.

PUBLIC HEALTH'S DEBT TO EXPERIMENTAL RESEARCH

LECTURE BY SIR WILLIAM SAVAGE

The Research Defence Society on Oct. 12 resumed its series of annual Stephen Paget memorial lectures, which had, been interrupted by the war. This, the fourteenth, lecture was given by Sir William Savage, lately County M.O.H. for Somerset and a former president of the Society of Medical Officers of Health. He took as his subject "Public Health and its Debt to Experimental Medical Research." The chair was occupied by Lord Hailey, president of the Society.

Sir William began by pointing out that public health was not a pure science, or indeed a science at all; it embraced the application of all scientific knowledge which might be turned to its purposes. The chief contributing sciences to public health had been bacteriology, physiology (including biochemistry), and, to a less extent, chemistry. The development of many sciences, particularly physiology and bacteriology, had depended mainly upon experimental research requiring animal experiments, and many of the striking advances in public health merely reflected this knowledge as applied administratively. The whole of the indebtedness of public health to experimental medical research could not be comprehended in a single lecture; therefore he took some illustrative examples.

Control of Acute Infectious Diseases

Control over acute infectious diseases was rightly placed in the forefront of the work of a medical officer of health. Such control depended for its success upon the application of precise knowledge of causation, methods of dissemination of organisms responsible, control over spread of infection, and application of methods of immunization. Until bacteriologists and epidemiologists had established the factors concerned in this spread satisfactory progress was impossible. This potent weapon of accurate knowledge was largely due to bacteriology, and had been forged by laboratory workers with animal experiment as the necessary tool.

We now know enough to control the majority of infectious diseases, but to apply such knowledge was not always possible, and sometimes not worth while because of complicating social questions such as interference with the liberty of the subject, the reluctance of many persons to respond to preventive measures, and the likelihood that the inconveniences of control would loom larger than the damage resulting from infection.

His first example of a controlled disease was the enteric fevers. Deaths from typhoid and paratyphoid fevers numbered 371 to the million of population in 1871-5, and fell to 67 by 1911, and to 3 in 1939 and 1940. The initial decline was largely due to improved water supplies and sewage disposal. Meanwhile, field investigations and bacteriological studies showed infected shellfish and milk to be important conveyers of infection; but, while the vehicles were recognized, only rarely could the reservoir of infection and the path from reservoir to vehicle be traced. This knowledge presently emerged as the result of direct bacteriological studies which demonstrated that a material proportion of cured cases continued to harbour the typhoid bacillus and became chronic carriers. It thus became clear that, apart from direct contact infection, the chronic carrier was the key to the infection of

new cases, though in paratyphoid fever the chronic carrier was often less important as an agent of spread than the symptomless recently infected person. It was also shown that food such as cream and milk was much more to blame than water as a disseminator of infection.

Recently it had been recognized that both typhoid and paratyphoid bacilli were not one and indivisible, but included a number of types to be differentiated by phage typing, thus enabling the association of a particular outbreak with infection from a carrier to be demonstrated with accuracy. Here Sir William Savage referred to the work of Bradley¹ in tracing the relationship of 22 cases, mostly in Buckinghamshire, notified over two years. These proved to be all of phage type D (an uncommon type), and all were directly traced to a milk producer who was a persistent typhoid carrier on a farm in Wiltshire, a hundred miles from the main cases in Buckinghamshire, the vehicle being milk.

Immunization against Diphtheria

Diphtheria illustrated a different point. Here, while there had been a marked decline in case mortality, until quite recently there had been no serious decline in prevalence. The deaths per million over the period 1856-65 were 247, gradually falling to 120 in 1910, to 88 in 1930, and to an average of 66 in 1936-40. The control covered three stages. The first stage was the recognition of the disease as a clinical entity, without any great knowledge as to its spread and with no specific method of treatment. The second stage started in 1894 with the introduction of diphtheria antitoxin and by the recognition that the usual method of spread was from case to case and could partly be controlled by swabbing and by other methods founded on bacteriological knowledge. Antitoxin, imperfectly used as it was at first, dramatically reduced case mortality. In Metropolitan Asylums Board hospitals the case mortality, which had ranged from 33 to 22 in 1890-5, had fallen to between 8.6 and 5.0 in 1920-5, and the greater part of this decline was due to the use of antitoxin; there was still no corresponding reduction in prevalence. The third stage was the introduction of specific immunization. This was introduced in 1926 in the U.S.A. and Canada, but in this country it had been widely practised only during the recent war. Sir William showed a table of the Canadian figures. In 1901 the deaths per 100,000 population were 35.4, and in 1920 they were still 25.7; in 1925 they were 8.1, and fell steadily until in 1940 they stood at 0.3. The incidence, which was as high as 205 per 100,000 population in 1920, was for the years 1938, 1939, and 1940 respectively 6, 4, and 2.

While efficient immunization protected the individual almost completely, statistical evidence of a general reduction in incidence was unlikely until a material proportion of the susceptible (school and pre-school) population—said by some authorities to be 50%, but he believed it to be higher—was protected; so that it was rather early to look for significant reductions in Great Britain, but the available figures were encouraging.

An Uncontrolled Disease

The lecturer's final example was whooping-cough, chosen as an illustration of the extent to which control depends upon having effective tools. Whooping-cough had been notifiable only for the last few years, so that exact figures of prevalence were not to hand; but there was little evidence of any decline in incidence. As a result of much greater care in management the deaths per million had declined from about 500, at which they stood in 1860-90, to below 100 from 1923 onwards. Deaths per million at ages 1 to 5 still remained considerable. The bacterial cause had been known for nearly forty years, but whooping-cough was so difficult to diagnose before spread of infection had taken place that it was doubtful whether control by ordinary measures was practicable. General immunization would not be worth while; on the other hand, immunization of children under 5, and especially under 2, would eliminate nearly all deaths and the bad after-effects. For this purpose a process of immunization was needed which was both effective and easy to operate.

These three diseases—the enteric fevers, diphtheria, and whooping-cough—illustrated contrasts. The first of the three

¹ *British Medical Journal*, 1943, 1, 438.