THE EPIDEMIC OUTLOOK IN EUROPE*

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During the more than five years of destruction and privation, accompanied by forcible or voluntary displacement of a large fraction of a populous continent's inhabitants, there has been no pandemic of first magnitude. Gratifying though this is, the fact must not be taken to mean that the epidemic situation is as satisfactory as it was before the war, nor as indicating a favourable outlook for the first years of transition to stable peace. The absence of real disasters may be traced to the low endemic level of most diseases during the years preceding the war, in conjunction with the advance of preventive medicine and the application of its principles on a large scale. On the other hand, caution against over-optimism is dictated by the disastrous aftermath of World War I.

During the four years of World War I Europe witnessed a rise in the endemic level of infectious diseases, and there were various pestilential outbreaks, such as that of cholera in Galicia in 1915, which caused over 17,000 deaths. A devastating typhus epidemic broke out in Serbia in 1915, causing 150,000 deaths in six months, and there were severe typhus epidemics in Egypt. Moreover, typhus caused several hundred thousand deaths in Rumania during the winter of 1917-18. There were extensive smallpox epidemics in various countries. Nevertheless, it was after the cessation of hostilities and following the disintegration of established government over wide areas that typhus, relapsing fever, cholera, malaria, dysentery, and typhoid fever swept across Eastern Europe, leaving millions of victims, and made serious inroads also in Southern and Central Europe. Whether directly due to conditions of war or not, it was at the time of the Armistice that the influenza pandemic struck, causing in less than half a year twenty million deaths throughout the world.

With World War II entering its final stage, civil administration is now in a fluid state in many areas and refugee movements are gathering momentum. These conditions, propitious to the propagation of epidemics, are likely to grow worse during the current year. They will further complicate the return to their native countries of millions of prisoners of war, shanghaied labourers, forcibly displaced people, and other uprooted men, women, and children, in themselves constituting grave potentialities so far as epidemics are concerned.

Appreciation of the problems at hand may be based on: (1) the trend of epidemic diseases in recent years in areas for which fairly accurate epidemiological data are available; (2) fragmentary information regarding the areas where no precise records of recent date exist; and (3) various estimates of displaced persons. The last-mentioned problem, which has other angles than the epidemiological, will not be dealt with in this summary.

Recent Trend of Epidemic Diseases

It may be said at once that among the five pestilential diseases covered by the International Sanitary Conventions only louse-borne typhus presents an immediate and grave danger to Europe. *Cholera*, which is a serious problem in Asia, has not appeared within recent years west of India and Afghanistan. *Yellow fever* seems hardly to have spread during the war, and has not been observed north of the North African desert belt. It should be added, moreover, that had no precautions been taken, the extension of these diseases would probably have been different.

Plague.—So far as we know, plague has not been introduced into any European port during the war. Nevertheless, this may happen at any time, as it did after World War I, because several large ports in North Africa and the Near East have become infected. The most important near-by foci are in the Suez Canal zone and at Dakar. Although they are quiescent at present on account of the season, these foci may flare up again. Meanwhile infection has spread to other ports, such as Haifa and Jaffa in Palestine, Ferryville in Tunis, Algiers and Oran in Algeria. The old plague centres in Morocco, especially at Casablanca, and in the Azores have also shown renewed activity in recent years. The outbreak in the Suez Canal zone from

Nov., 1943, to Sept., 1944, was the worst on record, 712 cases being reported, as against 359 in 1917. There were over 500 plague cases at Dakar in 1944, which is equal to the number notified in 1931, the worst year since 1920.

Smallpox.—Europe has remained practically free from smallpox during the war except for the 1944 outbreak in Sicily and Southern Italy, and an extension of the Near East epidemic into European Turkey and the neighbouring parts of Greece. The latter epidemic, which was of the classical type, has now come to an end. The Italian epidemic, the first case of which appeared in March, 1944, has centred at Palermo and at Naples and the vicinity. Although there have been some 1,500 cases all told, the epidemic is apparently not of prime importance, because all cases have been of the mild type. Only six deaths were reported, all among debilitated children. In this connexion it may be of interest that mild-type smallpox seems to have gained ground in French North Africa, while the classical type still prevails in the Near East. In the Iberian Peninsula, where smallpox was widespread during the early years of the war, there are now only sporadic cases of variola minor. The most encouraging element in the whole epidemic situation is that there were only 3 cases of smallpox in 1944 (7 cases in 1943) among the more than 200 million inhabitants of Continental Europe outside the Soviet Union and the Mediterranean peninsular areas. In 1919 there were nearly 50,000 cases of smallpox in this area.

Typhus.—Typhus presents a far greater danger than smallpox. In certain areas severe epidemics are already under way, and in much larger areas the danger is potential because for several years there has been an insidious spread of sporadic infection throughout Central Europe. It should also be remembered that North Africa and the Near East are just emerging from an epidemic wave extending from Morocco to Iran, which has been among the worst on record in several of the countries. The Soviet Union was the principal sufferer from typhus after World War I, but has apparently succeeded in keeping this disease under close control during the present conflict. The publication of records was discontinued, however, a couple of years before the outbreak of the war. In Poland typhus is known to have been on the increase during the German occupation, but numerical indications are not available for the last four years.

There are three main epidemic foci of typhus in South-Eastern Europe: the Rumanian, with centre in Bessarabia and Eastern Moldavia; the Sub-Carpathian, with centre in Sub-Carpathian Rutenia and extending into North-Eastern Hungary; the Croatian, with centre in Bosnia and probably extending into Serbia. All of these foci were in rapid evolution in the spring of last year, and there was a serious epidemic in Croatia and Bosnia, extending late into the summer. Information for recent winter months is not available for the Sub-Carpathian area. An epidemic reminiscent of the World War I disaster has broken out in Rumania. Unofficial information gives 30,000 cases in Moldavia alone, and the epidemic is likely to increase up to April or May. So far, this is undoubtedly the most serious epidemic outburst of any disease during the war. In recent years the epidemic level has been rising also in Bulgaria and Greece, and typhus was epidemic in Turkey in 1943. On the other hand, the typhus epidemic which visited Spain in 1941 and 1942, causing over 11,000 cases, has now been reduced to an endemic level. The outbreak in and around Naples during the winter of 1943-4 (somewhat over 1,000 cases all told) was brought under control in the course of a few months, and at present there is hardly any typhus in Italy. In Germany, where typhus was formerly unknown, there were over 5,000 cases in 1943, mostly among foreign workers. The cases were spread over the entire area of the Reich as far west as the Rhineland. Information for recent months is not available, but present conditions obviously favour the spread of infection. The typhus-free area of the European continent now consists only of the three Scandinavian countries, Finland, Switzerland, and, aside from relatively rare sporadic cases, the Netherlands, Belgium, and France.

With the exception of an outbreak in Tunis in March and April, 1944, and the tick-borne cases in Spain, *relapsing fever*, which followed on the great typhus epidemics of 1919-21, has not been heard from during the present war.

The above-mentioned diseases specially dealt with by the Sanitary Conventions—namely, cholera, yellow fever, plague, smallpox, and typhus—are international quarantine diseases not merely because they are the most dangerous, but also because they are of limited geographical extension and their introduction into uninfected areas is consequently feared. Various other epidemic diseases, such as typhoid fever, diphtheria, scarlet fever, and influenza, are numerically more important in Europe, but they are normally endemic in all countries. International transmission thus becomes of importance only when they develop particularly virulent strains locally or attain an unusually high incidence.

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Increase in Incidence of Common Infectious Diseases

Apart from the menace of typhus, the most significant fact of the epidemic situation is that the incidence of all the common infectious diseases has doubled or trebled in that part of the European continent for which statistics are available, and this means chiefly among the resident population of the less desperately afflicted countries. The table below, which covers mainly Central, Northern, and Western Europe, is based on the regular official returns of 12 countries where the public health services have never ceased to function and where the statistics may be considered reasonably accurate. Returns for 1943 have been used because the 1944 data are not yet complete. The pre-war data employed for comparison cover a period sufficient to include unfavourable years.

Cases of Certain Epidemic Diseases Reported in 12 Continental European Countries

	Median, 1928-38	Cases, 1943	1943 Incidence in Units of Pre-war Level
Cerebrospinal meningitis (in 15 countries)	2,561	7,996	3.1
Poliomyelitis	4,546	11,292	2.5
Typhoid fever	28,681	44,316	1.5
Dysentery (in 8 countries) ..	10,965	23,110	2.1
Diphtheria	168,354	501,911	3.0
Scarlet fever	176,275	566,398	3.2

The significant fact brought out by the above table is that there has been a heavy increase in the incidence of not merely some but all these diseases. It is unusual that entirely unrelated diseases should reach a peak during the same year and on a whole continent. The increase has probably been even greater than shown, because reporting is likely to have deteriorated in most countries, fewer physicians being available to notify civilian cases than in peacetime. Furthermore, there are excluded from the statistics the huge number of men in the armed Forces and, in several countries, also certain categories of non-resident population. There is thus a greatly increased amount of infection of all kinds, which doubtless results also in an increased ratio of carriers. It is in this polluted atmosphere that the war will have to be wound up.

Typhoid.—Efforts to control typhoid fever have been partly successful, and the increase of this disease has been the least spectacular among those shown in the table. However, the table does not include Italy, which in 1942 was responsible for one-half of the typhoid fever cases reported in all of Europe outside the U.S.S.R. and the Iberian Peninsula. The rate of increase is further lowered by the returns for Hungary, where the pre-war level has been maintained by systematic vaccination. In other Central European countries the incidence of typhoid fever has doubled, and in France it has almost trebled. Typhoid fever remains as rare in the Scandinavian countries as in the United Kingdom; in a general way, its incidence increases from north to south. While in Denmark and Sweden there was less than 1 case per 100,000 inhabitants in 1943, there were 6 in the Netherlands, 10 in pre-war Germany, 27 in Bohemia-Moravia, 36 in France (highest in the south), over 200 in Spain and probably not less in Italy, and 133 in Greece with only a fraction of the actual cases reported. Switzerland remained an area of low incidence. The problem of typhoid fever will naturally become more acute in areas where actual fighting has caused destruction of water supplies and herding of refugees.

Paratyphoid Fevers.—Paratyphoid fevers, on the other hand, are at least relatively more prevalent in the northern part of Europe, where cases are from 2 to 5 times more numerous than typhoid cases. In pre-war Germany the score is about even. In Southern Europe, on the other hand, paratyphoid cases are only a small fraction of the total enteric fever group.

Dysentery.—Dysentery is perhaps to be feared even more than typhoid fever during the immediate post-war period. The figures for this disease in the above table represent only the cases actually reported in Great Germany, Bohemia-Moravia, Hungary, Switzerland, the Netherlands, and the three Scandinavian countries, and these reports are everywhere defective. The big increase of dysentery cases over the pre-war level which took place in the Netherlands suggests that only a fraction of the cases occurring elsewhere in Central Europe have been notified. Fortunately, the type most commonly met with among the resident civilian population is the mild Sonne E. In the German Army, however, Flexner and Hiss-Y have prevailed, and there have been outbreaks of the Shiga type among prisoners of war. Their return from Central Europe may therefore give rise to epidemics of severe types, especially should

such return occur in autumn. The spread of winter dysentery for some years past in the North Sea and Scandinavian areas is a new development, the significance of which is not yet clear. Amoebic dysentery seems nowhere to have attained epidemic proportions and is unimportant in Northern and Central Europe.

Epidemic Jaundice (Infectious Hepatitis).—The "new" disease of this war has been epidemic jaundice. From an obscure existence among the garrison of Malta and in a few German Army units, it assumed proportions to interfere occasionally with military operations, and spread among the civilian population from the Libyan desert to North Cape. The disease was really not new, but was known already from World War I, when at times it was confused with Weil's disease. It occurred also among civilians in various countries, but had never been considered capable of setting up veritable epidemics. The reported incidence has for each of the last two years been as high as 1% of the civilian population in Norway and 4% in some of the provinces. Even higher rates of incidence have been reported in certain military units in North Africa. It appears to have been widespread in Germany, but if it has been made notifiable the number of cases has remained a secret. Epidemic jaundice is notifiable only in the three Scandinavian countries, Finland, and Switzerland. About 65,000 cases were reported in these five countries in 1943, and returns for 1944 are on the whole not lower. The case-mortality rate has fortunately, at least hitherto, been fairly low, usually ranging from 1 per 1,000 to 1%, but there is some evidence that it increases with age. Epidemic jaundice is clearly a virus disease of an extremely high degree of infectivity and capacity for covering distances, which may have to do with the long period of incubation (3 or 4 weeks). Since its potentialities are unknown, and means of combating it have not so far been devised, this disease deserves to be closely watched.

Among other diseases of Mediterranean origin *papataci*, or sand-fly fever, has given some trouble in the Balkans and in Italy. *Undulant fever*, whether of the Mediterranean or the Bang type, does not seem to have increased to any noteworthy extent during the war.

Poliomyelitis.—During the 20 years between the two world wars poliomyelitis has slowly spread from north to south in Europe, moving by patches of varying intensity. During the war years this spread has apparently become accelerated. The incidence is considerably higher on the Continent than in the British Isles. The most important poliomyelitis epidemics of 1943 occurred in Sweden, the Netherlands, and Central France. In 1944 Denmark, Sweden, and Switzerland were the principal sufferers, and in the former two countries the outbreaks reached their peaks only in November.

As might be expected, *cerebrospinal meningitis* has been much above its normal level ever since the beginning of the concentration of troops leading up to the war. Since 1941, however, there has been a gradual decrease in incidence, which, with minor exceptions, has constantly remained lower on the Continent than in the British Isles.

Encephalitis lethargica has not been heard from, except for the usual sporadic cases.

Diphtheria.—So far, diphtheria has turned out to be the leading epidemic disease of the war on the European continent, as a cause both of morbidity and of mortality. It is estimated that there were at least one million cases in 1943 outside of the U.S.S.R., and the case-mortality rate can at present not be set at less than 5%. In Germany alone nearly 300,000 cases were reported in 1943, with the rise continuing also in 1944, and there were 15,000 deaths from diphtheria in 1942. The incidence of carriers has increased enormously. The rise of diphtheria in Germany has been steady over a number of years, while in several other countries, and especially in Norway and the Netherlands, it has been explosive—attaining in 1943, respectively, 24 and 14 times the normal level. During the last three years there have been about 150,000 cases of diphtheria in the Netherlands. With a case-mortality rate in that country of nearly 7%, diphtheria has become one of the leading causes of death, running not very much behind tuberculosis, in spite of the rapid increase of the latter disease. A severe epidemic is prevailing also in Finland. The contrast with the experience in England, where diphtheria has actually been reduced during the war years, is most striking. On the Continent, a reduction has been attained—through vaccination—only in Hungary. Denmark, Sweden, and Switzerland have also maintained a relatively low incidence. The most serious development of diphtheria, however, is not so much its spread as the change in type and its increasing gravity. The proportion of severe croupous cases has increased, and particularly noteworthy is the increase of cases refractory even to early serum treatment. In a series of diphtheria necropsies performed in Germany 64% showed interstitial myocarditis, while this condition had formerly been found in only one-fourth of the post-mortem examinations. There has also been a shifting of the age incidence. At Rostock, in 1943, 30% of the diphtheria deaths occurred in persons over 15 years of age (6% before 1940), and 9% over 60. Diphtheria has been among the most important causes of fatal illness in the German Army, and it has also proved a fatal complication of typhus as well as of chest wounds.

Scarlet Fever.—Scarlet fever has spread almost as much as diphtheria, and with few exceptions its incidence is from two to five times the pre-war level. Nevertheless, there has been no explosive epidemic comparable to the diphtheria outbreaks in the Netherlands and Norway. There seems to have been no change in type or gravity of the disease. A heavy increase of measles has also been noted, especially during the earlier years of the war.

Influenza.—The only important epidemic disease which seems to have remained unaffected by the war is influenza. The usual winter waves have come and passed, the most recent reaching its peak during the early part of the winter of 1943-4. In spite of abnormal living conditions none of them attained the gravity of the three or four most serious inter-war epidemics. The change from influenza B to influenza A reported to have taken place in England between the 1942-3 outbreak and that of 1943-4 does not seem to have had any visible effect upon the mortality. Nevertheless, the danger of major epidemics cannot be entirely disregarded.

Endemic Diseases

In addition to the epidemic perils, the increasing incidence of endemic diseases, such as malaria, syphilis, and tuberculosis, must be carefully considered. *Malaria* is the leading cause of morbidity in a large part of the Mediterranean basin, and it is reported to have assumed epidemic proportions in Greece during the last couple of years. The areas of high endemicity in the Balkans and in Italy have probably by this time returned to their lamentable pre-control state, and further spread must be counted on, especially in view of the forced migrations. *Falciparum* infection predominates in autumn in truly Mediterranean countries, while further north *vivax* malaria prevails. The latter form may extend northward into Europe as it did after the last war.

Reports relating to the Scandinavian countries, Finland, France, and Germany indicate that the incidence of *syphilis* has increased threefold to ninefold, and the achievements of the 20 years of peace in venereal disease control have practically been wiped out. While the spread of *gonorrhoea* was checked for some years by successful sulphonamide treatments, virulent sulphonamide-resistant strains are now reported to be developing and spreading. Penicillin treatment has not yet become generalized. *Infectious skin diseases*, such as scabies, have also spread at an extraordinary rate, but the removal of soap from the list of luxuries should bring about a downward trend.

The war had no effect upon the *tuberculosis* mortality in 1939 and 1940, but an increase began in 1941 in several countries and became more or less general from 1942 and on. The situation is now much the same as during the period immediately after World War I, except that the increase this time started from a lower level. The part of the improvement gained from 1920 to 1939 which has been lost varies greatly. Great Britain, the Scandinavian countries, and Switzerland have withstood the years of trial remarkably well, although their tuberculosis problems may require increased attention during the first post-war years. The number of tuberculosis cases has increased greatly in France, Belgium, the Netherlands, Germany, Austria, Czechoslovakia, and Hungary, and it has doubled in many parts of this area. Among these countries the Netherlands are undoubtedly the worst sufferers. The Balkans, where the tuberculosis mortality was high also before the war, are probably back to the conditions of 25 years ago. In Italy the situation is likely to become worse than ever before, and Poland faces an unprecedented calamity.

Conclusion

In general, the epidemic outlook is not unlike the forecast which might have been made this day 27 years ago. As then, the general endemic level of nearly every kind of infection has risen, and serious epidemics have already appeared. In February, 1918, no one could have forecast the influenza pandemic, but other developments might have been foreseen had sufficient information been currently available. Unpredictable epidemics may occur, war or no war, but our knowledge of the existing situation is far more complete and up to date than then.

In several ways the outlook is darker than in 1918 because destruction of buildings and displacement of persons are far more widespread than during World War I. On the other hand, the endemic level was lower to start with in 1939 than it was in 1914, and the world is now better equipped to deal with many of the important infectious diseases. On the public health front World War I lasted not four but more nearly ten years. However, it was gloriously won. Many years of effort in combating infectious diseases have once more been lost so far as Europe is concerned. To make up for backsliding will take several years after the cessation of active hostilities, but the public health profession and services can win their war now as then.

Reports of Societies

THE VITAMIN B COMPLEX

A joint conference of the Biochemical Society and Nutrition Society was held on April 28 at the London School of Hygiene and Tropical Medicine. Prof. R. A. PETERS, who presided during the morning session, opened the proceedings with an expression of sympathy for the starving people in North Holland, and of the desire of all nutrition workers to give active help. After referring to the pioneer work of Eijkman and other Dutch investigators, Prof. Peters spoke of his own early work and that of Dr. Harriette Chick, of the Lister Institute, in the first steps towards the differentiation of the various members of the vitamin B complex. He emphasized that the labels vitamin B₁, B₂, B₃, etc., were originally adopted for the immediate convenience of the workers concerned. If the terminology had been changed in the light of additional knowledge it must not be implied that the original conclusions were necessarily at fault.

Dr. L. J. HARRIS, with Dr. E. KODICEK, in an introductory survey of the vitamin B complex, showed how, nearly 20 years ago, it had been found, mainly in work with rats and pigeons, that when sources of the original "water-soluble B" were heated until their antineuritic properties were lost certain other nutritive properties remained. This led to the postulation of two vitamins. The heat-labile factor was described as vitamin B₁, and has since been isolated and synthesized in the form of aneurin. The second factor was termed vitamin B₂. It was soon found that riboflavin, a yellow fluorescent substance isolated from milk whey, and now known to be very widely distributed in living tissues, could restore growth in animals restricted to diets deficient in vitamin B₂. The responses were not complete, however, and it became obvious that other factors were involved. Thus on treatment of concentrates of vitamin B₂ with charcoal and other adsorbents some factors were adsorbed while others passed through into the filtrate. The list of the better-known members of the complex was now as follows: *Heat-labile*, vitamin B₁ or aneurin. *Heat-stable*, vitamin B₂, which resolved into *adsorbed factors*, riboflavin, nicotinamide, and pyridoxine; *filtrate factors*, pantothenic acid, p-aminobenzoic acid, inositol, and choline; *unclassified factors*, biotin, folic acid, and grass-juice factors. The structural formulae for about nine of these vitamins were known. Biochemical roles in some specific enzyme action had been found in five cases. The essential roles of vitamin B₁, nicotinamide, and riboflavin were well known in relation to the deficiency symptoms of beriberi, pellagra, and cheilosis respectively. Pyridoxine and biotin were also probably required by the human subject. On the other hand, p-aminobenzoic acid and inositol might be required only for the well-being of the intestinal bacteria, which in turn might produce vitamins essential to the host. For such factors the term "secondary factors" might be appropriate.

Action in Enzyme Systems

Dr. J. H. QUASTEL, summarizing the many parts played by members of the vitamin B complex in enzyme systems, pointed out that the highly important relationship which existed between aneurin and carbohydrate metabolism was discovered by Peters and his colleagues. They found that in avitaminosis B₁ the brain could not metabolize glucose or lactic acid at the normal rate. This defect might be observed with the isolated tissues *in vitro*, and be remedied by the addition of small quantities of the vitamin. The precise point of failure was in the utilization of pyruvic acid, which accumulated in the tissues as a result of aneurin deprivation. The next important step was the discovery by Lohmann and Schuster that co-carboxylase, which was essential for the activity of yeast carboxylase, was aneurin pyrophosphate. This substance, rather than aneurin itself, was then found to be coenzyme of pyruvate oxidation. This comparatively simple situation, however, had been greatly elaborated as the result of subsequent research.

Nicotinic acid was obtained by early workers during attempts to isolate the antineuritic vitamin from yeast or rice polishings.