

THE EPIDEMIOLOGY OF INFLUENZA.

WITH the exception of a chapter on the clinical aspects, to which reference is made elsewhere, the first part of the Ministry of Health's Report on the Pandemic of Influenza¹ is devoted to the epidemiological study of influenza. The modern history of the disease is first recounted, then the statistics of 1918-19 are examined, next the clinical and the bacteriological features are described. In the four following chapters particular problems—namely, the extent of protection conferred by previous attack, the relation between meteorological variations and epidemic influenza, the epidemiological significance of domestic overcrowding, and the special prophylaxis of the disease—are considered. In the last chapter an attempt is made to summarize the lessons to be learned.

HISTORY.

The historical chapter does not profess to be exhaustive, but examines in some detail the sequence of events from the time of Sydenham. The writers point out the difficulty, amounting to impossibility, of providing a logically complete definition of "influenza," but remark that "if into the definition of influenza, while maintaining the characteristics of *apparent* suddenness, undoubted rapidity of evolution, and usually low fatality, we import the conception of peculiar attendant circumstances, such, for instance, as a break in the uniformity of epidemiological history prior to the outburst, and also keep in mind the catarrhal element of the explosive disease as a frequent clinical experience, we shall reach a plan of identification which is not logically assailable." Following this clue, it is shown that both in the experience of Sydenham and in that of his greatest successor as a medical analyst, Huxham, epidemic influenzas were dramatic incidents occurring in series of years characterized by less striking but yet distinct abnormalities of the public health.

"We think," say the compilers, "Huxham's narrative establishes the proposition that the epidemiological features of the cycle of years within which influenza exploded once or more were, *apart from such explosion*, different from the characteristics of the influenza-free epochs. Huxham's crowded references to intermittents around the explosive manifestation of influenza in 1743, his silence between 1745 and 1752, the paucity of his remarks on the subject during the quiet years 1739-42, are paralleled in the story told by Sydenham. We are also justified in making a comparison between the strange nervous fevers incidental to Huxham's narrative and Sydenham's new fever of 1685. With these long-sustained chronologies by skillful observers to guide us, it is not fantastic to suppose that the inter-relation of 'sgues' and influenzas to which Dr. Creighton called attention in the section of his history dealing with the sixteenth and seventeenth centuries, is more than casual and not a mere reflection of some theoretical pathology."

It is shown that similar but less complete evidence exists respecting the influenzas of 1762 and 1782, but that no adequate chronologies of the pandemics of 1803 and of 1831-37 have survived. Both for 1847 and for 1918, there is evidence of an abnormal condition of the public health apart from influenza, but the same remark hardly applies to the years which ushered in the great epidemics of the last ten years of the nineteenth century. Still, even for this latter period—which, as the authors candidly emphasize, constitutes the most formidable objection to the view that influenza is not an isolated event but an incident in a series of related events—prior to the supposed importation of influenza very remarkable localized outbreaks of disease had occurred, such as that at Northallerton in 1887 and the fatal epidemic of pneumonia in Middlesbrough more than a year before the pandemic. The general conclusions drawn by the compilers are in essential agreement with those reached by Dr. Hamer and by Dr. Crookshank; they doubt whether the ravages of influenza can be stayed by the discovery and destruction of some remote endemic focus of the disease, and hold that

"The problem of epidemic influenza is largely an internal problem of each nation; there is no question of shutting the wolf out of the sheepfold, he has been regularly lying down with the lamb for years; his ravages depend as much upon the disposition of the sheep within the fold as upon his appetite. Thus broadly stated, the hypothesis neglects some portion of the truth; however combustible the material, there can be no fire without a spark, and when the fire has been started it may spread to material not naturally combustible. We must not ignore this consideration, but it has perhaps been over-emphasized in current discussion."

¹H.M. Stationery Office. (10s. net.)

RECENT STATISTICS.

In the following chapter the general statistics of 1918-19 are examined. It is pointed out that: "(1) The mortality in England and Wales, as a whole, attributable directly or indirectly to influenza, is without any precedent in magnitude; (2) that that of the metropolis affords no parallel more recent than 1847; (3) that the toll taken at the young adult ages of life is without any known West European or North American precedent." The relation between the death rates from influenza in the three waves and the normal pre-epidemic standardized rates (all causes) of the county and metropolitan boroughs is studied by the method of correlation. It is shown that the death rates in the first wave were substantially correlated with the normal death rates, a finding comparable with that of Professor Raymond Pearl of Baltimore, who showed that in America "an essential factor in determining the degree of explosiveness of the outbreak of epidemic influenza in a particular city were the normal mortality conditions prevailing in that city"; but, for reasons explained in the report, the compilers do not regard their arithmetical results as deserving of much confidence, and suspect that the heterogeneity of the data has influenced the numerical magnitudes of the correlations. The writers devote attention to the form of the epidemic wave in time. They remark that the data of epidemics on ships, carefully compiled by the health authorities of the Commonwealth of Australia, are particularly instructive, that the forms of these curves are complex, almost suggesting in each a triple wave reproducing in miniature the world evolution of the pandemic.

"On the ship we do really have ordinary social life in isolation from the great world, a real microcosm. The remarkable point is that within this microcosm we have seen in miniature a triple wave, such as the whole world experienced, but running through its phases in weeks instead of months. But this evolution was not parallel with the world evolution, since the voyage started after the first act of the world drama. Whatever organism was 'carried,' it must have belonged to the autumn variety, not to the summer vintage. Hence, if this threefold wave phenomenon is not a mere illusion, it would seem to be a function of the organism as modified by passage, a modification determined by the environmental conditions."

BACTERIOLOGY.

The chapter on bacteriology, by Sir Frederick Andrewes, is worthy of its author's reputation. At the outset Sir Frederick warns the reader that "the germ theory of disease is now so firmly established that we are in danger of too readily accepting a microbe as the causal agent of a disease, and of neglecting the rigid proofs which should be demanded." He points out that from the experience gained between 1890 and 1918, "it cannot be said that the status of Pfeiffer's bacillus as the cause of epidemic influenza had materially altered. No further confirmation had been obtained, nor had the observed facts disproved a possible relationship." The results in 1918 did not suffice to settle the question. The failures to recover Pfeiffer's bacillus in the summer could not, in Sir Frederick's opinion, be referred to a faulty choice of medium or defective technique.

"Amongst those who have recorded their failure to find the organism are bacteriologists of the highest repute: the failures were perhaps more numerous in Germany than elsewhere: such men as Kolle, Gruber, Friedemann, and many others, failed to find it, while Uhlenhuth and Pfeiffer himself were puzzled at their want of regularity in finding it. It is expressly stated by Sobernheim that, using precisely the same technique, he uniformly failed to find it in the summer epidemic and almost uniformly succeeded in October." "The evidence," says Sir Frederick, "does not carry conviction as to the primary causal relationship of Pfeiffer's bacillus to epidemic influenza. The varying results cannot be correlated with the competence of the observers. The observed facts, notably the earlier negative findings in certain localities, and the more general positive results in the autumn outbreak, would be better explained on the assumption that the bacillus played a very important secondary rôle in the disease, and was not the primary infecting agent." Decisive significance cannot be assigned to the results of agglutination or complement fixation tests because Pfeiffer's organism is at least so commonly present as a definitely pathogenic invader "that it would be strange indeed if antibodies were not formed against it."

Important evidence might be furnished by unequivocally successful results of prophylactic immunization by vaccines containing Pfeiffer's bacillus. Sir Frederick Andrewes calls attention to the apparently striking results of large scale inoculations, but notes the desirability of

statistical criticism. This point is in fact taken up elsewhere in the report, where it is remarked that "no inferences can be drawn from a lower attack rate upon inoculated than upon uninoculated persons if the inoculations were carried out during the epidemic, without due allowance for variations of length of exposure." This simple consideration rules out most of the published data. For the rest, the compilers say:

"Such evidence as we have in favour of any practical advantage points to the efficacy of vaccines derived from organisms cultivated from cases existing in the neighbourhood of the tested population. This is illustrated by the example quoted in the section on influenza in the annual report of the Chief Medical Officer. A pure Pfeiffer vaccine was used for the inoculation of employees (volunteers) in a London business house, and the inoculated escaped the disease, while their co-workers experienced a normal incidence. It appears doubtful whether any simple stock vaccine derived from a limited number of strains of micro-organisms implicated in the clinical evolution of influenza is likely to be of value."

It cannot be said that the evidence derived from prophylactic inoculation much strengthens the case against Pfeiffer's organism as the primary pathogenic agent.

Sir Frederick Andrewes thinks that the evidence in favour of a filter-passing organism as the essential cause is suggestive but unconvincing.

"The strength of the case argued by Gibson and his colleagues lies in the fact that there was a definite incubation period in their experiments, that they succeeded in carrying on the effects through more than one generation of animals, and that they produced them with cultures. The weakness lies in the fact that the lesions in their animals do not afford convincing proof of influenza. . . . The cultivation of filter-passing organisms is notoriously a difficult thing, and beset with many fallacies, as Arkwright has well pointed out in his recent criticism of the subject. The results so far recorded in influenza must be received with caution."

Whether or not a primary significance can be assigned to Pfeiffer's bacillus, Sir Frederick believes "there can be no doubt that it played a part of vast importance in the recent epidemic of influenza. Though we know it, at normal times, as a mere agent of catarrh, the more virulent types which prevail in epidemic times are more highly toxic, and seem especially to lead to escape of blood from the smaller vessels in the lungs and bronchi. It seems probable that we must regard Pfeiffer's bacillus as the chief cause of the haemorrhagic oedema and the localized haemorrhagic areas in the lungs which have been so conspicuous a feature of the late epidemic." Next in importance come certain types of streptococci; *Streptococcus haemolyticus* has been often found in the pulmonary lesions, and its presence there has "been a distinguishing feature of the epidemic, especially in the autumn, when the disease exhibited its highest fatality, and it was found in the worst cases."

IS IMMUNITY CONFERRED BY A PREVIOUS ATTACK?

In the next chapter the compilers discuss the question whether those who had been attacked by influenza in one phase of the pandemic were, on that account, less liable to attack in a subsequent outbreak. This matter is examined in detail and perhaps constitutes the most original section of the report. Briefly, the method adopted was this. The histories of considerable samples of different populations were followed through all the phases of the epidemic, and it was determined whether the attack rates in, say, the autumn were significantly different (from the statistical point of view) upon those who had and those who had not been attacked in the summer. It was found that the after-histories of the exposed to risk were very different in different places. In some cases—for instance, in Leicester—those attacked in the summer came off far better in the autumn than those who had not been attacked in the summer; in other cases—for instance, in Manchester—the summer victims experienced an identical rate with that suffered by those not attacked in the summer. The possible reasons for these differences are discussed in detail, and the conclusion is reached that the immunizing value of the strains of organisms probably differed in different parts of the country. The method of analysis is subject to a theoretical criticism. Thus it is assumed that if the attack rates in the autumn upon those who were and were not attacked in the summer are the same, then the summer attack conferred no protection. But if those singled out for attack by the disease in the

summer were so singled out because their resisting power was low, then, *ceteris paribus*, they should again have a higher attack rate in the autumn; if they have only an equal attack rate, the summer experience helped them. But it may be urged in reply that there is little or no evidence that the first phase of the pandemic did select those who, judged by any extrinsic criterion, were peculiarly liable to respiratory attacks. In any event, the practical result that whatever protection was conferred was far from being absolute, is plain. Upon the whole, there is a balance of probability that the summer influenza had some immunizing value; less reason can be shown for thinking that autumn attacks shielded their victims in the third phase.

THE WEATHER.

The following chapter deals with the weather and disease. This chapter contains an interesting summary of traditional opinions and brings out the relation between changes of temperature and variations of mortality from respiratory disease. It also shows that before each of the three waves of influenza warmth was deficient, but, as might have been expected, the compilers hold that whatever part was played by meteorological factors in the genesis of the pandemic must have been quite a minor one.

OVERCROWDING.

In the next chapter the relation between domestic overcrowding and the incidence of influenza is studied; no close statistical relation was found and the tentative conclusion is reached

"that the natural infectivity of the germ may be so high that the necessary exposures and contacts of all persons living under urban conditions are sufficiently numerous to provide opportunities of transfer so effective that any increase above the average is relatively a factor of negligible order."

It is, however, specifically stated that these conclusions apply solely to incidence, not to fatality, it being probable that the fatality amongst patients grossly overcrowded (as, for instance, upon war transports) was far above the average.

Chapter IX deals with general prophylaxis. The compilers remark that

"from what has been said in this report it follows that to avoid crowds, to shield the mouth and nose when coughing or sneezing, not wantonly to thrust one's face into the face of one's interlocutor, are essentially rational and appropriate methods of reducing the risk to take influenza. It even appears probable that the one form of overcrowding which in some little measure can be controlled by the individual is the form most potent to spread the disease. In the present state of the nation, to advise the avoidance of overcrowded tenements and lodgings is indeed a counsel of perfection; it is likewise a vain quest to seek for public conveyances not grossly overcrowded; but it is quite easy not to frequent theatres, music halls, and picture houses; it is even possible to avoid bargain sales, political meetings, and assemblies. These forms of congestion belong to the extra-domestic group which, by a process of exclusion, we have discovered to be more influential than intradomestic conditions admittedly hard to control now."

Much importance is attached to the hygiene of the nasopharynx, and attention is directed to the researches of Dr. Leonard Hill (described in his reports to the Medical Research Council, and also in our columns). Due weight is given to the importance of further research into the immediate etiology of the disease, but "the public should not suppose either that nothing of service can be attempted until the authentic *materies morbi* of influenza has been unequivocally defined or that the recognition and successful isolation of the authentic microbe would necessarily be followed by elimination of the influenza scourge."

SUMMARY AND FINAL HYPOTHESIS.

The last chapter of this part is a general summary of those we have discussed, and a provisional statement of a hypothesis which covers the facts. This hypothesis is that there have been three phases in the development of influenza.

"The first, which lasted for many centuries, was, if we may be permitted to use teleological language, a series of attempts to maintain a high level of infectivity or dispersiveness, which attempts were unsuccessful. The second phase, ushered in by the year 1889, is marked by a partial victory of the germ, a fairly constant infective power has been secured, and much infection is produced throughout the world at frequent intervals, but the toxicity relative to the infectivity is still slight. The final phase is of complete victory; infective power is maintained, even enhanced, and to this is added a toxicity surpassed

by few epidemiological competitors. Viewed as a contest between man and 'germ,' it would seem that in the congestion of public transport and the multiplication of public assemblies and entertainments, features which increasingly characterize the development of the European type of civilization, a strategical advantage was given to the enemy. Finally, in the provision of countless incubators, whether in garrisons, war-time factories, or abnormally overcrowded and ill-ventilated means of transport and places of entertainment, the opportunity was afforded for the development of destructive powers which secured to the enemy a decisive and overwhelming victory."

These reflections suggest that there are dangers ahead.

"The dangers to the world from epidemic sickness in this matter of influenza are enhanced in two ways. The inevitable trend of the movement of population will keep the infectivity of the organism at a high level. This we may face with equanimity. But if anywhere in the world there be large collections of men, whether through war or economic strife, or through that dissolution of society which a certain degree of collective misery and disorganization entails, herded together *en masse*, there will be opportunities for the other modification of the *materies morbi*, which renders it apt to conquer the world. No sanitary cordon, no quarantine, will shield us from this danger. The porters of the infection may not be sick; to exclude even the sick has often been found a task beyond the power of a quarantine authority; land quarantine has, in fact, never yet succeeded. To realize that the material well-being of the inhabitants of a foreign—perhaps even a hostile—country is a pressing concern of ours is very hard. Yet the teaching of this pandemic is that it is a hard truth. Any supra-national organization for the control of epidemics will need to face it. The popular belief that misery breeds disease is strictly true, and the influenza of 1918-19 is no exception to the rule. The history of the world has never yet provided an instance of a mortal and highly dispersive illness among the antecedents of which human misery did not assume a prominent place."

In his introduction to the volume Sir George Newman emphasizes one aspect of this doctrine—namely, that, as he puts it,

"The fundamental requirement to make us masters of our fate is a universal improvement in the standard of health and the conditions of life. No technical device, no narrow or specific remedy for pestilence, can ultimately, triumph apart from a sanitary environment for the community and the sound nutrition of the individual. They are the bed-rock. Out of them spring the sources of national vitality. Hardly less certain is it that we require, and must seek till we find, more knowledge. We have in substantial degree the means of controlling tuberculosis and syphilis, malaria and plague; we fail to control these four pestilences largely because we do not use the means; and education is perhaps the answer to that. But in the case of influenza and its allies we are not yet in possession of the means, and whilst we press forward with the improvement of sanitation, of nutrition, and of the conditions of life, we must apply ourselves anew to search and research into the causes of primary and secondary infections, into epidemic catarrh, and the common cold, into carriers, and into immunity. That is perhaps the principal lesson which is taught us by our experience of the great pandemic."

With this quotation from the preface by the Chief Medical Officer we shall conclude our notice of the report. The second part, compiled by Dr. Bruce Low, C.B., and Dr. S. P. James, which compresses within less than 200 pages a vast amount of statistical and other information respecting influenza abroad, does not lend itself to summarization, but is not the less worthy of perusal. The same remark applies to the valuable collection of scientific papers by medical officers of health, as well as by officers of the Ministry, which form appendices to the report.

We believe that Sir George Newman was justified in characterizing this report as a "contribution of exceptional interest and suggestiveness," and that its authors, both the medical members of the Ministry's staff and the other medical men, not civil servants, who have collaborated, deserve the thanks of their colleagues. A volume of 577 pages which announces no sensational discovery and promises no conquest of influenza in the near future cannot render its authors popular heroes. They will, however, be sufficiently rewarded if the outcome of their labours is of use to other students of a menacing yet fascinating problem.

THE Hispano-Portugese Association for the Advancement of Science will meet at Oporto in June.

A SCIENTIFIC expedition to Central Asia, under the direction of Dr. Roy C. Andrews, has been organized in the United States by the American Museum of Natural History to carry out researches in anthropology, archaeology, zoology, and medical geography in the less explored regions of Turkestan, Tibet, and Mongolia.

UNIVERSITY GRANTS.

THE University Grants Committee appointed in July, 1919, to inquire into the financial needs of university education in the United Kingdom, and to advise the Government as to the application of any grants that may be made by Parliament towards meeting them, has made a report,¹ after giving full consideration to all the representations made to it, and after carrying out a series of visitations to all the universities and colleges in England, Scotland and Wales. The parliamentary grant is now £1,000,000 a year; in 1919-20 a special grant of £500,000 in addition was made, and in 1920-21 the unexpended balance of this, amounting to £196,000, was available. During the past year nearly the whole of this unexpended balance has been distributed. The Chancellor of the Exchequer has promised that the annual vote this year shall be increased to £1,500,000.

The medical member of the University Grants Committee is Sir Wilmot Herringham, who succeeded the late Sir William Osler in November, 1919.

The Committee begins by expressing its sense of the efficiency maintained in the universities and colleges generally in face of many and serious difficulties, but is convinced that the present resources of the universities are inadequate, in spite of the facts that since the armistice the Treasury grants have been increased by 83 per cent., that tuition fees have been increased, that a few local education authorities have increased their support, and that many of the universities are endeavouring also to supplement their revenues by public appeals. On the other hand, it is pointed out that all expenditure, in particular unavoidable expenditure on wages and material, has grown enormously, and that even if the pre-war income were doubled, it is doubtful whether the universities would be as well off as they were before the war.

The report goes on to point out that the number of students since the armistice has been unprecedented; the total number of full-time students in attendance at grant-aided institutions and colleges rose from 23,872 in the academic session 1913-14 to 36,423 in 1919-20, and the number was raised to 37,748 by the addition of certain colleges to the list. Of this total 11,682 were ex-service students, but it is pointed out that a permanent increase over 1913-14 is to be expected, owing to the larger number of secondary schools and to the operation of the Education Act, 1918.

An important part of the present financial embarrassments of the universities and colleges arises out of the need for increased salaries and improved superannuation. The Committee agrees that the present salaries of many university teachers are inadequate, and has evidence that many members of the university staffs are living in circumstances incompatible with continued efficiency; many teachers are not in a position to enjoy the advantages essential to the proper discharge of their duties, such as books, travel and membership of learned societies. Further, many are compelled to supplement their income by dissipating their energies in outside work. The Committee does not commend the scheme of salaries and increases proposed by the Association of University Teachers; it agrees that it would be an advantage if all the grant-aided institutions agreed upon minimum salaries, but does not agree to a dead level of uniformity as between institutions. The Committee also agrees that it is important to establish an equitable system of superannuation. The Federated Superannuation System for the Universities in England, established in 1912, provided that 5 per cent. should be paid by the institution and 5 per cent. by the beneficiary. The contribution of the institution has now been increased to 10 per cent. The youth of the scheme renders it desirable to make special provision for many of the senior teachers. The position in Scotland is special, and is, the Committee thinks, unsatisfactory.

An important section of the report deals with equipment and accommodation, and it is declared that the character and efficiency of a university may be gauged by its treatment of its central organ—the library—which is essential to the well-being alike of the arts and science. Ampler funds are needed and the status of the librarian should be improved. For the subjects included in the faculty of pure science additional staff and improved accommodation and equipment are required. In the

¹ Cd. 1163. H.M. Stationery Office. Price 3d. net.