

REPORT ON THE PANDEMIC OF INFLUENZA, 1918-19.

CHIEF MEDICAL OFFICER'S INTRODUCTION.

To the Right Hon.

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Minister of Health.

SIR,

1. I HAVE the honour to submit a report on the Influenza Epidemic of 1918 and 1919. This report, taken in conjunction with the *Report on the Mortality from Influenza in England and Wales during the Epidemic of 1918-19* recently issued by the Registrar-General (Cmd. 700), constitutes the official record which it is necessary to make concerning the outbreak. The report has been reduced to the narrowest compass compatible with an adequate presentation of the facts and the inclusion of records from various parts of the world. There can be no doubt that as an historical survey it will prove invaluable for future reference in the event of subsequent epidemics.

2. This document deals with one of the great historic scourges of our time, a pestilence which affected the well-being of millions of men and women and destroyed more human lives in a few months than did the European war in five years, carrying off upwards of 150,000 persons in England and Wales alone. The report is divided into three parts. Part I. has been prepared by Dr. Major Greenwood, with the assistance of Dr. Thomas Carnwath, both of them Medical Officers of the Ministry, and with the collaboration of Dr. Herbert French (Physician to His Majesty's Household and to Guy's Hospital) and Sir Frederick Andrewes (Professor of Pathology and Bacteriology at St. Bartholomew's Hospital, University of London). It deals with Influenza in Great Britain and Ireland, and will be found to be a contribution of exceptional interest and suggestiveness. I desire to express my high appreciation of its value, and of the public service its writers have rendered in its preparation. Part II. has been compiled by Dr. Robert Bruce Low, C.B., and Dr. S. P. James, Medical Officers of the Ministry. It presents an account by the former of the incidence of Influenza in Europe and the Western Hemisphere, and by the latter of its incidence in Australasia and parts of Africa and Asia. The section contains a large amount of information not hitherto collected respecting the epidemic in many parts of the world.

Part III. contains 12 special papers reporting inquiries into different aspects of Influenza as it occurred in this country. Several of them are by Medical Officers of the Ministry, but we are fortunate in being able to include papers from Dr. James Niven, the Medical Officer of Health of Manchester, and some of his colleagues in the Public Health Service, and a paper by Dr. Brownlee.

3. This Report does not contain a detailed history of the previous outbreaks of Influenza in this or other countries. In 1852 Dr. Theophilus Thompson described, in his *Annals of Influenza in Great Britain*, the record as it concerns this country from 1510 to 1837 ; the epidemic of 1847 was described by Dr. T. B. Peacock ; Hirsch published in his *Geographical and Historical Pathology* a list of outbreaks in different countries from 1173 to 1875; in 1890 Dr. Clemow ventured even further back and discussed the probable influenza epidemics from 877 to 1481; in the following year (1891) was issued an official report to the Local Government Board by Dr. Franklin Parsons on the epidemics of 1889-92 (also recorded by Dr. Dixey) ; and in 1891 and 1894 there appeared the two volumes of Dr. Charles Creighton's book on the *History of Epidemics in Great Britain*, containing his review of the occurrences of the disease in this country. Speaking generally it is evident that since early times there have been outbreaks of epidemic sickness not distinguishable from what we now think of as influenza, though it is certain that the generic term has been used to cover a wide variety of catarrhal conditions. Creighton begins his list of influenza epidemics with 1173, and his examples include the epidemics of 1510, 1540, 1557, 1580, and that of 70 years later, the outbreak of 1657, which was described by Willis in what Creighton characterises as " the first systematic piece of epidemiology written in England." Then we come to the period of Thomas Sydenham and his description of the "epidemic coughs" and subsequent *febris comatosa* of 1675 and 1679. He argued that one epidemic constitution passed gradually into another. There followed at irregular intervals a series of outbreaks throughout the 18th century; in 1833 a severe epidemic of influenza occurred, succeeded by less conspicuous prevalences until the pandemic of 1847. This was reported to have caused an excess of 5,000 deaths during the six weeks that it lasted. In the three worst weeks (December) it raised the deaths at the age of childhood 83 per cent., among adults 104 per cent., and in old age 247 per cent.

The subsequent course of the disease may be traced on the accompanying chart. Except for a small epidemic in 1855, the trend of prevalence was steadily downward until 1870. During the two following decades influenza almost disappeared from the death records of this country. Then came the great pandemic of 1889-1892, which initiated a new phase in the

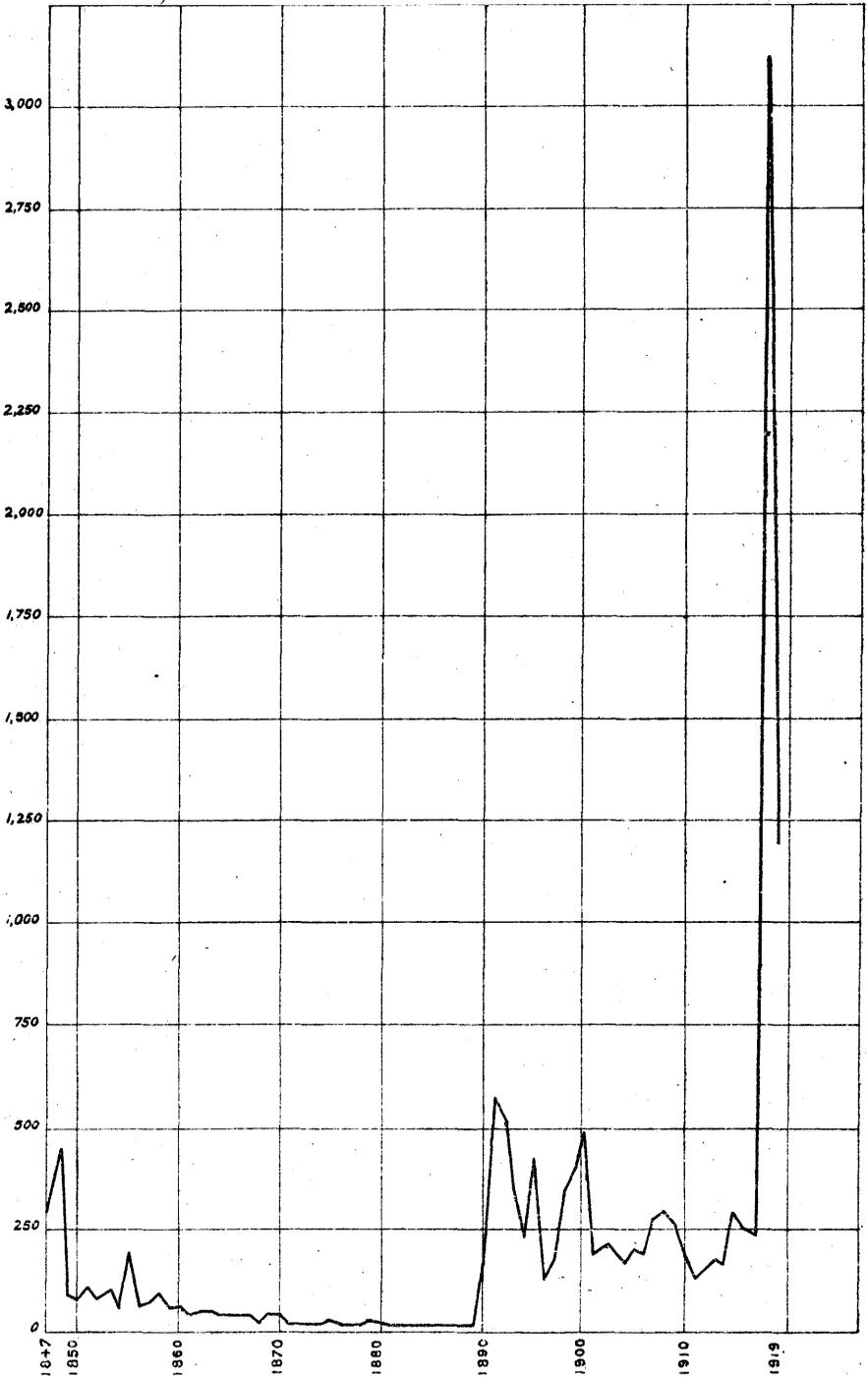
evolution of the disease—the phase of complete victory in which "infective power is maintained, even enhanced, and" to this is added a toxicity surpassed by few epidemiological "competitors." Since 1890 influenza has maintained its position as a factor of great importance in the causation of mortality. Outbreaks of considerable magnitude occurred in 1895, 1900, 1908, and 1915, but that in 1918-19, which is the subject of the present report, far surpassed anything previously experienced. In 1918 there were 3,129 deaths from influenza per million of population in England and Wales. The corresponding figure for 1919 was 1,170.

The pandemic of 1889-92 revealed for the first time the disease in successive waves separated by short intervals. Dr. Franklin Parsons furnished a lengthy report on the epidemic of 1889-92, treating of its occurrence both in this and other countries. He also discussed the etiology (Pfeiffer's bacillus had not then been isolated), incidence, and local behaviour of the disease, giving brief notes on some of its clinical features. Dr. Klein added an appendix on the pathological aspects. Dr. Parsons concluded that the disease was imported (probably from Russia), that it followed the lines of human intercourse, that it was spread from person to person, that it prevailed independently of season and climate, that the first cases were mild and the subsequent cases more severe. Whilst the report did not greatly add to our knowledge of clinical influenza, it dealt fully with incidence, and it effectually dispelled the then prevalent belief that the disease was miasmatic. Parsons showed, by his detailed records of the behaviour of the disease in areas and in institutions, that it spread, independently of the weather, from person to person.

The Clinical Character of Influenza.

4. The influenza of the 17th century had, as its most constant symptoms, cough, vomiting, hæmoptysis, aches and weariness in the head, back, and limbs, and some fever. In addition there was frequently thrush and epistaxis. According to Sydenham the disease was of the nature of "epidemic ague" up to 1685, but afterwards changed its character to that of "pestilential fever." In 1729 Huxham, of Plymouth, described the disease as "a catarrhal febricula, racking pain in the head, "delirium with incessant cough, slight dyspepsia, anorexia, "langour, and rheumatic pains"; a few years later he characterised it as having also rigors, "flying pains" in the back, and violent headaches; and once more after ten years, he adds pains in the joints and universal lassitude as the leading features. In 1767 Heberden described the attack seen by him as beginning with severe chills, then a troublesome cough, acute pains in the head, back, and abdomen, with fever, and prostration. Fifteen years later the College of Physicians

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said that "the universal and almost pathognomonic symptom was a distressing pain and sense of constriction in the forehead, temples, and sometimes in the whole face, accompanied with a sense of soreness about the cheek-bones under the muscles," with languor of body and depression of mind. The influenza of 1833 assumed a catarrhal character—sudden attack, headache, coryza, and cough, pain in the chest, and depression; and in the great epidemic of 1847 these characters predominated, accompanied by pneumonia and bronchitis.

5. We have many contemporaneous accounts of the Influenza of 1889-92. The catarrhal symptoms receded into the background; extreme prostration, weakness, and nervous depression were the outstanding features. Frontal headache, pain in the eyeballs, and muscular pains were also common. In the later phases of that epidemic a tendency to lung complications was manifested, especially "a low and insidious form of pneumonia, to which the mortality from influenza was in large part due" (Parsons). Pye-Smith wrote a description in 1890 based on the first two years of the epidemic. He said that most of the symptoms were those of "a common feverish cold, attended with greater pyrexia and with more severe depression of strength." The attack began suddenly with rigors, and pain "behind the eyes," prostration, pains in the limbs, and some faintness, and often an irritating dry cough. Sometimes there was great dyspnoea and loss of appetite. The attack passed off at the end of three to five days. If it continued longer, pneumonia or bronchitis supervened. Convalescence was slow, with muscular weakness and malaise. The fatality was low. In the 25 years following 1890, influenza was widely prevalent in England and Wales—a condition totally different from its relatively quiescent stage between 1850 and 1889.

6. The clinical descriptions and records of the epidemic of 1918-19 far surpass in detail and accuracy any previous accounts of the disease. There was, moreover, a remarkable uniformity of incidence and clinical character whether the cases occurred in Great Britain, in France, in the Near East, in India, in North or in South America. We are thus authorised to believe that the view of clinical influenza set out in the present report by Dr. Herbert French, who had special opportunities of studying its characteristics, is of typical instances. Medical reporters have of course chosen different ways of presentation of their clinical experience. Dr. French sets before us a picture of the disease which brings into bold relief the principal features of the first and second waves. Elsewhere Dr. Small, of Edinburgh, has described the clinical aspects of the epidemic as it occurred in France—the simple three-day type of ordinary influenza, the pulmonary, malarial, gastric, septicaemic, and cerebral types in order of frequency in the first wave; the simple, though more severe, ordinary influenza and the grave pulmonary-septicemic

type of the second wave. Dr. Burnford, in Macedonia, found that soldiers from various parts of the world suffered clinically from (a) pharyngitis, with or without implication of the mucosa of the nose and sinuses, (b) laryngitis, (c) tracheitis, (d) bronchitis, (e) bronchiolitis, or (f) pneumonitis, with involvement of the whole lung tissue—indicating a progressive infection of the respiratory tract.

7. All observers are agreed as to the differentiating characteristics of the two waves, the first in June and July, 1918, the second in October and November, 1918 (the third presenting the features of the second, in February, 1919). The *first wave* was one of "the three-day-fever" type. There was sudden onset, lassitude and prostration, general aching, a rapid rise in temperature, a relatively slow but unstable pulse, coated tongue, loss of appetite, a sore throat, and a congested nasopharynx, headaches, a rapid convalescence, and a low mortality. Though the respiration was quickened there was no dyspnoea, gastrointestinal symptoms were common but not severe, and, as a rule, there was no albuminuria. There were, of course, variations and complications, the most frequent involvement being the respiratory tract. Whilst coryza was rare, epistaxis and other haemorrhages were common; substernal pain occurred, and was worse owing to cough, which was almost universal. The progressive changes in the sputum were significant. The chief nervous conditions were psychical, and sleeplessness was common.

On its clinical side the outbreak was remarkable, not for its virulence or mortality, both of which were low, but for its complete change of age incidence. It attacked youth. On its pathological side a damaged condition of the capillary vascular system was distinctive, leading to haemorrhages in the mucous and serous membranes, the respiratory tract, and the lungs. In some ways it seemed to be a "bacteriaemia" localised in particular in the pulmonary blood vessels, and haemorrhage paved the way for secondary infections.

8. The clinical features of the *second wave* ushered in much more severe forms of the disease. As Dr. French points out, of a thousand individuals attacked in the autumn, about 800 suffered from the three-day-fever type, though of somewhat unusual severity; the remaining 200 displayed pulmonary complications, and of these 80 may be thought of as moderately severe and 120 as desperately ill. Of the 120, between 60 and 80 would prove fatal (Abrahams). Many cases began as in the first wave, though epistaxis appeared to be particularly common. Some cases became pulmonary at the outset, others in a few hours or days. The pulmonary involvement was an acute infective inflammation, sometimes progressing as a bronchopneumonia, at other times it swept through the body like a virulent toxæmia or septicaemia. In some cases there were

few or no physical signs, in others dulness, bronchial breathing, crackling rales, bronchophony, and pectoriloquy; in others signs of coagulative oedema, haemorrhage, abscess, and collapse. The normal progress of a pneumonia case was rare. There was pain, headache "behind the eyes," ear-ache, cough, a high respiration rate ("polypnoea"), variable fever, followed by a toxæmic or pulmonary complication on the third or fourth day. The toxæmia was heralded by early cyanosis, delirium, a rapid pulse and epistaxis. The heliotrope cyanosis indicated a bad prognosis; it was evidently not cardiac in origin, but an intoxication, recalling the "purulent bronchitis" experienced in 1916-17 at Aldershot (expectoration of enormous quantities of purulent sputum, heliotrope cyanosis, and high fatality), itself an infection due in part to *B. Influenzae* and in part to the *Micrococcus catarrhalis*, streptococcus, or associated organisms. There are grounds for believing that both forms of cyanosis were caused by an albuminous exudate in the alveoli and interstitial tissue of the lung. The pulmonary complications which arose were various, and included oedema, broncho-pneumonia, haemorrhage, effusions, and sometimes abscess. The onset of the lung changes was indicated by alteration in the character of the sputum, increased respiration rate, pain, and diminished respiratory movements and air entry (Sundell). The mild type of the first wave and the contrasting type of the second and third waves seem to have been very much the same everywhere, except that different stages of the epidemic did not occur at quite the same periods or with uniform sequence in different countries.

9. It should be added that in February 1920 there was, after nine months' quiescence, a further rise in influenza in this country, and a sharp outbreak in some of the chief cities of the United States (beginning in January) and in Switzerland and Denmark. The disease was mild and caused relatively few deaths, the age incidence reverted, with some exceptions, to that of pre-epidemic years (a high incidence in childhood and old age, and low in early adult life).

The Causation of Influenza.

10. The problem of the cause of influenza is not yet solved. Clinicians, bacteriologists, and epidemiologists are all agreed that Pfeiffer's bacillus is associated with the disease, but whether it is the cause remains unproven. Dr. French thinks it has not yet been deposed from its place as the causal organism, but Sir Frederick Andrewes considers that its position as the primary cause has been in no way strengthened by the experience of the recent pandemic. Many observers would be found to agree with Dr. French that in all probability this organism was the primary one responsible for the three-day-fever type of influenza common in the summer and autumn of 1918; but

that the graver cases were due to a combination between the Pfeiffer bacillus and an additional organism or organisms (streptococcus, diplococcus, or diplo-streptococcus) virulently or symbiotically associated with it. In a word they would suggest that the "influenza" cases were caused by Pfeiffer's bacillus, whilst the septicaemia or pneumonia types were due to an associated group of organisms. The significance of this association, however, requires further investigation.

11. As Sir Frederick Andrewes points out in his lucid and able review of the bacteriology of influenza, there are three means at hand enabling us to form a useful opinion on the part played by a specific organism. First, there is its presence in cases of the disease—its presence, isolation, separate culture, and subsequent inoculation and reproduction of the disease. The fourth of these postulates has not been even approximately satisfied, but the presence of the organism in clinical cases of the disease, its isolation from the body, before or after death, and its cultivation have all been verified in an absolutely and relatively considerable number of instances. Even here, however, we are met with the substantial difficulty that in the summer of 1918 the presence of the bacillus was not uniformly or universally demonstrated. During the earlier outbreaks of the disease in 1918 Pfeiffer's bacillus was found in some countries in a large proportion of cases; in other countries it was sometimes found and sometimes not; in Germany only quite exceptionally was it found. Speaking generally, the *B. Influenzae* was absent in post-mortem examination and diplo-streptococcus was present. It is difficult to believe that differences of media or method fully explain this discrepancy, for though the bacillus is not easily demonstrated, it had been frequently isolated in previous outbreaks of the disease. However that may be, we are in fact faced with (a) the absence of a universal and uniform demonstration of it, which we get, for instance of the tubercle bacillus in tuberculosis, (b) an absence of specific result invariably following its inoculation in animals, and (c) even the relative failure to convey the disease to man by spraying with cultures of Pfeiffer's bacillus.

The second means at our disposal is a study of the specific immunity reactions. We know that particular antibodies arise in the blood of the patient suffering from influenza, as a result of the activity of the causal organism in the body; in a word, an expression of the body's attempt at defence. Now it is known that, both by agglutination and by the complement fixation test, the serum of the patient suffering from influenza shows specific reaction to Pfeiffer's bacillus (between the second and sixth days of the disease), a reaction which blood from the normal person fails to produce. Whilst such a reaction demonstrates the frequent intervention of Pfeiffer's bacillus it does not establish that, organism to be the primary cause of the disease. A third line

of evidence is sometimes obtainable in the effect which a pure vaccine has upon the disease. If it could be shown that a vaccine prepared from pure cultures of Pfeiffer's organism cured or prevented the disease in a large number of trials, this fact would be strong evidence in favour of its etiological importance. In truth, however, such pure vaccines have been too rarely used to furnish us with a basis of general reasoning. It is true that our experience of mixed vaccines is wider ; this experience, however, is hard to interpret, and even had such vaccines been proved to be of great value in influenza, their polyvalence would make it impossible to assign to each constituent its correct role in the etiology of the disease. We are, therefore, left at the end of the pandemic with our previous knowledge of Pfeiffer's bacillus confirmed but not much extended. Sir F. Andrewes summarises our present knowledge of this bacillus as follows • —

- (1) It is not infrequently present in the pharynx of normal persons, living there as a temporary and apparently harmless saprophyte.
- (2) It is still more commonly found in catarrhal conditions of the respiratory tract, and its presence under such circumstances may, or may not, be associated with fever and constitutional symptoms.
- (3) It is the apparent cause of certain chronic inflammatory conditions of the throat, nose, and accessory sinuses.
- (4) Certain cases of meningitis have been associated with the presence of this bacillus or of one closely related to it.
- (5) In rare instances it has been found to be the exciting cause of malignant vegetative endocarditis.
- (6) It is closely and profusely associated with lesions of the respiratory tract in human influenza and is toxic for animals, though specific influenza has not been truly reproduced in them. It is frequently present in the respiratory complications of the disease in man. "Its case remains unproven, and the crucial tests to which it has been submitted seem to indicate it rather as a secondary infection of the highest importance and significance than as the primary 'materies morbi.' At the same time it cannot be asserted that as a primary cause it is wholly out of court." On the other hand " the complications to which the epidemic has owed its abnormal fatality have been due to secondary infections, in which Pfeiffer's bacillus and the haemolytic streptococcus have played a predominant part."

Sir F. Andrewes explains in his chapter why the evidence in favour of a " filter-passing" virus as the primary cause of the disease, suggestive though it may be, is not at present of a conclusive nature.

12. It is 28 years since Pfeiffer announced, at the end of the last pandemic, his discovery of the bacillus known by his name. It may appear at first sight to be somewhat disappointing that we have not been able within a generation to decide finally as to its relation to the disease. This is due in the main to our limited knowledge of the natural history of the disease, its lack of definition, its protean manifestations, and its liability to numerous complications which tend to confuse the issue for the bacteriologist. But his technique and methods are improving and his scope is rapidly widening. Protozoology, bacteriology, parasitology, immunology, agglutinins, filter-passing viruses, the carriage by healthy persons of pathogenic and saprophytic organisms, the assumption of virulence by saprophytes, secondary infections—all these now come within the ambit of the bacteriologist as well as the study of the nature of bacteria themselves. Nor must we forget to avail ourselves of the aid of epidemiological, statistical, and clinical study. Nothing is more certain than that the growth of knowledge in pathology in any direction advances growth in all directions; and the investigation of the cause of diseases allied influenza, to common cold, all the catarrhal conditions, all the diseases which accompany it as predecessors or successors is of first rate importance in solving the problem of the etiology of influenza itself.

The Epidemiology of Influenza.

13; The epidemiological features of the pandemic are even more complex and puzzling than the clinical characteristics, and the present report does little more than present a large body of data which await interpretation. Some facts concerning the incidence and behaviour of the disease we certainly possess, though a satisfying explanation of them may be lacking; other data are of insular or local interest and do not throw much light on the pandemic; a further group of observations remains as yet unverified. Almost all our data—and this report presents but a selection of them—require careful and prolonged study, a judicious co-ordination and much further research. We have passed, it is true, from the former theories regarding origin—the miasmatic theory, the telluric and climatic theories; the importation theory; or the idea that influenza is a specific disease like anthrax, arising and progressing within narrow and definitely circumscribed limits. These are hypotheses no longer confidently held. They do not answer the fundamental questions raised by the pandemic through which we have passed.

14. With the object of obtaining a bird's-eye view of the problem we may briefly summarise some of the principal features of the epidemiology of the recent outbreak, without discussing at length their causation or significance.

15. And in the first place we have to do with an *epidemic wave-form* in influenza. The outbreak of 1918-19 expressed

itself in a *three-wave type*, of which the second wave was much the most severe. The first wave, as measured by mortality, began in this country at the end of June, reached its zenith in the first half of July, and fell by the end of July ; the second wave commenced in October and reached its summit early in November, remaining high for two to three weeks, and falling slowly to the end of December; the third wave began at the beginning of February 1919, rose to its summit (higher than that of the first wave but not so high as that of the second) in the third week of February, and fell slowly to the end of March. As regards period of wave the first occupied approximately six weeks (with eight weeks' quiescence), the second twelve weeks (followed by four weeks' quiescence), and the third eight weeks. As regards mortality the Registrar-General states that during the 46 weeks from June 23, 1918, to May 10, 1919, the total deaths attributed to the disease in England and Wales were 151,446, approximately three quarters of which occurred in the second wave. It will be understood that whilst this is the record as a whole for this country, and particularly for its urban communities, there were considerable local variations in periodicity, incidence, and case mortality. For example, at Liverpool the first wave, as measured by mortality, was less and the third wave greater than in the country as a whole; at Birmingham and at Manchester the third wave reached its highest in March ; at Cardiff and at Portsmouth there were practically only two waves, in October and March; at Coventry there was one substantial wave reaching its summit in November ; and at Sheffield there were three waves—July, November, and March, but the November wave was incomparably the most severe. So also in Stockholm there was an August wave and an October one ; at Chicago a very high incidence (with a relatively low mortality) in October only; in other countries also variations occurred. The broad facts remain that the epidemic presented three waves and that they differed in form. The first short, sharp and high ; the second slower in formulation, flatter, higher and more destructive of life ; the third also slow in formulation, lower, prolonged in decline, and partially reverting to the older influenzal form—a condition of things which suggests a biological factor modified by environment, but not, unhappily, directly controllable by human agency.

16. In the second place we must recognise that in many parts of the world influenza broke out in the summer of 1918 with *apparent suddenness and showing an undoubted rapidity of evolution*. It is true that in 1915, in England and Wales, an excess of deaths was attributed to influenza, but the excess disappeared in 1916 and 1917, to be followed in the summer of 1918 by a sudden explosion at the end of June. As in 1890-92 the primary wave thus generated after some years of relative quiescence spent itself after a few weeks, though it attained a

great elevation. The secondary wave passed much more slowly-through its phases, and whether anticipated or not it came with much less suddenness. In Germany and in Austria there were outbreaks of influenza in 1915-1916 and in 1917, but in both countries the outbreak of 1918 exploded in July. In America, too, influenza had been occurring in greater or less degree in 1915, 1916, and 1917, but it became epidemic in mild form in April and May, 1918, and in September developed more virulent characters and swept over the country, mainly from east to west. In Paris the epidemic broke out in July; in Spain at the end of May; in Italy in April; in Greece in May; in Persia and Mesopotamia in June; in India in June; in Australia and New Zealand in July. Such was the universal experience of emergence and the rapid evolution was similar to it. The disease simply had its way. It came like a thief in the night and stole treasure.

17. Thirdly, the epidemic was remarkable in respect of the *mortality*. It should be borne in mind that the fatality of influenza is low, but its incidence is so vast that the number of deaths create an excessive mortality. Thus, it comes about that the epidemic destroyed more lives in the whole world than did the European war in five years. The peculiar character of this pandemic was that the type of age distribution which had consistently characterised influenza mortality for many years suddenly and completely changed with the onset of the summer epidemic of 1918. Deaths at 0-15 years of age increased from 7 to 11 per cent, (of the epidemic of 1889-92) to 25 per cent.; at 15-35 years of age, from 8 to 10 per cent, to 45 per cent.; at 35-55 years of age there was little or no change; but deaths at 55-75 years of age and upwards, which formerly provided 60 to 70 per cent, of the total registered, contributed in this epidemic only 10 per cent, up to 75 and 2 per cent, over 75 years. In a word, this epidemic presented a sudden and very remarkable change in the behaviour of influenza. It destroyed not the very young or the old, but the adolescent and the adult. What is the explanation of this complete change of age incidence? The customary explanation is that the older persons in the population may have enjoyed an immunity, owing to attacks in a previous epidemic (in this case 28 years before) or in intervening prevalence. But the obtainable evidence is to the effect that the degree and extent of such acquired immunity is slight, transient, variable, and incomplete. A second explanatory suggestion attributes the change in age incidence to alterations in the circumstances of the population. Soldiers have been aggregated for war purposes, young men and women in munition works, large sections of adult populations have moved in bulk owing to trade or transport exigencies, and thus the disease had greater opportunity of fastening upon these aggregated populations under exceptional surroundings. But this epidemic was a pandemic, and all classes came within its ambit, the

change of age incidence occurred in non-belligerent countries not directly affected by the privations of war, and in all parts of the world ; lastly, it occurred suddenly at the outset (and not as a sequela), differentiating itself clearly from the influenzas of 1917. A third explanation is that the adolescent and adult population were suffering from the debilitating influences of war, from strain, and from exposure. No doubt this factor played a part, but we cannot escape the knowledge that the epidemic ravaged populations of this age-period who were not subjected to these unfavourable circumstances. A fourth suggestion is of a more narrowly biological character. It propounds the view that the epidemic was the pathological expression of a new strain of infecting virus, or one to which adolescent and adult tissues were particularly susceptible. This seems to require for its support evidence of importation or of origin of such a virus, and we have few or no facts in that behalf; moreover, the characters of the disease which proved most fatal and which we must assume would be attributable to such a new or enhanced virus had already manifested themselves sporadically and even epidemically in England, France, and America in the years immediately preceding the pandemic ; and, still further, it must not be forgotten that the changed age incidence obtained at the beginning of the first wave of the pandemic and in the mild three-day type of influenza, as well as during the second and more severe wave of fatal septicaemia. The age incidence, in short, was peculiar to the whole emergence of the pandemic, mild or severe, and it was almost universal, under diverse conditions of economic, social, and racial environment.

18. A fourth characteristic of the recent epidemic was its relation to the *social conditions of the people* affected. In 1847 Farr recorded the fact that the influenza of that periodic epidemic was more deadly to people living in insanitary conditions and attacked in particular "persons labouring under zymotic diseases," such as whooping cough, measles, and typhus fever. It is interesting therefore to find that in the recent epidemic neither of these propositions can be proved to hold good. The mortality fell alike upon "the sanitarily just and unjust;" the Registrar-General's report makes this clear in a set of valuable tables showing the incidence on the towns and in the London boroughs ; it was not associated with, nor apparently did it increase the severity of, zymotic sicknesses or tuberculosis. The facts did not even demonstrate, as will be seen in the discussions in the present report, that domestic overcrowding was a principal factor in the spread of the disease. It must not be supposed, however, that social conditions played no part in the matter. The great probability is that the social evolution proceeding in the later years of the nineteenth century raised the sum of the etiological factors to near their critical values, and maintained them closer to those critical values than in any

earlier age. Even in a world-wide pandemic the problem of epidemic influenza may be largely an internal problem of each, nation, a problem of social relationship, of social factors, of domestic habit and life. The materials of the conflagration come from within. As the compilers warn us, the wolf is in the fold all the time. "His ravages depend as much upon the disposition of the sheep within the fold as upon his appetite."

19. There is a fifth point of great interest and importance which has led to much discussion respecting the epidemic, and that is the *relation of influenza to other contemporary diseases*. Is there an "epidemic constitution" of influenza? Is it an epidemiological entity by and of itself, or is it a manifestation of an infection or group of infections also represented in other diseases? To answer these questions we must consider our growing experience of the "setting" of an influenza epidemic. Attention is drawn in the report to various epidemiological records, which go far to establish—

- (a) that the epidemiological features of the cycle of years within which influenza explodes are different from those of the influenza-free cycles ;
- (b) that preceding epidemic influenza there is often a rise in general morbidity of the population, an "epidemic constitution" develops favourable to influenza, there are early though often mild and atypical clinical forerunners of the disease, and parallel or allied clinical maladies are seen ;
- (c) that there are concurrences, similarities, and inter-relationships between outbreaks of cerebro-spinal fever, poliomyelitis, and outbreaks of influenza, bronchitis, and pneumonia.

Many facts lead us in the direction suggested in these three propositions. For example, the epidemiological history of England and Wales for several years previous to 1918, as previous to 1847, was different from the normal. In his special report on Influenza to the London County Council in June 1919, Dr. W. H. Hamer furnished evidence of such differences in London ; the present report discusses the subject still more widely ; and we have ample indications of the incidence of disease elsewhere which preceded the influenza outbreak. There were outbreaks of infectious pneumonia in German prisons and camps in 1915 ; cerebro-spinal fever and poliomyelitis had been increasing in Great Britain in 1915-1917 ; there was exceptional prevalence of "influenza" or "pseudo-influenza" in the United States of America in 1915 and 1916 ; obscure but extensive febrile "pneumonic" outbreaks occurred on both eastern and western war fronts in 1916 and 1917 ; in the same years there were the epidemics of purulent bronchitis, bronchiolitis, and pneumonia at Aldershot (Hallows, Eyre, Abrahams, and French), apparently a primary influenzal infection followed by strepto-

coccus; in the winter of 1917-18 there was much purulent bronchitis among young soldiers in France, as there had been at Aldershot, with pneumonia, pleurisy, empyema, and toxæmia (Abercrombie, Hammond, Rolland, and Shore), and showing cyanosis, nummular sputum, pyrexia, and high mortality; and there was, in England and Wales at least, a continuous smouldering of influenza itself which in 1915 caused more deaths than in any previous year of this century. It seems impossible to escape the conclusion that these various conditions bore a fundamental relationship to each other and to the pandemic of influenza. Or we may consider another group of facts. There is an essential similarity between the epidemic incidence curves of influenza and bronchitis; an increased incidence of bronchitis and pneumonia not infrequently precede an increased incidence of influenza; the true curve of influenza mortality can apparently only be constructed by combining with it the simultaneous waves of pneumonia and broncho-pneumonia. A similar relationship seems to obtain, though it cannot at present be measured, between the incidence of "common colds" of feverish type and of influenza itself. Again, we have also to bear in mind that not only do historic records associate chronologically outbreaks of influenza with the sporadic or even epidemic occurrence of obscure nervous illness, but that the more exact clinical methods of modern times reveal close analogies between the general and nervous symptoms of acute poliomyelitis, of lethargic encephalitis, and of cerebro-spinal fever and those of the more severe forms of influenza. The convergence of these paths of investigation leads to the surmise that the admittedly vague concept of an "epidemic constitution" does indeed correspond to something in nature; that there really is a development over a series of years of various clinical forms of infective disease which tend to assume a generic type and to prevail before and after an epidemic of influenza.

20. Generalisations are valuable though often unreliable—particularly unreliable when founded upon a slender basis of established facts. But in the present situation we must not decline to attempt the formulation of an outline of the possible or probable cause of the pandemic. Taking into consideration the data furnished in this report we may hazard the view that the recent visitation—its character and degree as well as its age incidence—was due to the operation of an exalted virus (possibly an infecting agent, parasite or saprophyte, the virulence of which had been increased by human passage) or an unusual infection of associated or symbiotic organisms, the potential virulence of which had for many months, perhaps years, been rising to a critical and stable level. This specialised agent acted upon the adolescent and adult human tissues, which had an inherent susceptibility of response to its toxic effects engendered by a complex of factors—lowered vitality or resistance owing to strain, exposure, deprivation, or physical disability: or a virginity

of tissue soil to the particular infecting agency ; or the unsuspected carriage by sick or healthy persons of saprophytic or benign organisms awakened to pathogenic virulence by the infecting virus ; or tissues rendered susceptible or vulnerable by the influence of other organisms. Social factors no doubt played a part in preparing the infecting seed or the soil, and in bringing to the critical and dispersive point the conditions which had hitherto been sporadic and restricted. Among these we must in particular include the extra-domestic aggregations of persons. I cannot do better than quote the general theory of the epidemiology of influenza which the compilers of the report suggest as a " working hypothesis." They say:—

" The story, then, of the germ of influenza is divided into three phases. 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 relatively 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 characterise the development of the European type of civilisation, 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.

" The first inference from our hypothesis is that in the seeming conflict between man and his microscopic competitors, there can never be a time when man is securely master of the universe. Intoxicated by the victories achieved over the plague (in Europe), over the enteric group, over typhus (in western Europe), and over small-pox, we are too apt to suppose that the campaign has ended in our favour, that we have little more to fear from the typically epidemic diseases and may concentrate against the endemic group. That we have just passed through one of the great sicknesses of history, a plague which within a few months has destroyed more lives than were directly sacrificed in four years of a destructive war, is an experience which should dispel any easy optimism of the kind. No instructed epidemiologist can say that the world may not have to endure during the next half century other plagues of the first order of severity.

" The second inference is the essential solidarity of all mankind in the matter of epidemic sickness. In a narrow sense this solidarity has been realised since the beginnings of western civilisation. The conception of a sanitary cordon, the barring out or sealing up of an infected territory, is, indeed, an old notion. But our hypothesis extends this conception greatly, and enables us to see that the sanitary cordon is but a very small part indeed of a supra-national system of preventive medicine. 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 civil society which a certain degree of collective misery and disorganisation 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 powers of a quarantine authority; land quarantine has, in fact, never yet succeeded. To realise 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 organisation for the control of epidemics will need to face it."

Means of Investigation and Prevention.

21. At the beginning of 1919, immediately on your appointment as President of the Local Government Board, you will remember, Sir, that you called for vigorous official action in regard to influenza, and it is desirable that a brief summary of the administration of the Board at that time, and of the Ministry subsequently, should be recorded. In the first place the *means of information* were revised. Primary pneumonia and acute influenza pneumonia were both made notifiable by the issue in January, 1919, of the Public Health (Pneumonia, Malaria, Dysentery, &c.) Regulations, which had been prepared by the Board in 1918. A system was instituted of cables from consular and other agents in various parts of the world, and of weekly returns in the army, navy, air force, and civil communities (including schools, institutions, factories, &c.), to overcome, as far as might be, the absence of compulsory notification of influenza, which was deemed impracticable owing to difficulties of definition. The returns received were systematically charted, studied, and published, and in this way the foundations of an Intelligence Department were prepared. Secondly, we appointed a *Standing Committee* of the medical heads of the various Departments in Whitehall concerned in the matter, including the Army, Navy, and Air Force Medical Services and the Medical Research Committee, which met weekly for "intelligence," consultation and co-ordination. It was also thus possible jointly to provide and supervise numerous local inquiries in different parts of the country, which had been commenced by the Local Government Board in 1918. Thirdly, the Ministry *advised local authorities* throughout the country to organise treatment, nursing, and "home-help" for influenza-stricken houses, and issued a revised circular of advice (with popular leaflets), pressing on the public and on local authorities the precautions which preventive medicine suggested as advisable in regard both to protection and treatment. Numerous

examples of such advisory publications will be found in the present report. Fourthly, the Ministry, in conjunction with the Medical Research Council, made arrangements for the first time for *linking up medical officers of health with bacteriological expe7'ts* in different parts of the country for the systematic clinical, pathological, and epidemiological study of the disease. In this way was instituted an organisation for co-ordinated research and investigation ready to deal with the epidemic in its *local foci* of prevalence and in its varied forms. Lastly, the Ministry supplied *an anti-influenzal vaccine*. A large quantity of the vaccine (*circa* 1,850 litres) was prepared for the Ministry, partly at the Lister Institute and partly by arrangement with the War Office, at the Royal Army Medical College, Millbank, in accordance with the following formula: —

400 million	Bacilli Influenzae	(Pfeiffer),
200 ,,	Pneumococci,	
60 ,,	Streptococci,	

per cubic centimetre of vaccine.

Several strains of the influenza bacillus were employed, and Types I. and II. of the pneumococcus. The vaccine was intended primarily for use as a prophylactic, and was recommended to be given in two doses separated by an interval of 10 days. For adults the first dose was 1/2 c.c. and the second dose 1 c.c. The vaccine was distributed through the Government Lymph Establishment to medical officers of health, free of cost, for issue to medical practitioners within their districts. It was also supplied direct to schools and hospitals, and made available to medical officers of passenger ships bound for infected ports. Up to the end of October, 1920, 23,559 bottles—sufficient for the preventive inoculation of 377,000 adults—were distributed in response to 1,248 applications. Each bottle of vaccine was accompanied by a form, on which the medical practitioner was asked to record, in respect of each person inoculated, certain particulars, including dates of previous attacks of influenza, date of inoculation, and subsequent history.

22. It was, of course, recognised that such a vaccine had but limited possibilities ; for, first, we do not know the cause of the disease, and thus we are ignorant of the basic element for such a vaccine ; secondly, the presence of the disease in the individual is not followed by a stable and complete natural immunity, and we are therefore without substantial grounds of hope, in any artificially prepared vaccine, for the production of an acquired immunity ; and thirdly, it must not be forgotten that to introduce a prophylactic vaccine in the midst, and, indeed, at a late stage, of an epidemic is to court failure and imperil the credit of the vaccine. On a balance of considerations, however, it was thought desirable to attempt to meet the public demand by providing a polyvalent vaccine of the nature described above.

As was anticipated, the results have not been sufficiently substantial or uniform to lead us to any definite conclusions, though there are indications that the use of the vaccine did reduce in some cases the risk of fatality. Various forms of vaccine have been tried in different countries, hitherto without much success, for the reasons already given.

• *The Prospect of the Future.*

23. "The problem of influenza is still unsolved," write the compilers of this report; "its solution will be one of the great events in the history of medicine." And they go on to ask the inevitable question which arises in men's minds, What is the world's outlook upon future pestilences or dangers of pestilence? The answer is that it is gloomy. "The conclusion to which we are led is that the generation of a great pestilence such as influenza or pneumonic plague is dependent upon disturbance of social order involving for absolutely large numbers of human beings the endurance of conditions of insalubrity which afford for invading parasites a suitable field of modification. So soon as the new properties have been stabilised no barrier against the pandemic or epidemic extension will avail, nor will those individuals or nations who have not suffered the primary evils be more resistant to the disease than their fellows. No impartial spectator can doubt that at the present time, and almost certainly for a generation to come, there will exist in many nations and over wide tracts of country precisely the type of misery which we suspect to be the appropriate forcing house of a virulent and dispersive germ."

24. The prospect is not cheerful, but we must face it with equanimity and all the resourcefulness of the spirit of adventure and quest. One thing is certain, that 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.

25. Two other practical steps remain. First we must fortify our administrative methods for dealing with such scourges as influenza, and secondly, we must instruct the whole population, child and adult, in the laws of preventive medicine. The administrative arrangements introduced in 1919 by the Ministry require to be consolidated and perfected, particularly in relation to (a) the development of a system of "intelligence," (b) the effective co-ordination of central and local agencies for the synthetic study and prevention of the disease, and (c) the provision of further means of adequate treatment and nursing. Lastly, there is public instruction in the practice of preventive methods. The infection of influenza and its allies appears to be conveyed by the secretions of the respiratory surfaces. In coughing, sneezing, and even in loud talking these are transmitted through the air for considerable distances in the form of fine spray. The channels of reception are also normally the respiratory surfaces of mouth, nose, and throat—though dust, unclean hands, and infected materials may be the means of conveying infection. It is manifest, therefore, that the closer the bodily contact the more readily will transmissions occur; hence the paramount importance of persons abstaining thus directly to infect each other, and also of avoiding overcrowding and thronging of every sort, whether in places of public resort, public conveyances, or factories. Well-ventilated rooms, nourishing food, and an open-air life afford some defence; and in times of prevalence of respiratory catarrh or sore throat the frequent use of an appropriate gargle (for example, 20 drops of liquor sodae chlorinatae in a tumbler of warm water) and nasal wash may be recommended. In regard to individual prophylaxis, both the clinical experience of Dr. French and the epidemiological inferences drawn by the staff of the Ministry concur in supporting the belief that a simple hygiene of the mouth and nose is of more value than any specific medication. At the first feeling of illness, or rise of temperature, it is the private and public duty of the patient to go to bed at once, to remain at rest and in warmth, and to place himself under medical supervision, for it cannot be too clearly understood that it is the complications of influenza which disable or destroy life. Thus it seems probable that, though our knowledge of influenza is strictly limited, we are not wholly without means of reducing its incidence and mitigating its consequences.

26. So far as concerns the provision of some simple and infallible prophylactic against this terrible disease—the use of the adjective is, unhappily, fully justified—the outcome of this report must fairly be described as meagre. But in one particular, and that not the least important, this intensive study of a great and historic epidemic is well worthy of public attention. In the general annual digest which I had the honour

of submitting to you a few months since, a document founded upon a review of the whole volume of mortality and morbidity in this country, I emphasised the unitary character of the problems of health and disease—the fact that there are no short cuts to a sanitary millennium. The story of influenza as unfolded in the present report teaches the same lesson. A drama which is acted in a few weeks seems to be the product of years of preparation. There can be no question as to the deduction to be drawn. The only sure defence against sudden and devastating epidemics is to raise the whole standard of life of this nation, indeed of the whole comity of nations. That conclusion from the present evidence will, I believe, still stand long after the specific hypotheses of etiology and epidemiology here suggested have become merged in the wider synthesis which future research must render possible.

I have the honour to be,

Sir,

Your obedient Servant,

Ministry of Health,
Whitehall,
October, 1920.

GEORGE NEWMAN.