THE LONG-TIME CYCLES OF PANDEMIC INFLUENZA[1]

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The object of this paper is to present briefly some observations on the occurrence, in point of time, of the great influenza pandemics, and to indicate certain phases, the statistical study of which may prove valuable. For this purpose the term "pandemic" is applied to those great epidemics which have not only affected a whole country, continent, or hemisphere, but have, in a series of great waves, encircled the entire globe. The term "influenza" is here used to designate the disease or clinical entity usually known by that name to physicians; it refers also to the same disease known by other names before the term influenza came into general use.

The study of these phenomena in the light of history is of course limited in precision by the absence of mortality statistics in modern form previous to about the last century and a half. Nevertheless, the pandemics stand out so clearly in the history of the last four centuries that one may endeavor to measure them roughly and to interpret their relationship to each other. Viewed in this perspective they present a picture characterized by unmistakable features.

Our sources of data are chiefly the descriptive and critical studies of Hirsch, Creighton, Leichtenstern, Thompson, and others, and official vital statistics. Previous to the seventeenth century the records were made for the most part by lay chroniclers; subsequent to the days of the great Sydenham, in the early seventeenth century, physicians in increasing numbers recorded their findings; and during the nineteenth century there accumulated an extensive literature including descriptive official statistics. It must be noted that before the last century the scientific writers on influenza, chiefly physicians, compensated for their lack of the precise methods and resources of modern clinics, laboratories, and official records, not only by comprehensive and minute observations, but also by a thorough mastery of language in presenting them.

The method used to identify and relate to each other the historic influenza epidemics cannot be stated in exact detail in this brief paper, but it will be described sufficiently to make clear the procedure. We selected the records of England and Wales as a measure of the pande-

[1] Read at the Eighty-third Annual Meeting of the American Statistical Association at Pittsburgh, Pa., December, 1921.

micity of influenza because they cover a long period of time and are readily available, including critical studies of them, especially by Creighton.

The first step is to chart the annual influenza death rates of England and Wales since 1838 from data in the yearly reports of the Registrar-General, with the exception of a negligible interval of four years during which no epidemic occurred and for which figures are not available. The English "bills of mortality" were printed first in 1629, although the parish registers of deaths had been kept since 1538 and various parish bills of mortality were compiled as early as 1532. Next, from Creighton's study of the records and other sources of information, we are able roughly to estimate the mortality [1] of these various epidemics from 1510 to 1838: (1) of definite influenza; (2) of indefinite but very probable influenza; (3) of mild and doubtful character which may possibly have been influenza. These three classes must be held clearly in mind in our subsequent discussion. (See Charts I and II.)

In this connection, the nomenclature of influenza is important because throughout its history it appears under a great variety of names, many of them popular designations indicating either the severity or the mildness of the disease. In 1782 the term "influenza" was formally adopted by the College of Physicians in England and since then has been in general use in the English literature. But the wealth of medical and lay descriptions of the epidemics previous to 1782 establishes clearly the clinical character of the important influenza outbreaks.

For charting and comparison the epidemics may then be classified as follows, with regard to their relative severity and probable annual mortality from influenza per 100,000 population for the entire year in which each epidemic occurred:

1. Very mild; rate under 15.
2. Mild; rate over 15 and under 30.
3. Moderately severe; rate over 30 and under 45.
4. Very severe; rate 45 or over.

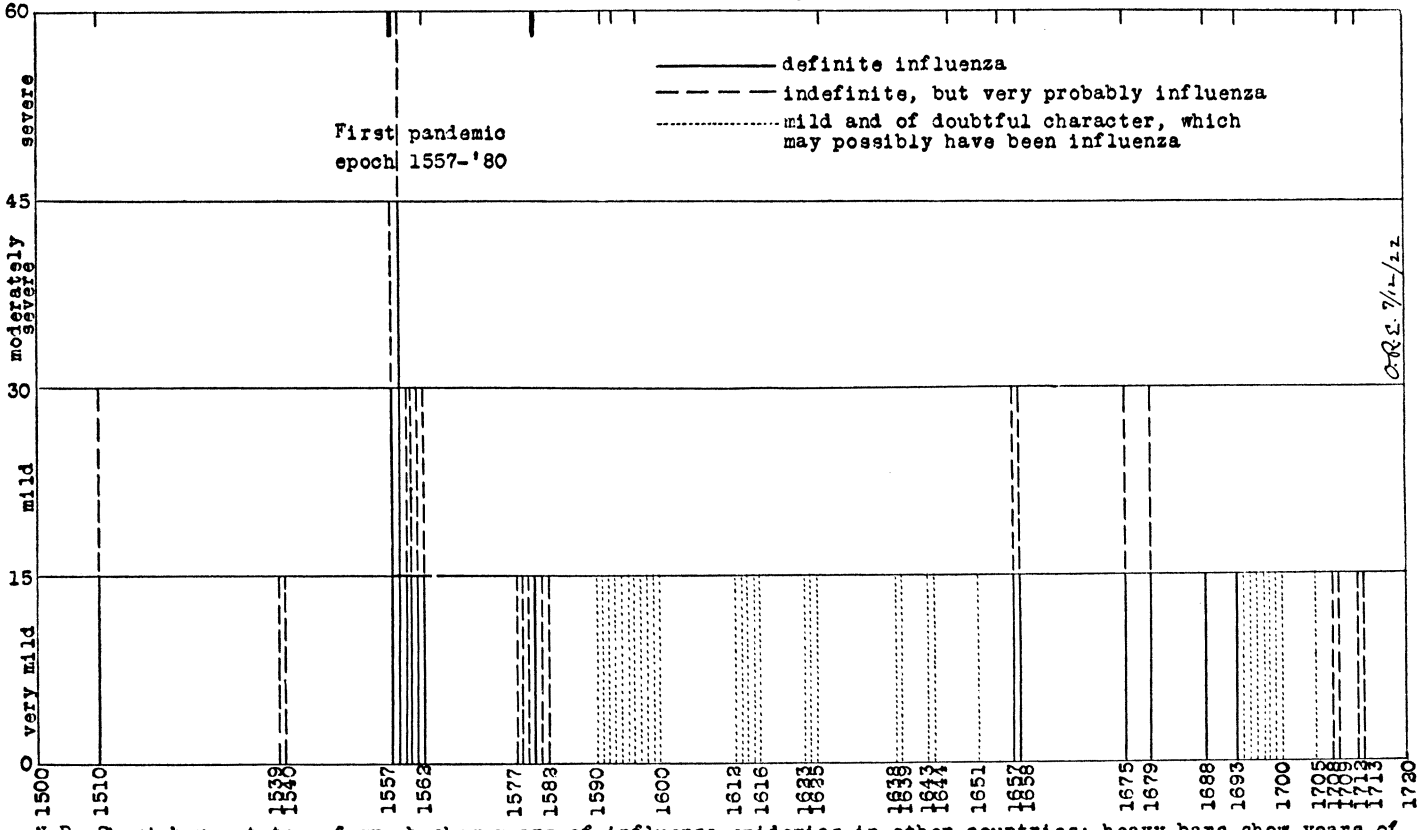
Although the definitions involve assumptions, derived from study of the annual statistics of the Registrars-General since 1838, in order to designate the relative severity of each epidemic preceding that year, it is not a matter of moment for our purpose whether such designations do accurately represent the real mortality. These groups might be reduced to 2 or 3, or extended to 6, and the corresponding mortality values likewise raised or lowered, and it would still be possible readily to allocate to them any of the historic epidemics with regard to their severity *as compared with each other* and with those which followed

[1] The term "mortality" is used in this paper to indicate deaths in proportion to population.

Chart I

THE LONG TIME CYCLES OF INFLUENZA IN ENGLAND AND WALES

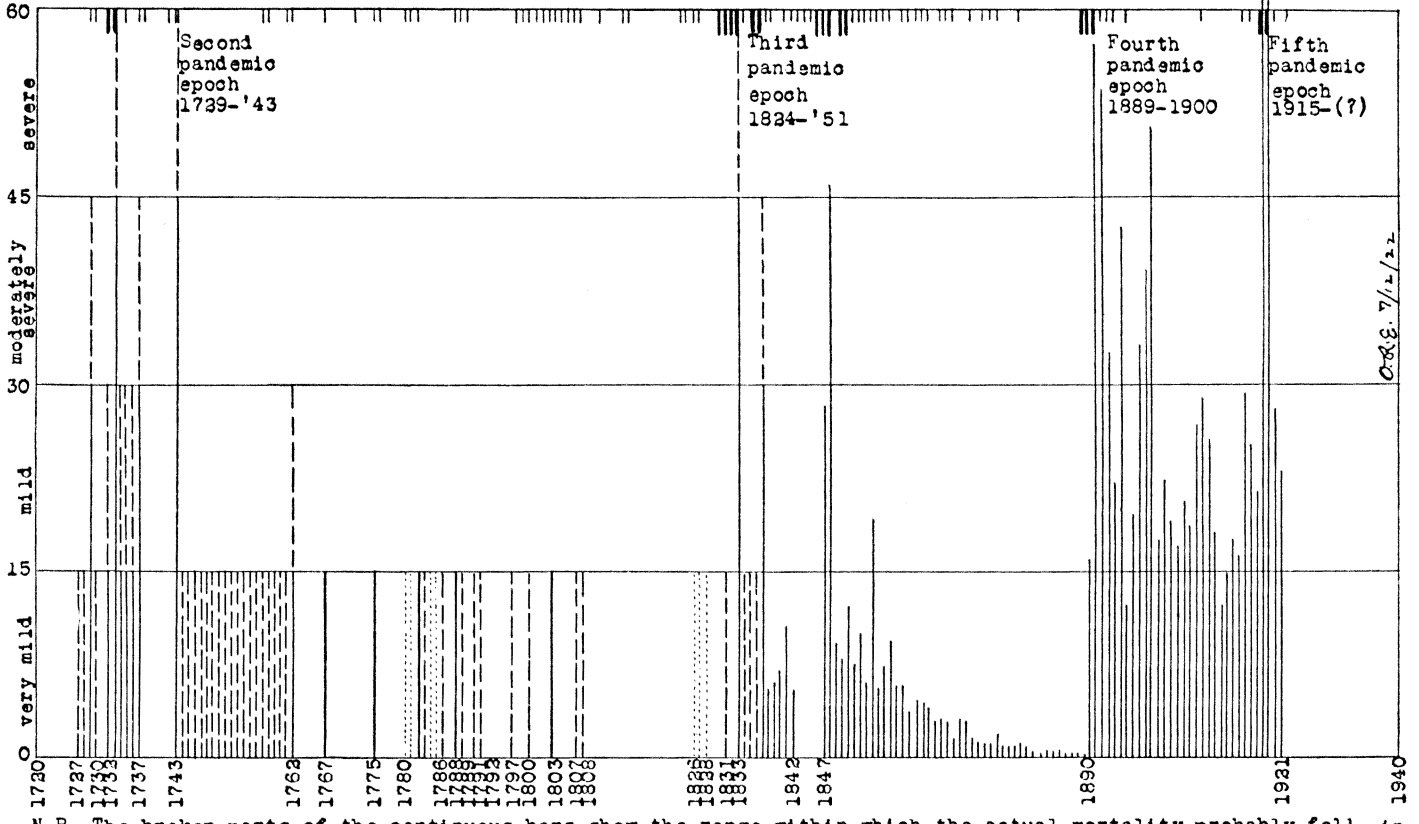
Annual death rates per 100,000 population
estimated 1510-1837; from reports of Registrars-General 1838-1921



N.B. Short bars at top of graph show years of influenza epidemics in other countries; heavy bars show years of world-wide outbreaks, or real pandemics. (Also see foot note to Chart II.)

Chart II

THE LONG TIME CYCLES OF INFLUENZA IN ENGLAND AND WALES (Concluded from Chart I)



N.B. The broken parts of the continuous bars show the range within which the actual mortality probably fell, in both Charts I and II. (Also see foot note to Chart I.)

The actual rate for 1918 is over five times as high as that shown on the chart, and the rate for 1919 is nearly twice that represented.

1838. Even if opinion should differ as to whether a certain epidemic was mild or moderately severe, or otherwise, or whether or not it was true influenza, it would be found that it could be allocated approximately, according to the definitions formulated, both as to severity and to the certainty of its being true influenza. Allowing for wide differences of judgment, the resulting graphic pictures in each instance would still present the same significant features.

The data thus prepared are then plotted in their proper places on the chart constructed to show the annual influenza death rates since 1838 and according to the same scale.

Inasmuch as very extensive outbreaks [1] occurred which left little or no impress on the bills of mortality or the later official statistics, these questions now arise: (1) For the present purpose, is the mortality a reliable index of epidemicity? (2) Are great epidemics causing heavy mortality *in Britain* a reliable index to the pandemics?

The answers to these questions are evident from the fact that the years of severe outbreaks with high influenza mortality in Britain coincide with those periods during which the disease was encircling the globe and causing high mortality everywhere. Such pandemic periods or "epochs" (a term suggested by Leichtenstern) were followed by *occasional* less fatal outbreaks in the long interval of time before the next pandemic epoch began, some of which were very extensive, indicating a high degree of communicability, and affected large proportions of the people of a country, or even a continent or hemisphere.[2] Not only was the mortality low but the fatality (*i. e.*, percentage of fatal cases) also must have been low—a condition characteristic of the terminal phase of severe epidemics of various diseases. These mild and extensive epidemics did not coincide with periods of truly world-wide diffusion, but they are very confusing in the chronological history of the disease and seem to have obscured the picture of the real pandemic waves and their rise and subsidence. These waves form a remarkable and consistent sequence of events when viewed quantitatively.

In 1510 there occurred in Europe (then, of course, the chiefly known portion of the world) a wave of influenza which many students regard as the first real outbreak which ever occurred. In the chronicles of earlier epidemics there is evidence of influenza outbreaks, but this is much confused because of the frequent recurrence of pestilences during the Middle Ages. Creighton quotes Short's statement that in 1510 "none died except some children"; Short failed to state his authority,

[1] The word "outbreak" is used synonymously with "epidemic" in this paper.

[2] For example, the outbreaks of 1767, 1781, 1802–3, and 1874–75.

but Creighton surmised it was probably the continental chroniclers. Therefore, as the mortality was doubtless low, we may suspect that the 1510 wave was only an incident in the decline of some great previous pandemic, perhaps that of 1173 (regarded by Hirsch as the first authentic epidemic) which was recorded in Britain, Italy, and Germany and doubtless appeared elsewhere on the Continent. The reason for suspecting this sequence would be its apparent consistency with the course of events in the subsequent history of the disease.

For practical purposes a pandemic epoch may be defined as beginning with that year in which those first authentic outbreaks occurred anywhere in the world which developed into waves of pandemic proportions, after a series of years in which apparently no epidemic occurred anywhere; the end of the epoch may be dated as either the last year of high (or severe) influenza mortality in Great Britain or of world-wide, or nearly world-wide, epidemic diffusion of the disease before a general decline of the mortality begins.

After the opening of the sixteenth century the first giant wave of influenza arose in 1557, rapidly spreading over the then known world. This outbreak persisted in Britain during 1558, taking a heavy toll of lives, and was followed by revivals up to the year 1580 both in Britain and on the Continent. This may be regarded as the first definitely known pandemic epoch. It covered a period of 24 years.

The second epoch began in 1729 and persisted to 1743, a period of 15 years, in the midst of which there occurred in Britain, in 1733 and in 1743, two very severe epidemics, which were believed by Creighton to be the most severe in the history of Britain previous to the time of his writing (1894). During this epoch, in various years, there occurred similar severe outbreaks in other countries, including North America. One writer stated that 80,000 persons were sick in Rome in 1743, and that 500 were buried in one day.

The third epoch began about 1824 and persisted to 1851, a term of 28 years, during which there occurred in different years and in various countries of the entire world very severe epidemics resulting in heavy mortality from the disease.

The fourth epoch may be regarded as that of 1889 to 1900, a term of 12 years, the details of which are recent knowledge.

The fifth epoch began in 1915 [1] and *is still in progress.* The first pandemic invasion was the great wave of 1918, which has been followed by several revivals in various countries, some of serious proportions as to mortality. This, doubtless, was the most fatal of all influenza pan-

[1] Influenza appeared widely in epidemic form in the United States in December, 1915, and January, 1916, being reported definitely from 22 states. See U. S. Public Health Reports for January 7, 1916.

demics and was perhaps the greatest single catastrophe of modern times, not excepting wars.

Therefore the duration of the first four epochs being roughly 24, 15, 28, and 12 years respectively, or an average of 19.8 years, it is clear that the epoch beginning in 1915 will very probably contain one or more severe epidemics, or pandemic waves, in addition to that of 1918. These outbreaks should be anticipated during the 10 to 20 years following 1915.

A curious fact in connection with each of these great epochs is that upon the occurrence of the first severe epidemic phase, both the laity and the medical world immediately questioned the identity of the infection with that of other previous outbreaks. In former times these epidemics were frequently referred to in Britain as epidemics of a "new disease," "strange disease," etc., and, indeed, even during the present pandemic period able observers have questioned whether the disease is the same as that of other years, or in one recent epidemic as compared with another. Regardless of clinical and pathological differences observed in the study of individual patients, a quantitative review of the mass of mortality data may be of value. Each of the five pandemic epochs just described was immediately followed by a series of years during which the mortality from the disease remained generally high. This mortality for each year is definitely known in England and Wales since 1838. In the outbreak of 1847 the influenza death rate per million was 285, in 1848 it was 460; and it remained above 75 for the next five years. In 1851 a recrudescence of the disease raised the rate to 193; the next year it was 55, after which it *declined continuously*, with minor variations, for many years until the decade 1880–89, when it was below 10. During the second half of that decade it fell to only *2 per million!* Then another pandemic invasion caused rates in 1890 and 1891 of 157 and 572 respectively. If depicted graphically (Chart II), this decline during the 40 years from 1850 to 1889 (or beginning approximately with the end of a pandemic epoch) makes a hyperbolic curve if smoothed. This seems to represent a natural phenomenon uninfluenced by human factors and obeying a law susceptible of mathematical expression.

During the interpandemic period from 1889 to 1918 the annual influenza mortality of England as a whole remained on a very much higher level than during the 40 years preceding 1889, and although characterized by extreme fluctuations it nevertheless presents a picture of general decline from 1890 to 1918. Perhaps the most striking and the most interesting feature of the estimated mortality of the epochs previous to 1838 is that each of them contains various minor epidemics

with moderately high mortality, in addition to very severe pandemic waves; and each such epoch is immediately followed, for a series of years, by a concentration of moderately high influenza mortality. After the severe outbreak of 1743 in Britain (which marked the end of a pandemic epoch) there occurred during the 19 succeeding years many minor epidemics of influenza and colds, with a well-marked effect on the general mortality, which corresponds to a similar condition observable in the official statistics after the epochs of 1824–51 and 1889–1900. Minor or secondary epidemics after the pandemic wave of 1918–19 were noted during 1919–22 in several countries.

After these periods of high mortality, which followed the great epochs, there still occurred in isolated years in Britain mild epidemics, occasionally very widespread, some of which are doubtful as to identity and some unmistakably real influenza. These, however, left but slight impress upon the bills of mortality and the later official statistics. Thus, as a whole, these periods fit into the picture as do the declining annual death rates in the Registrar-General's statistics during the 40 years before 1890. During the years from 1762 to 1809, when the very mild and unimportant outbreaks were disappearing, it will be noted that these *become less frequent* as the distance becomes greater from the pandemic epoch; so that in 1807–8 slight epidemics of "catarrhal" diseases prevailed in Britain, the character of which was doubtful and the identity with influenza disputed. *These mild outbreaks were followed by a term of 17 successive years during which there occurred no epidemic of any disease resembling influenza.* Then during the 6 years from 1826 to 1832, mild epidemics of a "catarrhal" type of sickness again appeared, and in 1833 there was a very serious influenza epidemic. These slight "catarrhal" outbreaks may be regarded as preliminary to the oncoming storm and as being related directly to the wide diffusion of mild influenza outbreaks in the United States in 1824–25, and in all the Western Hemisphere, Russia, and Siberia in 1826–27, which preceded the universal appearance of the disease in the giant waves of another pandemic epoch. A similar phenomenon preceded 1918, in the constantly increasing pneumonia mortality during several preceding years. One may well consider whether such apparently unimportant but constantly increasing respiratory mortality is not essentially the beginning phase of the pandemic and susceptible of statistical definition.

When the similar events of the great epoch of 1729–43, and its slow disappearance over many years to 1824, are charted, the picture presents features unmistakably like those in the origin of the next pandemic epoch, beginning in 1824, and its subsequent decline down to

1889. It would require but little imagination to construct curves which would represent roughly the long interpandemic declines.

From the foregoing it may be clear why the mild outbreak of 1510 (mentioned early in this paper) may be viewed as an isolated incident in a long curve of decline from a previous great wave. Analagous declines of the mortality from other epidemic infections over long periods of years will be recalled, *e. g.*, plague and leprosy.

One of the many other interesting observations which might be made as to the great influenza epochs is the *apparent* shortening of the time intervals between them during the last four centuries. This relative shortening will be found to exist, regardless of the exact years used to measure the pandemic epochs. These intervals, *or long-time cycles*, may be defined as follows, from the beginning of one epoch to that of the next:

From the epoch of	1557–80	to that of	1729–43	.....	172	years
" " "	1729–43	" " "	1824–51	.....	95	"
" " "	1824–51	" " "	1889–1900	.....	65	"
" " "	1889–1900	" " "	1915–(?)	.....	26	"

We may supplement this interpretation of the statistical evidence of influenza with these judgments:

1. Pandemic influenza is identical with the influenza of the interpandemic periods: it is an intensely virulent and highly communicable form of the same disease. The disease may differ in clinical or pathological manifestations in various outbreaks.

2. Influenza exists constantly in mild or severe form in one or more countries of the world, or subdivisions of them; and factors, at present unknown, occasionally operate to increase the virulence and communicability of the disease, thus causing either epidemics or pandemics. (This condition becomes apparent when the influenza mortality of Britain is studied in comparison with the historic epidemics.)

3. There is increasing severity and frequency of local outbreaks in one or more countries for several years preceding the first invasion of a pandemic epoch; these preliminary outbreaks seem to begin after a series of years entirely free from epidemics, and may be susceptible of sanitary recognition, if not statistical demonstration.

4. The appearance of influenza in pandemic form is evidence of the presence of a pandemic epoch, during which period of years one or more other severe epidemics or pandemics will occur at intervals of a few months to a few years.

5. The rise and fall of the pandemic epochs, in long-time cycles, indicates that the fundamental causative factors probably have been uninfluenced by preventive measures.