HISTORY OF INFLUENZA EPIDEMICS*

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IN tracing the history of the etiology of influenza one finds much of interest. For one can thus visualize the history of the etiology of disease in general; from the belief in ancient times of its origin in some impending fate or superstitious dread, on through the intervening stages to the more modern ideas of errors of sanitation and infection by bacteria, for

> . . . the ravages of epidemics like the great cataclysms of nature have in all ages appealed to the imagination and excited the terror of mankind. To the simple savage of the earlier generations, as among the savage tribes of the present day, an obvious similarity must exist between the havoc wrought by the fury of the elements—and that no less fatal—accomplished by the sudden outbreak of some malignant disease spreading with inconceivable rapidity and making countless victims.
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> Earthquake and pestilence, meteors, volcanic eruptions and storms being alike abnormal and mysterious occurrences, the direct intervention of some supernatural agencies were deemed requisite to account for their apparent deviations from the settled order of the universe; all were attributed to the anger of an offended diety, as when Zeus, for an insult to his priest, by his thunder, sent sickness into the Argive camp.
>
> On mules and dogs the infection first began
> And last the vengeful arrows fix'd in man.

As knowledge increased the medical men of ancient days assumed other causes of influenza. Some held the cause to be a morbid miasma that floats in the air,[20] others held that it was "a gaseous emanation of telluric origin"[19]; and later it was thought to be some volatile or fixed principle emanating from the bodies of men and animals.[20] Baron de Tott claimed immunity from these emanations by directing, with his cane, the removal of the bodies that had died of the plague in Constantinople.[20]

In 1411 the French physicians claimed that the cause was a contagion *de l'air*, in 1414 a contagion *de le bise* or north wind.[19] This epidemic and the one of 1427 were supposed to be airborne.

Dr. Johnson quotes Van Swieten who calls it "a malignant catarrh that arose as it were from a certain vapor, since thick clouds of an ill smell preceded it for some days, then it suddenly broke out seizing almost instantly a thousand persons."[20] This description resembles the disease that recently occurred from some ill-smelling gas of unknown origin. It was called nebelsouch or fog plague in 1889–90, when the fog was supposed to have caused many deaths.[19]

Hildanus, becoming more concrete, supposed that the cause of the Plague at Lausanne and the neighboring districts was not only a contagion, but also some vicious quality of the air, which travelled from the sick to the well "sitting near."[20] In the monthly report of the Paris Faculty of Medicine in 1658 we find a paragraph stating that the disease was due to "les variations de l'atmosphere." In Italy, at the same time, the same view was held. The theory of its

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causation from temperature variations received further support from Sprengel, who, writing of the epidemics of 1742 and of 1782, said that influenza was due to a "sudden change from sudden heat followed by sudden cold," while Muncio, writing of the 1762 epidemic, expressed the same thought, when he said that it was caused by sudden cold followed by sudden heat.[19]

The chemical composition of the air was again advocated as a cause in 1742, when influenza was said to be due to a phlogistic gas, over-stimulating the weakened body, producing a catarrh. And, when the chemistry of the air was still better known, Most, in 1820, becoming more specific, claimed that influenza was due to an excess of oxygen in the air.[19]

But a real advance in the contagious theory was made in 1762, when the disease was traced to people coming from infected areas; and in 1782, to persons, clothing and articles coming from infected districts. It was then said "that it began in a town or city and spread to the neighboring villages; that both on land and sea isolated imported cases invariably preceded the general outbreak," thus bringing forward prominently the contagious cause.

And so it went, miasma or contagion, contagion or miasma, but actually the miasmatists were hard pressed to explain the transference of influenza observed clinically, and the contagion advocates were equally hard pressed when confronted with records of whole communities succumbing in a night, as was recently illustrated at Cape Town in 1918.[17] Therefore, as clinicians we might hold to the contagious view, while as epidemiologists we turn to the miasmatic hypothesis.[19] But it was not until the 18th century that contagion, as opposed to the miasmatic cause, was clearly defined by Haygarth.[4]

Dr. Johnson, writing of the 1793 epidemic, gives instances of influenza occurring on vessels that had left a healthy port with a healthy crew, and weeks later had influenza break out. He says that while the warship *Atlas* was in the China Sea influenza broke out on board ship, and that it was later found to have started in Canton, China, at the same time. But as an argument against the theory of contagion, he gives reports of influenza breaking out in isolated, widely separated huts in the mountains with no communication between them. This fact, and the instance of the warship *Atlas*, may lead one to believe in the Epidemic Constitution, which idea will be developed later.

We find that in 1782 the Medical Council of Vienna declared that influenza was caused by persons inhaling air-borne or swallowing water-borne insects.[19] The name la grippe was also said to refer to insects, which by contaminating the air were supposed to cause the influenza. The same, with respect to insects, has been said of dengue.[4]

From early ages, in 1529, food poisoning has been blamed as the cause of some of the manifestations of influenza, as in Germany it has been said to have been caused by eating fish. In 1752 Swabian sausages were thought to be the cause; or it was thought to be due to ergot, causing Kriebelkrankheit; or to radish seed causing raphania. It was also said to be due to partaking of rye, peas, chickens, and many other articles of food or drink; all of which were declared to have caused illnesses now diagnosed as influenza, with this pecu-

liarity, that many of the cases of food poisoning were found to be nervous or cephalic in their symptomatology, "die Nervenkrankheit, as Haberkron in 1772 called it." These epidemics were also called Kreibelkrankheit in Germany, and Raphania in Sweden, Scandinavia and Russia until 1800.[7]

The bacterial cause was, of course, not understood in the early history of influenza, but Seiffert in 1883 was one of the first to study the bacteriology of this disease. He found a Streptococcus pyocyaneus to be the cause. In the 1889 epidemic Klebs discovered the flagellata, while Rilbert, Vaillant and Vincent found the cause to be a streptococcus, but Weichselbaum, Kruse, Pansini and Marmorek ascribed influenza to the diplococcus of pneumonia.[19]

We have studied the parasites which develop under laboratory conditions and have held disease to be bound up with them. For instance, Creighton claimed that "the bacillus influenza was the sine qua non of influenza," but, says Hamer, "we forget that a particular parasite may be merely one of a series, and that it may in some cases be replaced in that series by another parasite, and for the time being and under the local conditions in question cease to have any connection with the disease at all. The records of epidemics suggest that some such explanation must be looked for, in order to reconcile the extraordinary persistence of disease types, with the no less remarkable variability of the organism to which the bacteriologist attaches importance, as the cause of the disease."[7]

Then an idea, that has since gained many adherents, was brought forward by Robert Donaldson. He thought that the streptococcus in the epidemics was of an unstable variety, which on culture became stable; that it was a pleomorphic organism.[9] That the disease is closely associated with a pleomorphus streptococcus of the pneumococcus group is now held by many; Donaldson thought that it belonged to type IV.[3,17]

This view was also held by Rajchmann who predicted the 1918 pandemic.[3,17]

Crookshank says that bacteriologically the pandemics of influenza are due to some bacillus or filter-passing virus,[7] and that epidemics of specialized| types are caused by association with other organisms; or that the cause of the epidemic may be a pleomorphus coccus or some physical condition that actuates that pleomorphus coccus.[17] Others have held that the prevalence, between the pandemics of influenza, depends upon some interaction between the "primary cause," whatever that is, and the various "satellite influences." Into this question symbiosis comes, "for the organism may be linked now with one and now with another ferment or enzyme." (Dixon.[7]) This doctrine may find application, for example, in the connection between the tubercle bacilli of bovine or of human origin; or the parasite or associated parasites of smallpox and vaccinia; of scarlet fever and diphtheria; (I have often seen these occur consecutively in the same house but not necessarily in the same patient); of dengue and influenza; of enteric fever and dysentery; of typhus and relapsing fever. We may even conjecture that immunity in some instances may mean that the parasite has been harnessed to some other parasite or enzyme which robs it of its virulence. (Hamer.[7])

Here, of course, we must not lose sight of the fact that the particular organism to which the bacteriologist has drawn attention, may of itself be a mere subparasite, capable of living symbiotically with the parasite in chief. Thus the influenza organism may at one time live in association now with one or more groups and then again with some other differently constituted groups of satellite influences, thus accounting for the variations in manifestations of influenza, especially during the interpandemic period. The manifestations of influenza are fairly constant in the agregate, at each pandemic phase, but undergo remarkable transformations in passing from one pandemic to another.[7]

So, one pandemic passed into another through the intervening trailers and precursors by means of the activation of carriers of the organism, whether this activation occurred by the influenza bacillus or by the streptococcus or otherwise. But only when this activation was due to the streptococcus did fatal and complicated cases occur.[8]

The prodromes and trailers of epidemics will be briefly referred to later.

In discussions of the bacteriology of influenza, Pfeiffer's bacillus has been prominent. But Donaldson in writing of "the bacteriology of influenza, with special reference to Pfeiffer's bacillus," says:

> In the 1918–19 pandemic of 19,145 examinations during life it was found in 34.4 per cent of cases and of 3056 post-mortem examinations it was found in 39.8 per cent of cases. These cases represent a majority of the cases examined in many countries by many bacteriologists.[9] . . . Taking an average of nearly 20,000 cases, 62.9 per cent were entirely negative as far as the Pfeiffer bacillus is concerned.

Pfeiffer himself of 217 cases examined during life obtained only 51.6 per cent positive and of 30 cases examined post mortem only 66.6 per cent positive.[9]

If Pfeiffer's bacillus is the causal organism of influenza, then there is also a pandemic of 62.9 per cent of total cases of some disease due to some other organism, according to an average of the findings of all bacteriologists except Pfeiffer.

Epidemics of Influenza

The epidemic of 1510 was accepted by all but there are accounts of diseases, that we now consider to have been influenza, that occurred in B.C. 412, and also in B.C. 393, when the Carthaginians were besieging Syracuse, and in B.C. 43 in Rome. In A.D. 591–92 the disease was characterized by much yawning and sneezing, which gave origin to the custom of making the sign of the cross over the mouth when yawning and saying "God preserve you" when anyone sneezed.[19]

Also there were epidemics in A.D. 837, 876, 889 and 932.[1] But authentic history begins with the epidemic of 1173, which was noted by Hirsh, for fatalities in pregnant women. In the epidemic of 1307 it was called by the French *le tac;* also *le horion.* The meaning of these names will be explained under Nomenclature. Other epidemics occurred in 1323 and 1327–28. In 1387 the disease was so prevalent that hardly one in ten remained healthy, but few succumbed. It occurred again in 1403–04 and 1410–11.[19]

Pasquier says that there were at least 100,000 cases in Paris in 1413–14; another epidemic occurred in 1427 and the 1510 epidemic was noted for frequent abortions in women, while in 1529 there was a pandemic of sweating sickness in all countries except France

and Italy.[1] It was then referred to as the *pestis Britannica.*

In 1551 the epidemic in France was called *le coqueluche,* or, the fad of the moment and the same frivolous term was applied to the terrible pandemic of 1580.[1]

In 1557 was another one of the English sweats; which, on account of its posting character, received the name of "stop gallant and know they master."[7] Some say that the "sweating sickness" was not the same as influenza. They may be right, but many physicians, of many periods of medical history, have identified them as being the same disease, on account of their possessing the characteristics known to be those of influenza.[7] Some say that the dates here given are not those of influenza epidemics but Dwight M. Lewis[8] says that "what are often thought to be independent diseases and independent complications of such diseases are seen on careful examination to be interdependent diseases and interdependent complications. Many physicians have correlated all the diseases here mentioned as being influenza.[6,7] The correlation of epidemics, the identification of the various epidemic illnesses, as being influenza, will be referred to later, when opinions by Heusinger, Willis, Camerarius, Scheifferlius and others will be quoted.

To continue the list of epidemics: The great epidemic of 1580 was noted especially for two symptoms, being so sudoral as to suggest the return of the English sweat and so encephalic as to be called by Brunner the *Hauptkrankheit.* There were other epidemics in 1593 and in 1647. Cases of influenza first occurred in North America in 1626–27, but-the first epidemic occurred in the western hemisphere in 1647.[19]

Epidemics occurred in 1675 and, in 1712, Camerarius called it *Schlafkrankheit.*[4] The nervous manifestations seem to crop out all along the line. There were epidemics in 1718, 1727, 1729, 1732–33, and 1741–42, in Edinburgh, "not one out of six or seven escaped."[19] They again occurred in 1767 and 1781–82. That of 1781–82 was most widespread. It started in the British army in India in November. It was in China during the same autumn; in Siberia and Russia in December; Germany in February, 1782; Denmark and Sweden in April; England and Scotland in May; France and Italy in June; and in Spain in August, again illustrating its posting character.[19]

The one in 1793 was described by Robert Johnson, who observed that epidemic and wrote of it.[20] There seems, then, to have been much influenza, a sort of epidemic constitution from 1799 to 1804, and the one that occurred in 1816 was especially fatal to children, killing in a few hours, as occurred in some of the cases in 1918. Epidemics also occurred in 1827, 1830–33, 1836–37, 1843 and the one in 1847–48 was noted for its bronchitis of the capillary form which was very fatal.[19] There were epidemics noted in 1850–51, 1855–58 and 1875–76, and in 1889–90 it was in both the western and eastern hemispheres, where it was called the *morbus maximus epidemicus.* Pandemic influenza again occurred in 1918–19.

Periodicity for epidemics has been claimed by some but has not been proved. Sydenham, I think, wrote on that feature.[19]

The average duration of a pandemic is about three months.[4,19]

Epidemics have not been proved to spread from east to west or from west

to east as some claim, but they spread radially and by leaps and bounds and always by roads of intercommunication, using the route of travel, by person to person and country to country, illustrating their posting character.[7] The posting character is defined by Crookshank[4] as involving large areas of the globe and prevailing in affected communities for some three or four months at one time.

Some epidemics are very widespread. The one of 1781 has already been geographically outlined but the one of 1580 also involved millions of people and a wide territory: Asia, Africa to Constantinople, Venice, Sicily, France, Portugal, Hungary, Bohemia, Denmark, Sweden and Russia.[19]

Influenza has often been called a *new disease, novus morbus,* on account of its diversity of manifestations. Epidemics are also diverse. Different epidemics seems to pick out different organs; the toxin picks out one type of tissue and seems to limit itself to that tissue, as in one epidemic pneumonia predominates, in another gastrointestinal involvement; while in another it may be mastoditis.[1,19] In different countries there are different manifestations, even in the same epidemic, as in 1718 it was called in Picardy, *surette du Midi;* in France *la fièvre miliare;* and in England the sweating sickness.[7] And the 1820 epidemic was identified with cholera sudorale; with this should be considered the great increase in cases of "mucous" and "ulcerative colitis" of 1918 and 1920, which were trailers of the 1918 pandemic.[4]

Thus we recognize many manifestations of influenza epidemics, but, in order that there may be no confusion, many observers have correlated the different typical epidemics as being all influenzal.[6,7] One brief reference: Heusinger in his "Commentatio Semiologica" connected Guidetti's account of the 1712 epidemic with that of Willis in 1658; and Camerarius that of 1712 with that of 1580. And Scheifferlius in 1727 in a rare essay entitled "De morbo epidemio convulsive, per Holsatiam grassante oppido raro," identified that malady with that of Willis (1652–58) and that of 1580. "He was severely criticized for this but was vindicated by the occurrence of recurrent waves of influenza from 1729 to 1733, that continued throughout the world."[6] Many others have drawn together under one disease the many different types of influenza as it has occurred from its first recognition until now.[7]

We are therefore impelled to quote Fernel, Schiller and Benedetto, to recognize that certain diverse special diseases represent the recto and verso of one and the same pathological and epidemiological concept.[4]

Prodromes and Trailers of Epidemics

With pandemics there were trailers that came after the pandemic, sometimes attacking the same people who had already been sick, repeating ten, twenty, or more times and often with different types of influenza in the recurrence. Hamer quoted several cases illustrative of these repetitions in the same patient. That epidemics have predecessors and trailers has long been noted. Hamer wrote learnedly on this subject. Crookshank has shown by historical survey that influenza has a characteristic tendency to herald itself in the form of predromes of paralysis or other manifestations of encephalomyelitis, but he recognized that the "epidemic stupors" are no

new disease but that they have been recorded with variations for 450 years, as predecessors or, as some say, *avant coureurs* or prodromes of a pandemic. Hippocrates recognized this when he said that the prevalence of encephalomyelitis has always stood in a certain relation to epidemics and endemics of "burning fevers," which we now call influenza.[7]

For instance, Malcoups of Brussels divided the historic influenza into two catagories; the one vernal, catarrhal and benign, as in 1658, 1742–43, and 1780; and the other autumnal or hermal and marked by "prodromes nerveux caractère adynamique gravité plus grande,"as in 1580, 1676, 1730, 1737, 1775 and 1837. The cases of encephalitis lethargica seen in May, 1918 should be reckoned among the *prodromes nerveux* of the pandemic of influenza of the autumn of 1918, which in point of fact combined Malcoup's two catagories.[6]

Literature is full of illustrations of physicians who have correlated the prodromes or *avant coureurs* and the trailers of epidemics and whose writings are too numerous to quote. However, Lombard expressed the aphorism that embodies the experiences of Hippocrates, Bellonious, Barthelini, the two Kammeisters and of Guidetti, when he said "La grippe est souvent précèdée par une constitution éminement nerveuse, dont les caractères principes sont de porter le trouble dans les fonctions du cerveau et des nerfs encephaliques," to which Ducros, Montain, Petroquin and Recamier agreed.[7] That is in brief, the opinion of many; a few illustrations are: The trailers of the 1550's epidemics were noted by Leichtenstein and avant coureurs of the 1580 epidemic by Bellonius. The trailers of the 1580 epidemic, occurring in 1581 were described by Ronsseus—they were like those in Belgium in 1557, which were supposed to be due to ergot; the illness began with spasticity or palsy of hands or feet, with half closed eyes, *oculi semi apertis*, open mouth filled with ropy mucous and tongue as if paralysed, all like botulism. This is parallelled by the account given by Breinl of the spasmodic form of Heine-Médin disease in Australia in 1917, occurring as prodromes of the 1918 pandemic; in both groups there were severe gastrointestinal disturbances.

Leichtenstein, writing of the 1550 epidemic, and also Blakiston and Graves, recognized and wrote of polymorphic nervous manifestations of influenza that occurred as trailers and *avant coureurs* of pandemic influenza.[1]

Many of the epidemics of 1825, called dengue, were incidences of "Spanish influenza" of the type seen in May and June of 1918, which were the precursors of the pandemic of that autumn.[7]

Huxham noted that the vernal catarrh of 1743 was followed by trailers in 1745 in the prisoners at Plymouth with a mortification of the feet.[4] This in 1889 was recognized as a sequela or trailer of influenza, a similar condition occurring after that epidemic.

NOMENCLATURE

It is curious to remark the regular and constant pace which the science of health and philosophy have kept with each other. As long as philosophers imagined the elements of natural bodies to be four, physicians supposed human bodies to consist of as many humors, but as soon as the corpuscular philosophy became pretty generally received, medicine had her acrimony, spiculae and salts of various sizes. In like manner when astrologers

took the lead of true science and people began to fancy all terrestial things to be governed by the heavens, some Italian doctor found that this distemper proceeded from the influences of the stars, and gave it the name of influenza. [Robt. Johnson.]

As Sir Thomas Watson says: "they put the cause for the effect."[1] Of these there are several illustrations, but I will name only four.

Buonissegui in 1357 called it, in Tuscany, the *grande influenza* and said that to save the patients the cost of doctor's visits, the doctors were allowed to visit their patients only once daily. Sozoma similarly named the famous epidemic of 1387, while Calenus declared the epidemic of 1579–80 to be *ab oculta coeli influentia.*[4] The fourth illustration is more descriptive: "In 1658, about the end of April, suddenly a distemper arose as if sent by some blast of the stars, which laid hold on very many together, that in some towns in the space of a week about one thousand fell sick together."[7]

The Venetian envoy in London in writing home of the sweating sickness of 1551 used the word *influsso; influxio* and *influsso* were then freely used in respect to all catarrhal and sudoral maladies. *Influsso* is therefore astrological and humoral in its connotations, while influenza is philosophical and astrological but not humoral.[1]

The word influenza was first used in professional English in 1767, in the translation of Professor Huxham's book, "De aere et morbis epidemicis," but the first allusion by an English physician to the word influenza, as the name of an epidemic, was in 1743 in an "Essay on Fevers," also by John Huxham.[4] However, it was not until 1918 that the Royal College of Physicians confirmed the word influenza in the place of Zeviani's *il catarro epidemico.*[1]

Thus we see that very early it was called "pest," "pestilence" or "a plague."[1] Then it was called catarrh in the 16th and 18th centuries, but was called influenza by the Italians as early as 1357; and finally influenza by everyone.

Those are the foremost names of influenza, though its names are legion; varying geographically and temporarilly.

Geographically it was called *morbus Hungarius, morbus Gallicus, suette de Midi, la suette de Picardo,* or the Picardy sweat, which in 1847–48 was thought to be essentially cholera sudorale (Hirsh); in Spain, *pantomima;* in France in 1772, *la fièvre miliare.* In Germany, especially in 1528, it was called the *sudor Anglicus* or the English sweat, or less euphoniously, the *pestis Britannica;* in Russia the Siberian fever, and the Chinese fever in Siberia. America called it influenza Europa, European catarrh or Spanish influenza.[4] Each country was blaming the other for it. It was called Malta fever where the two empires the empire of influenza and the empire of dengue, met.[7]

In 1580 in England it was called the "gentle correction" or later "the Jolly rant," the "Dunkirk rant," or in 1709 the "Dunkirk ague."[4] On account of the symptoms of the 1580 epidemic, the encephalitic forms, which were like those exhibited by a sheep with cysticerci within the skull it was then called *mal de castrone,* and in Germany in 1487 the *Haupweh,* the head trouble, was given as a name for the influenza trailers of the 1580 epidemic. And in 1775 Andral called

influenza "hydrophobia without the bite of a dog."[6]

Then there were names given to it on account of some particular symptom. The names *le tac*, meaning a *coup de fer*, and *l'horion*, meaning a sudden punch between the shoulders, are expressed by the Londoner as "getting the knock,"[5] or the "knock-me-down-fever." In Spain it was *trancaze*, a blow with a bar; the *Schnupfenfieber* in Germany and the *mal di castione*, or coughing sickness in Italy. In fact in 1173 it was called *tusso gravessimo*.[19]

The present name for whooping cough, *coqueluche*, was used by the French for influenza in 1414, 1551 and in the great epidemic of 1580.

That sickness follows as the result of sin was believed not only by the Jews of Christ's time, but by the French in 1411, when they thought that influenza came as a visitation on those for singing a lewd song then in vogue, "Tu as chantē la chanson."[19]

Dengue and influenza were by many supposed to be the same, dengue being the summer form of influenza. (Dengue is by some said to be derived from *dans le dos, le dando.*)[5]

Because the symptoms of influenza did not always correspond to or match the concept of influenza then held, a new epidemic was often thought to be a new disease; for instance Randolph, the English ambassador to the Scotch Court, writing to London in 1562, called it the "new acquanyntance," stating that it "spared neither lorde nor ladye."[19]

Hamer says that different manifestations of the same epidemic used to be thought to be different diseases. For instance, he finds historical records of cases of sausage poisoning in one village, ergotism in a neighboring valley and encephalitis or influenza in a town a few miles away.[1,7] He thinks that all of these cases were influenza.

Again, in 1915, there was in London an epidemic of influenza with lung and cerebrospinal complications that finds its analogy in "a new fever," described by Sydenham in 1685, also with lung and central nervous system symptoms; in each there was often a purpuric rash.[7]

SYMPTOMS

Of the symptoms of influenza Robert Johnson in 1793 said that one of the characteristics of this disease was "the sudden transformation from high health to sickness, often as it were instantaneously." "There is," he says, "no disease to which the human body is liable that is so extensive in range, so sudden in attack (the German *Blitzkatarrh* or lightening catarrh carries out that idea) and so furious at the beginning, so rapid in its course, and at the same time attended with so little danger."

Time permits of speaking only briefly of some of the symptoms.

The cough is especially prominent for its persistence, especially as a sequela. In 1410–11 in Paris, it was so severe as to cause in some cases rupture of the pregnant uterus.[19] In the epidemic of 1427 it prevented the people from attending church; but from the contemporaneous writings we learn that it did not prevent them from attending the theater.

Epistaxis was noted by Hippocrates and was regarded as a favorable symptom in the epidemics of 1414, 1580, 1729 and 1837. It was frequent in recurrence rather than persistent, in the epidemics of 1737, 1755, and 1803, and, in the 1918 epidemic, was noted by Conner in 25 per cent of cases in

some hospitals, especially in the cases that later developed pneumonia.[14] Johnson in 1793 mentioned a patient who lost 20 ounces of blood.

In 1580, on account of coincident symptoms referable to the bile duct, that epidemic was called by some *catarrhalis biliosus.*

Sometimes there was a bloody sputum[11] and cyanosis, the mauve or heliotrope cyanosis that was so fatally characteristic.[10] Some of these cases of cyanosis in the Russian epidemic of 1742–43 terminated in diarrhea or dysentery, which seems to show, in the terminal stage of the case, an affection of the vegetative nervous system innervating the gastrointestinal tract, as there was in the early stage a disturbance of the vago-autonomic nerves supplying the lungs. This affection of the vegetative system will be referred to later.

Diarrhea, pneumonia and rhinorrhea, a great flux from the nose, were noted in 1693.[11] Webster, in 1761, noted a running from the nose and Heimer in 1762 noted it as the cause of erysipeloid irritation of the upper lip.[14] Fernel, Benedetto and Ballonius regarded the catarrh as a distillation from the brain which came as a sweat, a flux, of the mucous membrane and which, if repulsed or arrested, choked the nervous system, producing what we now call encephalitis or myelitis.[6]

Camerarius in 1712 observed ptosis, the *oculi semi apertis*, a prominent symptom of the present-day cases.[10] That was the epidemic that he called *Schlafkrankheit* on account of the sleepy appearance.

Jelliffe advances an unique hypothesis in relation to causation of the symptoms. He says that, the involuntary functions of the body being under the opposing control of the sympathetic and the parasympathetic systems, an inhibition of one means an increase in the activity of the other. He also says that the most striking general feature of this autonomic or parasympathetic predominance is that bearing upon the complex factors of vascular wall function. As the result of the paresis of the constrictor fibers there is a dilatation of the vessels and a serous or hemorrhagic exudate.[11] If cephalic there is pain in the head, a serous or non-purulent meningitis (the "hydrophobia without the bite of a dog"). The head pain is at times intense, of a bursting character.[11] If the cranial nerves are involved there may be disturbances of smell, optic neuritis, ocular paralysis, deafness, vertigo, disturbances of taste, facial palsy and various fifth nerve neuralgias. Or, if peripheral spinal nerves are involved, we get neuritides or neuralgias from exudations in the nervi vasorum of the nerve sheaths.[11] In Scotland (and it is strange how symptoms occur to suit the people) there was a most characteristic sensation of tracheal excoriation that the imbibing of Scotch relieved. All of which, to go back to Jelliffe's explanation, are due to a vegetative disturbance, the most striking features of which are the disturbances of the pneumogastric and sympathetic adjustment. The sympathetic paresis with over-action of the autonomic causes the edematous flooding of the pure "influenza pneumonia," the pneumonia being thus not a complication, but a part of the disease.

The gastrointestinal symptoms from this vegetative disturbance are gastrosuccorrhea and the like.

Complications

The complications are many. Some are of interest.

In the throat there is sometimes a marked difference between the objective symptoms and the subjective symptoms, for at times, when there is little that can be seen, there is much subjective complaint, or vice versa.[14] Hoarseness and cough were prominently noted in the Roman epidemic in 1593, also in the epidemics of 1673, 1712 and 1737. Sometimes there occurs a paresis of some of the intralaryngeal muscles.[14] Years ago such a case was diagnosed in Charleston. The child's father thought that the condition was due to tuberculosis and moved to another city, changing the outlook and surroundings of his family.

Anosmia, if associated with disorders of taste, is apt to be permanent. Sinusitis occurs in 4–6 per cent of cases, but it tends to recover, even without treatment, in marked contrast with mastoiditis, which is serious, even with treatment. Middle ear complications were noted in the epidemics of 1580, 1732, 1788, 1789 and 1835, and it was early recognized that the eustachian tube caused the middle ear complication. H. Lawson Whale makes the interesting observation that an influenza mastoid may occur without an intervening middle ear involvement.[14] The epidemic of 1733 was noted for giddiness, an internal ear involvement.

Intracranial complications from otitis were early noted. Frances II, King of France, husband of Mary of Scotland, had an intracranial complication, a condition then recognized as due to the discharging ears (Alexander Dumas).

Neuralgias and neuritides with palsies and zosters[14] of every regional distribution, central as well as peripheral, have been seen.

Pregnancy has always been noted as one of the most serious complications, for it has been noted that a temperature of 103°F. or more, or especially a cyanosis, is particularly apt to make a uterus become active, and if abortion or premature labor occurs the mortality was as high as 80 per cent (Titus and Jamison) or as low as 50 per cent.[15] As has been mentioned, cough may cause the uterus to rupture. In 1510 women often aborted. In 1647 it was especially fatal to pregnant women. In the 1782 epidemic there were in London "many cases of miscarriage and some deaths."

Bradycardia is frequent in the early stages from involvement of the synapses in the mid-brain, and of the cromaffin tissues. Glossopalatine or spinal accessory involvement manifests itself as taste disturbances and a general disgust for food. This was especially noted in the 1742–43 and 1780 epidemics. Sciatica is also extremely common, being mentioned by many authors.[11]

CONCEPTS OF DISEASES: EPIDEMICS AND EPIDEMIC CONSTITUTION

As physicians we observe the phenomena presented by the patient. We then express their order of occurrence and their likenesses by means of concepts. The formation of a concept is not an act of perception but is an act of the mind. A disease concept, therefore, is a mental act and is as immaterial as an Euclidian line, but the disorders of function, their manifestations and their results, as attributed to the patient, are realities. Disease concepts are not realities but are bills of exchange on the counting house of medical practice, to be cashed, discounted, or rejected in accordance with their value at the

current rate of the bank of medical experience. A disease like influenza has no existence, except at most in the Aristotelean sense, anterior to the concept; just as a lawyer considers that a crime is only a crime as a result of a law. Anterior to the law the crime does not exist.[2]

We give a name to the disease concept, calling it scarlet fever, measles or influenza. When we match the symptoms presented by the patient with the disease concept we make our diagnosis and the patient is said to have a case of the disease. As we learn more, observe more and better, our disease concept changes. Because influenza did not match with the disease concept held at various times, influenza was frequently called a new disease; as a new delight, a new acquaintance, *morbus novus*, and *morbo neuvo* or *morbus insolitus*. New concepts mean new symptom groupings and rearrangement of our ideas concerning the manifestations of certain classes of sick persons. Just as a disease is a concept of symptoms plus an intracorporeal cause, so an epidemic concept is a concept of cases plus an extracorporeal cause, and a pandemic concept is a concept of epidemics plus an extracorporeal cause.[3]

We refer symptoms to the disease concept for diagnosis. We refer cases to the epidemic concept for diagnosis and we refer epidemics to the pandemic concept for diagnosis. The sufferer from the *epidemy* is not the person who harbors the disease but the community within whose terrain play the agencies that disseminate the germs and favor their pollulation; and the cause relates rather to the population and to the prevalence. As Brochin says: "Dans les epidemies, bénignes ou dangereuses, il ne s'agit pas d'un homme, mais de la cité, et même de tout un pays. Civitatem non virum curabis."[3] Epidemiologically we think of cases as symptoms of epidemics, and of epidemics as symptoms of pandemics.

Epidemic Constitution

The epidemic constitution was philosophized about by Hippocrates; idealized by Galen and materialized by Bellonius in the 16th century in his book called "Epidemies and Ephemerides." Sydenham practiced clinical analysis and epidemiological synthesis.

The epidemic constitution may be described as follows:

There appear many cases in a community which are often attributed to local conditions; as food poisoning (canned tomatoes, ergotism, botulism), drain errors, overcrowding, or rhaphania. Some of these may be nervous cases as solanism or they may be some form of meningitis. There are interesting and unusual forms of cerebral, bulbar, spinal and neurotic diseases. There are also respiratory cases which are diagnosed as pneumonia of a peculiar onset and course.

Others are gastrointestinal in their manifestations and have, as a diagnosis, some form of enteric fever, as typhoid, dysentery or gastric fever. There are also cases of gastroenteritis and of colitis (the scorbutus of the Renaissance period), or there is the serous effusion in the peritoneal cavity, "the tumid belly," as it was diagnosed by Sydenham, as a part of the epidemic constitution; or cases are seen of anomalous or peculiar forms of common specific fevers or of septic throat, of the fourth disease, of lastrim, of glandular fever and the like.[17]

"Many diseases appear new and mysterious and puzzling. Even the lower animals are affected, domestic as well as wild." These conditions succeed one another for a year or two or more and should be called by epidemiologist the *avant coureurs*. At this time the epidemic is often not looked for.

Then comes the general widespread and evident general disturbance of public health, a perfectly recognizable manifestation. In the pre-pandemic period the endemics and epidemics are less typical but become more typical as the pandemic period is approached and less typical after the pandemic ends. During the pandemic or "the influenza crisis" much happens that is afterwards forgotten. For instance; surgical operations "go wrong." There are odd forms of suppuration or peculiar inflammations of veins and of cellular tissues are seen with unusual frequency; anesthetists meet with difficulties; obstetricians have calamities; aural and ophthalmic specialists are puzzled; and alienists are consulted concerning baffling and strange psychoses.[17]

Moreover, the veterinary surgeons are busy; for there are epidemics here and there among horses, dogs, cats and rabbits and fowls; and paralytic affections such as "limber neck" are common in the stable and in the farmyard. [cf. Heusinger.[7]]

Nor is it only the domestic and captive animals that suffer; for, as in 1918, we heard of reindeer in Labrador and Lapland, and baboons at Gibraltar and the Cape dying mysteriously and in great numbers. And again there is indisputable evidence that during the great influenza periods there are widespread changes in the world of insects, of vegetables and of fungoid life.[17]

This fact is brought out in the etiology of influenza, as related to birds and in the Argive Camp where dogs and cattle were affected.[19] In 1833 influenza was called epizootique.

"Then the influenza pandemic all bubbles down as trailers, which in each succeeding year become more unlike the pandemic."[7]

Thus an epidemic constitution is not a material thing like a flower or vegetable; it is a concept of a condition, and by comparison of our observations with that concept a diagnosis is made of an epidemic constitution. An epidemic constitution, is, therefore, seen to consist of (1) the *avant coureurs*, (2) the pandemic, and (3) the trailers.

That brief exposition of an epidemic constitution may to some seem like a meaningless theory, but as a case in point, this is the epidemic constitution of the 1889–90 pandemic.

There were, according to Menitier, avant coureurs in the form of pneumonia in Paris in 1885; followed, according to Cordier, by an outbreak of poliomyelitis in France in 1886; and the same malady in Norway also in 1886, reaching Sweden in 1887–88. In the Mediterranean in 1888 it was called a "new disease" and according to Marathner, manifested itself as a disease similar to the Heine-Medin disease in Geneva and as a new form of pneumonia in Italy in 1888; in Virginia it was also called a new disease; some thought it to be dengue. In the Near and Middle East it was a vast epidemic, locally recognized as dengue, and the "dengue" at Honkong in September and October, 1888, was diagnosed by Sir James Catlie as true epidemic influenza. It was traced to Cairo, Palestine and Constantinople, then to Spain in 1889, as a new gastric and yellow fever; and also in Rio de Janeiro, as reported in the *Lancet*, it occurred as a new and comatose fever; in Germany as poliomyelitis; in Russia as rhaphania,

now called encephalitis lethargica. Then the trailing epidemic of poliomyelitis following in 1890–95.[17] It is of interest to note how many times it was called a "new disease." Crookshank described the epidemic constitution of the 1918 pandemic:

> It may, in a word, be said, that if the epidemiological happenings during an influenzal constitution be analyzed, we find that we may consider them as forming a series or sequence of epidemics grouped around a pandemic diffusion of the classical type. Influenza, then, is not the name of a specific disease and nothing more, but it denotes and must denote a complex concept, which essentially resembles in its construction the concept, for instance, of war. And, just as the notice of special wars, associated campaigns, battles, skirmishes and hand to hand encounters are embraced in the greater concept of war itself, so our notions of influenza embrace the subsidiary and constituent notions of certain kinds of epidemics, outbreaks, foci, and cases, and even of single symptoms such as epistaxis and hiccough.

In 1928–29 there were many cases of recurrent epistaxis and of low blood pressure from affections of the chromaffin, "which are of vast importance when studied from the viewpoint of the happenings with which they may be associated."[17]

All words, merely words, say some, but the account given by Quidetti of the epidemic constitution of 1712 parallelled word for word, as to some of the passages, with that in London in 1918.[6] The past checks with the present.

Mortality and Incidence

As has been said, influenza is a disease with an enormous morbidity and a relatively small mortality.[19] There have been exceptions to this, as in 1918; and in 1647, when in the Barbadoes and St. Kitt's there died 5000 and 6000 respectively. The most fatal complications are pneumonia,[19] and pregnancy.

As to incidence of infection, that also varies, but is generally high. In 1323 "all in Florence, Italy, were affected." In 1510 "not a family and scarcely a person escaped." In 1729, in Lausanne, 2000 of the 4000 inhabitants were sick and "in Plymouth, England, and district, not a house on the average was free." In Edinburgh in 1758 "not one in seven escaped." In 1410–11 Pasquier says there were at least 100,000 cases in Paris.[19]

But, for instance, in 1410–11, "except for cases with chronic disease and *que venesectione sunt*, hardly one in 1000 of those attacked died" (Weims). The excessive mortality of the earlier epidemics was due to the inordinate passion for venesection.[19] This may also account for the 20 to 60 per thousand mortality in Eulenburg in 1729. In 1510 bloodletting in Italy was followed by fatal results. Bleeding and purgatives are now said to have been injurious, but in 1580 in Italy and Spain bloodletting was practiced with dire results, killing 9000 in Rome (Schenkius) and depopulating Madrid and Barcelona (Vollalba). "Nearly all those who were bled died" (Saillant). In 1742–43 venesection caused many deaths in Italy as in previous epidemics.[19]

Andral thought influenza was itself never fatal, the deaths being due to secondary disease, or, I may add, to the treatment. The epidemic of 1833 was thought by contemporary writers to owe its high mortality to complications and sequelae and not to the disease.[4] But in 1847–48 the capillary bronchitis was very fatal, and in 1918 the mauve or heliotrope cyanosis was

particularly indicative of a fatal termination, even though the other symptoms then present did not appear serious. This symptom and its prognostic value were referred to by Peacock as early as 1847.[10]

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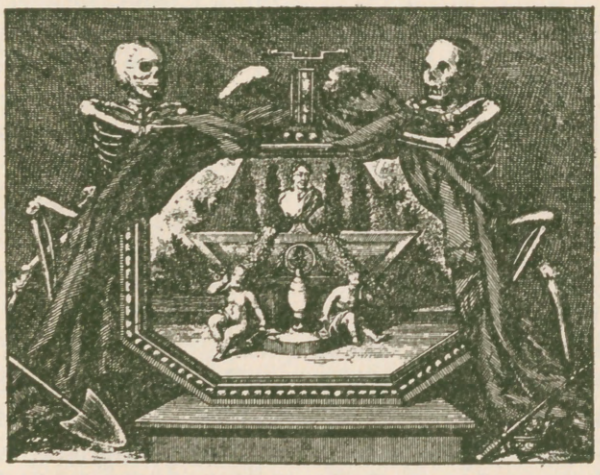

[COWPER: ANATONIA CORPORUM HUMANORUM. UTRECHT, 1750]