

A Further Investigation

INTO

INFLUENZO-PNEUMOCOCCAL AND INFLUENZO-STREPTOCOCCAL SEPTICÆMIA:

EPIDEMIC INFLUENZAL "PNEUMONIA" OF HIGHLY
FATAL TYPE AND ITS RELATION TO
"PURULENT BRONCHITIS."

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(With Coloured Plate.)

INTRODUCTION.

WHEN we published a paper upon "Purulent Bronchitis, its Influenzal and Pneumococcal Bacteriology," in conjunction with Dr. John Eyre, in THE LANCET of Sept. 8th, 1917, we were particularly desirous of drawing attention to the anomalous character of many of the cases of "pneumonia" that we had encountered in the Aldershot Command during the years 1915, 1916, and 1917, and because we felt that "pneumonia," in the sense of true croupous lobar pneumonia, was a misnomer in connexion with many of them. The "purulent bronchitis" type of certain of these anomalous cases that had up to that time been returned generally as "pneumonia" is now familiar to most Army physicians, but at the time of our own investigations, and those of Hammond, Rolland, and Shore,¹ the bacteriological nature of this severe purulent bronchitis, with its remarkable heliotrope cyanosis, abundant sputum, and high mortality, was not, we think, recognised generally.

Though it was occurring in the form of multiple small epidemics in France and in England, there was then no generalised epidemic to lead to the suspicion that it had an influenzal basis; and it was as the result of extended bacteriological research, *intra vitam* and *post mortem*, and not from the observation of clinical phenomena, that its causation was found to be primarily influenzal, with symbiotic or secondary invasion of the respiratory tract and circulating blood by either pneumococci or streptococci, the virulence of which, it seemed, had been so exalted by the coexistence of influenza bacilli that they caused death in a high percentage of cases by reason of a veritable pneumococcal or streptococcal septicæmia.

The condition, though labelled "purulent bronchitis" on account of the dominating characteristics—*viz.*, the severity of the chest symptoms, and particularly the appearance and quantity of the sputum—seemed to us, even at that time, to be an "influenzo-pneumococcal" or an "influenzo-streptococcal" septicæmia with a prominence of lung symptoms rather than a purely pulmonary disease. The question of the relationship of the streptococcal to the pneumococcal cases is elaborated later in this paper, but it may at once be stated that there is now much evidence in favour of the view that the streptococcal organisms described in certain epidemics may be really pneumococci growing temporarily in streptococcal form.

Since 1916, when the "purulent bronchitis" cases were differentiated more or less clearly from amongst the big group of anomalous "pneumonia" cases, we have had ample opportunities, more especially during the recent epidemics, for broadening and extending our views. We believe now that the "purulent bronchitis" type is merely one of many; that "influenzo-pneumococcal septicæmia" is responsible for much, if not all, of the fatal "influenzal pneumonia" which

is at the present moment (October, 1918) causing sickness and death, not only amongst troops in camps, but also, and to an almost greater extent, amongst the civil population, affecting Africa, America, and Asia as well as Europe, leaving few towns untouched in any country in which it has obtained a start, and spreading virulently amongst those who are aggregated closely together—for instance, when it breaks out on board ships on the high seas.

It is for others to deal with its epidemiology; we would confine our remarks to the clinical, bacteriological, and post-mortem aspects of the disease as we have seen it amongst troops at Aldershot and elsewhere. But once again, and even at the risk of becoming monotonously insistent, we would emphasise our view that in essentials the influenzopneumococcal "purulent bronchitis" that we and others described in 1916 and 1917 is fundamentally the same condition as the "influenzal pneumonia" of this present pandemic, and that it is only a matter of degree whether there is "purulent bronchitis," "capillary bronchitis," "broncho-pneumonia"—disseminated in some cases, lobar in distribution in others, multiple abscesses in the lungs, or even gangrene of the lungs. Few, if any, of the cases are true lobar pneumonia, and death seems due to an extreme toxæmia or septicæmia rather than to the extent of the lung lesion. In other words, the extent of pulmonary involvement is of comparatively little importance and bears no relation to the virulence of the essential septicæmic conditions.

Statistics: Incidence.—Owing to the extreme pressure of work, the overtaxed state of the medical staff, the variability of nomenclature in official returns, and other similar causes, it has been impossible to keep detailed records of all the cases encountered. In the aggregate we have seen several thousands, of which well over two thousand have been "pneumonic"; and have examined over four hundred autopsies. So variable, however, is the severity of the influenza itself in different units or hospitals at the same time, and so greatly does the mortality vary in troops from different countries that we make no attempt to give statistical details, beyond indicating that our experience is based on thousands of cases and not merely on hundreds.

Pneumonic incidence in the influenza cases.—Of the total number of cases seen in Aldershot and elsewhere during the last few weeks, the majority have been straightforward influenza. Roughly speaking, we may say that out of 1000 cases of "influenza" upwards of 800 have taken an ordinary simple uncomplicated course with fairly speedy recovery and without sequelæ. The remaining 200 have become more or less pulmonary—of these perhaps 80 being of moderate severity, the remaining 120 have been desperately ill; and of this last-named category somewhere between 60 and 80 have died.

These figures do not hold good throughout, for the lung complications and mortality have struck us as being very much higher amongst soldiers who have recently joined up than amongst those of longer service. They have been higher still amongst certain troops from overseas—South Africans, United States troops, and New Zealanders, *par excellence*—than amongst others.

The "pneumonic" cases and the mortality amongst them have also seemed to form a much higher percentage of the total "influenza" cases in a unit in which the epidemic has just started than after the epidemic has prevailed in the unit for a week or two. It is when the epidemic is in its earlier days that it is apt to spread like wild-fire and cause the greatest damage and the highest death-rate; although, so far as a whole Command is concerned, the daily sick and the daily mortality may continue at a high level for a longer time than it does in a single unit owing to the fact that the epidemic, whilst subsiding in one unit, tends to spread and break out in fresh units one after another.

THE SYMPTOMS.

(a) In the Straightforward Influenza Cases.

The symptoms in the straightforward influenza cases are precisely similar to those of ordinary influenza as it occurs in other places and at other times.

The onset has generally been sudden and acute. There have, of course, been many quite mild cases, but again and again a perfectly healthy man may be taken ill in the street or on duty with a sense of general malaise; he feels chilly, suffers from aches in his back, limbs, and head, and rapidly develops such a sense of prostration that wherever he is he has to lie down. He may rally sufficiently to be able to get himself back to his quarters with some difficulty, or he may be so bad that he has to be carried.

He gets to bed and is only too glad to stay there. He is nauseated at the sight of food and "feels rotten." Though drowsy, often he cannot sleep. His temperature is raised, generally as high as 104° F. or more. The pulse is full and firm, its rate is as rule not raised proportionately to his temperature, and his respiration-rate is between 18 and 30. Many cases have red injected palate and anterior fauces and complain of sore throat, but many have no such complaint, and on examination of the chest physical signs are absent. The tongue is almost invariably coated with a thick fur, superficially yellowish-brown at the back and on the dorsum, pale yellowish-white beneath the darker surface, and often with no fur on the margins and tip.

Epistaxis, sometimes of almost alarming degree, has been an unusually common phenomenon in this epidemic, sometimes at the

¹ THE LANCET, July 14th, 1917, p. 41.

beginning, more often after the patient has already gone to bed, and in quite a number of cases the hearing has become much impaired, a few cases having become temporarily stone deaf. Quinine prophylaxis may be a factor in this, but that there is middle-ear catarrh in at least some of the cases has been shown by subsequent ear discharge, and in one or two cases by considerable bleeding from each ear.

Vomiting has not been usual, but it has occurred often enough to attract attention. *Diarrhœa* to the extent of six or seven loose motions on the first day or two has been rather less uncommon.

Abdominal pain has not been a pronounced feature although occasionally it has existed of sufficiently severe character to lead to a provisional diagnosis of appendicitis, and even to some solicitude as to differentiation from an acute abdominal condition urgently needing operation.

In the earlier part of the recent epidemic *laryngeal symptoms* were not common to the same extent as in a curious outbreak of supposed "influenza" last year (not the "June, 1918," epidemic), but latterly quite a number of the men have been husky-voiced or even unable to phonate at all. These cases have not necessarily passed on to the "pneumonic" type.

The *temperature* has remained raised a variable number of days. (See Charts.)

Sometimes it fell suddenly as early as the second day, sometimes ending almost by crisis on the third, fourth, or fifth days, sometimes coming down more gradually to reach normal by lysis between the third and the fourteenth day of the attack. Speaking generally, the duration of the pyrexia has been far longer in the recent pandemic than in the cases encountered in June, and the subsequent prostration appears to be proportionately greater.

As long as the temperature has been up to anything like 101° the patient has continued to feel "rotten." With the fall of temperature rapid improvement sets in; the tongue cleans, the patient feels altogether better, begins to take his food with avidity, and convalesces in the ordinary way. Delayed convalescence has occurred either in those who have deferred taking to bed at the beginning, or, more usually, in those who, for duty's sake, have felt obliged to get up and work again before the acute stage of the disease has fully passed.

(b) *Symptoms in the "Pneumonic" Cases.*

The "pneumonic" or "bronchitic" complications, so much dreaded just now, come on at no fixed or definite period of the influenzal attack.

Frequently there is no distinct influenzal period at all, the case being then very similar to one of ordinary lobar pneumonia in the first day or two. Numbers of such cases have been diagnosed as true lobar pneumonia by those who are unfamiliar with the post-mortem findings, and it is remarkable how difficult it is to persuade those who have not seen such cases before that they are not dealing with ordinary pneumonia.

More often the patient has been ill for a day or two with simple influenza, often apparently not at all severe and indistinguishable from the general run of simple influenza cases, before acute or even fulminating pulmonary complications set in, and they may die so rapidly and with so little actual consolidation that it is clearly not the "pneumonia" but something more generalised, a veritable septicæmia, which kills them.

In a third type of case the "influenza" has nearly run its course, and the temperature may have returned to normal or nearly so for a day, or even several days, before it rises again with the onset of "pneumonic" complications.

All three types have been met with in abundance; the commonest is that in which the case has seemed to be one of simple "influenza," for one, two, or three days before it passes on into the much more serious phase of lung and general systemic complication.

There may or may not be a definite rigor; the temperature, already high, may or may not rise further. (See Charts.)

The patient complains in some way of his chest; he coughs with short dry hacking to begin with: the question of his sputum is discussed below. He often complains of pain in one or other side of his chest or in both sides, either in the region of the anterior axillary line about the level of the sixth and seventh ribs, or posteriorly at one or other base, or all over, or down the front of the manubrium sterni "as though he is all raw inside there."

Sometimes the skin is hot, dry, and pungent as in lobar pneumonia, occasionally a scarlatiniform rash of transient duration may be noted, but, on the other hand, it may be covered with profuse clammy sweat, the latter often leading to widespread sweat vesicles (sudamina and miliaria).

The breathing becomes rapid (often 30 per minute or thereabouts, but not seldom 40, 50, or even 60 per minute). The pulse-rate rises, but it is nearly always no faster than corresponds with the pyrexia, and often it is relatively infrequent except at the very end. There is no orthopnoea, and although there is rapid breathing there is no dyspnoea.

The facies is at first flushed and red, but in bad cases it speedily becomes less and less of a purely red tint and assumes more and more of a lavender, heliotrope, or violaceous hue mingled in the varying degrees of redness (pallor with heliotrope hue, redness with heliotrope hue, plethora with heliotrope hue, and all intervening degrees), this peculiar colouration being highly reminiscent of that of acutely gassed cases and an evil sign, for few cases recover when once this characteristic hue has become established.

The physical signs in the lungs.—Certain of the main symptoms will be discussed presently, but first we would refer to the physical signs in the lungs. These are extremely variable, and when a large number of cases have been seen one realises that neither the diagnosis nor the prognosis can be gauged by physical examination. Even at the risk of becoming wearisome we wish to emphasise this. A man with only a few rhonchi to be heard in either lung may die as certainly as another who has dullness, bronchial breathing,

bronchophony, pectoriloquy, and crackling râles over the whole of both lower lobes. The extent of consolidation is no measure of the severity of the infection; and a man may die of this disease with practically no lung symptoms during life and no evidence of consolidation post mortem.

In a considerable number of cases the clinical condition may be illustrated by saying that the patient when first seen looks so exactly like an example of lobar pneumonia that when one examines the chest and finds absolutely no abnormal signs at all one is inclined to say, "I am sure he is pneumonia all the same and I expect we shall find the signs of consolidation and probably rusty sputum by to-morrow." One examines the next day, and may again find no abnormal signs, or perhaps only a few scattered rhonchi in front, with subcrepitant râles at the bases behind without dullness or bronchial breathing. One may still expect consolidation signs the next day, and so on; and the case may run its entire course—to recovery after a week, ten days or a fortnight, or to death in one, two, three, four, five, six, seven, or even more days—without any further signs than the rhonchi in front and the non-sonating râles posteriorly.

On the other hand, the case may start as above, and in a day or two one may find markedly impaired percussion note at one or both bases, with bronchial breathing and sharp crackling râles, bronchophony and pectoriloquy, either of patchy distribution, or frankly all over a whole lower lobe or over a whole lung, or over both lower lobes. In such cases the unwary diagnose croupous lobar pneumonia simply because they are familiar with these signs in lobar pneumonia and forget that they may be also due to any other cause of extensive consolidation, or even to congestion only. In these cases the autopsy findings show this consolidation in the present cases to be due not to croupous pneumonia but to confluent broncho-pneumonia with varying admixtures of hæmorrhage, peribronchial infiltration even to the extent of abscess formation, œdema, turgid congestion, infarction, and pleurisy.

In other cases, again, the physical signs of some kind of consolidation may be pronounced almost from the start; and although these are to be found a hundred times in the lower lobes, especially behind, or in the middle lobe, for once they are found first in the upper lobes in front, there are occasional cases in which the dullness, bronchial breathing, and crepitant râles develop in one or other upper lobes and not in the lower lobes at all.

In another type of case there is no bronchial breathing anywhere, but both lungs—front and back alike—are full of crepitant or subcrepitant râles from apex to base, recalling the signs met with in some cases of generalised pulmonary tuberculosis.

In yet another type, whatever signs there may be elsewhere in the chest, one base becomes completely dull with silence as to breath and voice sounds; the dullness being of variable extent but generally extending a hand's breadth or more upwards from the base. Needling generally discovers turbid fluid in the chest in such cases, and small amounts of pleuritic effusion are common if the patient does not succumb too soon, although large pleural effusions are relatively rare.

Another phenomenon adds complexity to the picture.

This is the disappearance of bronchial breathing, which may have been pronounced and unmistakable a few hours previously, ordinary vesicular murmur now being heard instead. The bronchial breathing may re-develop perhaps a few hours later, or next day, either where it had been heard before, or in another lobe, and again it may disappear and be replaced by harsh vesicular murmur. The explanation of this seems to be the varying degrees of collapse that result from accumulation of thick muco-pus in the tubes. When a fair area of lung tissue becomes temporarily airless from this cause, bronchial breathing may be heard over it; within an hour the muco-pus in the tube coming to this part may have been displaced, and the alveoli have re-expanded with air, so that vesicular murmur is heard where a short time previously bronchial breathing was marked.

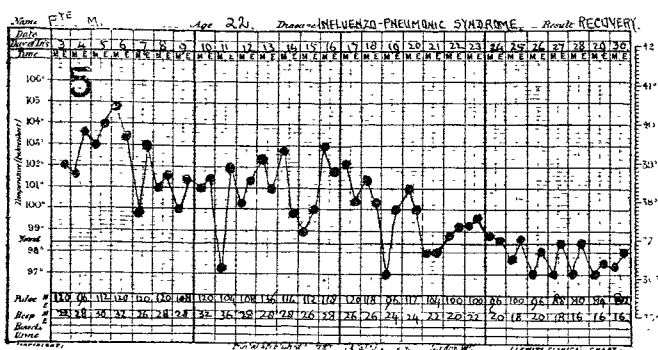
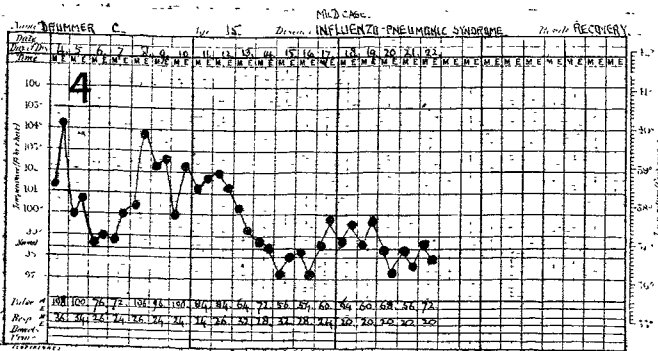
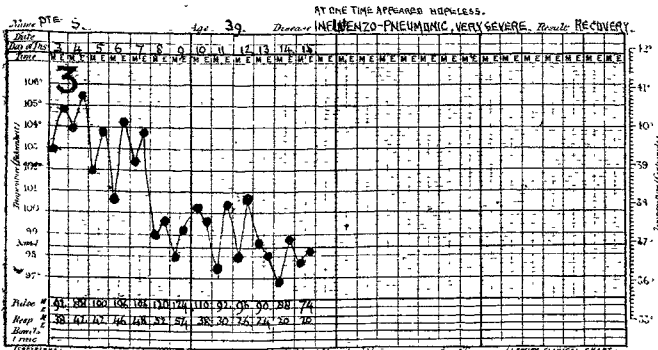
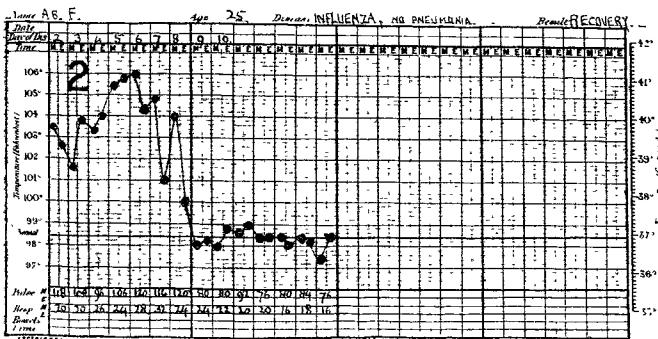
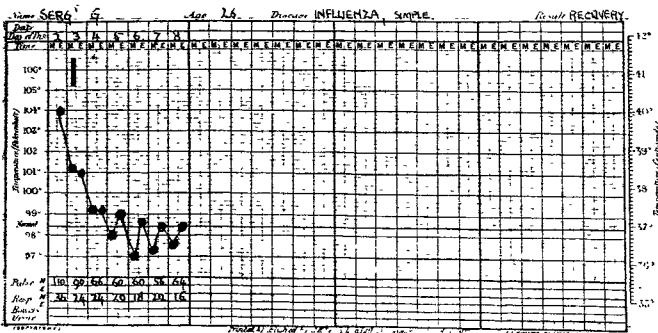
Apart from consolidation, the formation of fluid in the chest has been infrequent, remarkably so for cases in this Command, in which empyema is so common as to be almost the rule in all pneumococcal and streptococcal infections of the lungs. The coexistence of pleural effusions will be dealt with in the consideration of prognosis, suffice it to say here that its relative infrequency seems to indicate a high degree of virulence of the infecting organism and the incapacity of the tissues to react thereto. Towards the termination of the epidemic effusions became far more frequent in the pneumonic type of case with a high percentage of recoveries.

The sputum.—The cases of fatal "purulent bronchitis" of former years were characterised by the expectoration of immense amounts of sputum—often from 10 to 15 ounces in the 24 hours, this sputum being in the main pure pus, with little froth, with some blood, bright red in some cases, rusty in others, in a minority of the patients. Precisely similar sputum, necessitating the emptying of full sputum pots twice or more in the 24 hours has occurred in one group of cases we have seen in the present epidemic—the earlier and very fatal cases amongst United States troops; but in every other group we have been much struck by the relative paucity and even the entire absence of sputum.

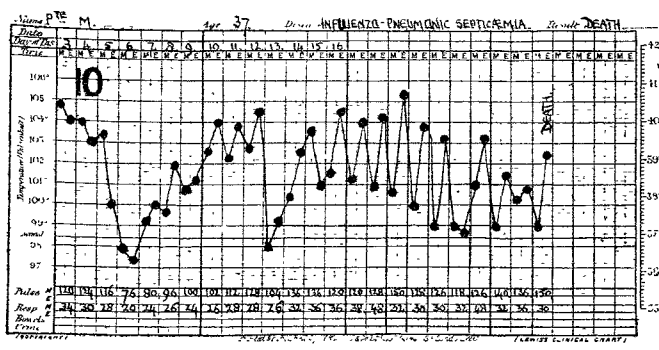
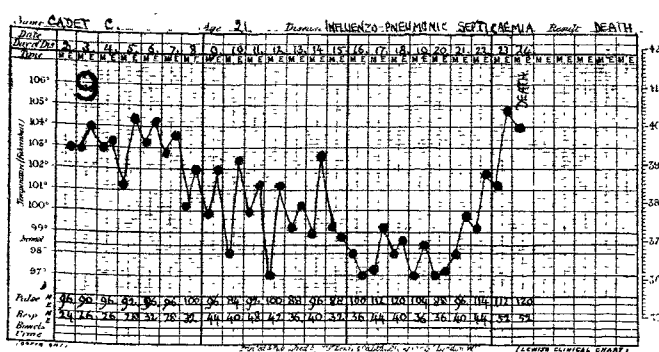
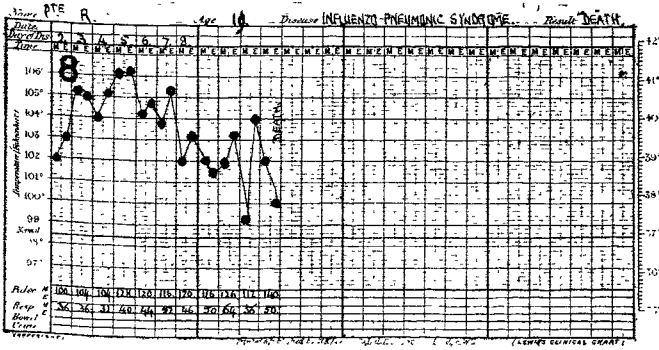
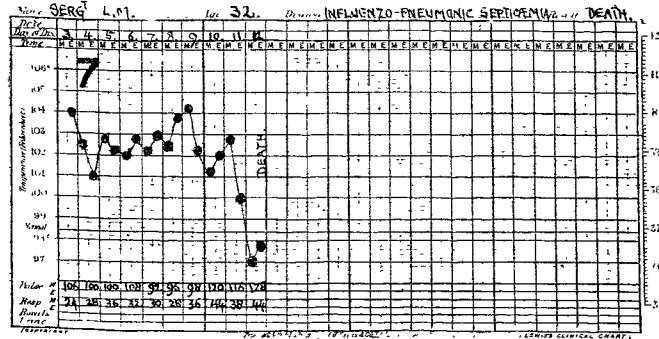
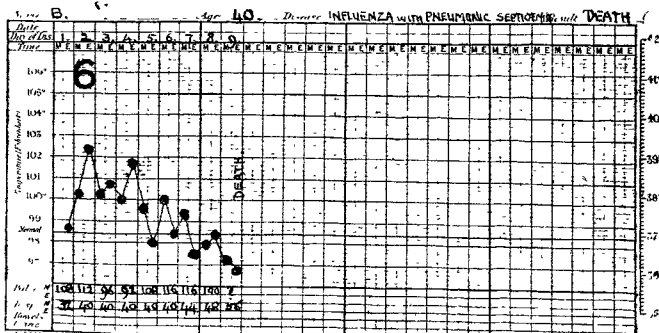
This paucity has not been confined to cases with any particular variety of predominant physical signs. Cases have been encountered with signs mainly of bronchitis with only a little frothy sputum; other cases with only bronchitic signs, and yet an expectoration of 15 ounces of pus a day; other cases in which the signs were those of extensive or confluent broncho-pneumonia with hardly any sputum; others, again, with physical signs of broncho-pneumonia of confluent type and lobar distribution with copious purulent expectoration equal to that which is familiar in "purulent bronchitis" cases.

There is no rule as to the amount of sputum, and those cases that have little sputum are, in other respects, especially as regards prognosis, very similar to those that produce half a pint in 24 hours. What has struck us a good deal in this connexion is that the cases that occur in any particular district tend to conform to one type in regard to the amount

Charts of 5 Cases of Recovery.



Charts of 5 Fatal Cases.



The temperature charts in the cases of influenza and influenzal "pneumonia" have been so extremely variable in type that a hundred or more would have to be reproduced if every species were to be depicted. The above serve to represent certain of the commoner types, however. The five on the left-hand side are from cases that recovered; the five on the right-hand side from cases that died. The authors think that the charts and their variability speak for themselves, so they have not commented on them in detail.

of sputum. Probably this is not a universal rule, but it has been a striking phenomenon in the present epidemic in which we have seen large collections of cases in widely-separated districts.

The sputum, when it is abundant, has generally consisted mainly of pus with or without blood; it is then not strikingly frothy. When it is not abundant it still contains pus, but it is often frothy and mucoid in addition. In neither case has it any strikingly offensive smell.

It is often free from blood, but occasionally it has a definitely rusty colour, simulating that of croupous pneumonia to some extent; though even when it is definitely rusty it is seldom of the glairy tenacious consistence that is so characteristic of true pneumonic sputum.

Hæmoptysis.—Apart from more or less altered blood in the sputum itself, actual hæmoptysis has been a very common phenomenon.

In the slighter cases with this condition the sputum pot exhibits frothy mucopurulent material in which occur streaks and splashes of bright red blood in varying quantity. This blood is spat up as a rule independently of the actual sputum, even if synchronously with it. In quite a considerable number of cases this hæmoptysis has attained a degree comparable to that of phthisis. The bed-clothes, wall, and floor have become blood-spattered during a coughing paroxysm, and as much as 10 ounces of bright red blood may be coughed up in a few minutes.

The conclusion has sometimes arisen that an old phthisical cavity must have become lit into activity by the new acute pulmonary infection, but post-mortem examination in such cases has not confirmed this suspicion, and there is little doubt that the hæmoptysis is due in many cases to the opening of small pulmonary arterioles by the acute infective process, in others it may be due to the infarcts in the lungs which are seen frequently at autopsy.

In cases of only slight hæmoptysis streaks and wisps of blood may come from the intensely engorged mucosa of the lower trachea and main bronchi, and in these the prognosis is not absolutely bad; when considerable hæmoptysis occurs it seems probable that it is due to localised lung destruction, with the opening of arterioles before they have time to thrombose, and the prognosis is grave.

We have only once seen a hæmoptysis so abundant immediately before death that the hæmorrhage itself could be regarded as actually the cause of death. On the other hand, we have seen cases with acute and considerable hæmoptysis recover, so that though a very grave sign it is not a hopeless one; when the hæmoptysis has been only in the form of wisps and streaks we do not think the prognosis any worse than it is in the cases generally.

A final reference as to hæmoptysis must be made to a few cases in which, after recovery has occurred and the patient has been apyrexial for several days, he has begun to expectorate quantities of comparatively fresh blood although no alteration in the symptoms occurs. In all these cases—we have seen perhaps eight in all—nothing untoward has developed.

Hæmorrhages.—Hæmoptysis has been common, as just described, but *epistaxis* has been far commoner.

This symptom is not confined to the "pneumonic" cases, but has been met with in a high percentage of the uncomplicated cases. We do not think that the occurrence of epistaxis indicates any special liability of the influenza to develop into the dreaded "pneumonic" or virulent type. In quite a number of cases the epistaxis has been really severe and difficult to control; more often, however, it has been merely a temporary nuisance liable to recur several times but invariably ceasing without treatment.

The blood from the nose has generally been bright red, such as would come from a small arteriole if it were ulcerated; and the prevalence of this epistaxis acquires additional significance when one realises how often the sphenoidal and ethmoidal sinuses contain pus at autopsy (see *Morbid Anatomy*, below), this pus being found to be teeming with pneumococci, sometimes associated with Pfeiffer's bacillus. The epistaxis occurs early; its character suggests erosion by an inflammatory process and encourages the suspicion that the pneumococci gain access not primarily from the lungs, but from the nose, naso-pharynx, and accessory nasal sinuses, and we would consequently advocate the wisdom of using simple antiseptic gargling and nasal douching as a therapeutic measure in all influenza cases in the first stages, and also emphatically as a prophylactic precaution in healthy individuals exposed to the infection.

Hæmatemesis has not been common, but we have met with it in approximately a dozen cases.

In some of these there has been the possibility of epistaxis occurring during sleep, the blood from the nose having passed down into the stomach until enough has accumulated there to make the patient vomit and bring up an alarming amount of blood not really derived from the stomach at all. In a few cases, on the other hand, the vomiting of swallowed blood could be excluded, and true hæmatemesis must have occurred.

In one such case, for instance, the patient was awake all the time; he vomited at 2 P.M., bringing up only mucus and partly digested milk; at 4 P.M., without any nose bleed or hæmoptysis in the interval or afterwards, he vomited again and brought up over a pint of pure blood, darker than fresh arterial. He had no particular abdominal pain, but in this case, and in several others, we felt sure that there was some bleeding breach of surface in the gastric mucosa, possibly of hæmorrhagic erosion type. Such hæmatemesis is not confined to the fatal cases.

Melæna has also been observed: but whether this has resulted from swallowed blood in every case we cannot say. We have, however, met with many cases in which a quantity of bright blood has been passed per rectum; this has particularly occurred shortly before death.

Hæmaturia has attracted notice very seldom. In a small number of cases the urine has been blood tinged or even red or blackish; but in all of these that we have seen the hæmaturia has been part of a definite acute nephritis; the latter has been very common, and blood cells may be found in the urine microscopically in a high percentage of the "pneumonic" cases. Hæmaturia apart from nephritis we have not met with.

Purpura or other form of hæmorrhage into the skin has been very uncommon indeed. In a malady associated with such severe toxæmia

we should have expected purpura to be common. We have met with no case of generalised purpura. One case had extensive purpura of the extremities; another exhibited severe purpura of the legs between knee and ankle, associated with a hæmorrhagic bullous eruption of the same parts. Both recovered.

Several cases have occurred of acute sudden painful œdema of one or both feet associated with diffuse dull red deep-seated purpuric tender spots beneath the skin of the dorsum of the swollen foot, similar to those described by Osler in cases of infective endocarditis; possibly both the swelling, the pain, and the tender purpuric spots on the feet in such patients are the result of local changes in the smaller vessels of the parts—thrombotic or embolic.

Hæmorrhage from the ears has been seen by us in one case only; the blood-staining of the pillow that resulted was extensive, but the total blood lost was not great. It was the result, we think, not of any special hæmorrhagic tendency, but of blood-discharge from very acute bilateral otitis media.

Other forms of hæmorrhage have not attracted notice; we have seen approximately 50 of the "pneumonic" cases in the female sex (mainly in the Nursing Staff), but in none has there been any special tendency to undue uterine bleeding.

A further indication of the hæmorrhagic tendency is afforded by those cases which have developed a pleural effusion. In the majority of these cases the prognosis is relatively good, the fluid has been sterile and the preponderating cell has been the lymphocyte. In a few cases the fluid, which has still been markedly hæmorrhagic, has contained pneumococci. In three cases a sterile hæmorrhagic fluid in considerable amount was obtained from one side of the chest and thick streptococcal pus from the other.

The colour of the patient: heliotrope cyanosis.—Of all the features of the "pneumonic" cases we would lay most stress on the colour of the patient. He may not have much colour at all, he may be flushed, he may be sunburnt, or he may be plethoric; but whatever the degree of his facial colour we have always been thankful when this colour has remained *red*. It may be a sallow face with redness of the lips and ears only, or the patient may be of a rubicund type with general redness of his whole face, or he may be flushed with the unnatural redness of fever; but so long as his lip and ear colour, whatever its degree, is *red* there is ample room for hope of recovery, no matter what the lung signs, the temperature, the pulse rate, or the respiration rate.

When, on the other hand, to reproduce the colour of the patient's facies, especially the lips and ears, one would need to mix some heliotrope, or lavender, or mauvy-blue with red paint to produce the right tint, the prospect is grave indeed, even if at the moment the patient seems comfortable, has no signs of consolidation in either lung, is sleeping fairly well and taking nourishment, has no more than an ordinary degree of pyrexia, a good pulse rate, not unduly fast, and a respiration rate that may not strike one as being unusual in the circumstances.

This colour may be confined to the lips and ears, or it may affect the rest of the face as well; in either case it is the surest basis on which to pick out those cases in a ward that are likely to be dead in a day or two from those who, unless they themselves develop the same hue later on, will most probably recover. It is not impossible for a "heliotrope cyanosis" patient to recover, but that he should do so has been the rare exception in this epidemic. The tint is precisely the same as that which struck us so much in the cases of fatal "purulent bronchitis" in 1916 and 1917; and it has been commented on by many other observers.

The actual colour of the patients differ greatly, because some have much, others little, blood in their superficial capillaries, and there is every intermediate degree; but common to them all is the mauve or heliotrope element that would have to be mixed with the red to reproduce the hue in a painting. We do not pretend that all the serious types are like the second of the coloured illustrations which we reproduce, but many of them are exactly like it, and we have taken an unmistakable case to illustrate with emphasis what we mean. We would also lay much stress upon the fact that the dreaded tint generally develops before the patient himself seems otherwise any more ill than those around him who are going to recover. Once the hue is there, however, treatment, as we have elaborated below, seems totally unavailing.

The change of colour may come on in a few hours. In the morning the man may be simply flushed but of good red colour, as in Plate I. By the evening or the next morning, not necessarily feeling much worse in himself and still quite cheerful and clear-headed though ill, he may have developed some degree of the colour of Plate II.; and then it is generally a matter only of hours, or at most a day or two before he becomes of ghastly appearance like Plate III.

At one time we thought the colour might be due to methæmoglobinæmia, but the spectroscopic shows no abnormal pigment in the blood in these cases, nor is there any defect in the oxygen-carrying capacity of the blood (see below); the condition is one apparently of what Professor Haldane terms "anoxæmia," precisely similar to what is seen in gassed cases at the Front and possibly due to analogous causes, to judge from the histological changes seen in the lungs.

The breathing.—One of the most striking features about the breathing in the "pneumonic" cases is the *absence of orthopnoea* even in patients who are breathing very rapidly.

Amongst female cases the desire to be propped up by pillows is not so uncommon, but in regard to men one can go round a hospital and see upwards of 500 cases in all stages of the disease, and it will be exceptional to find even one who is desirous of being so supported. The great majority lie at full length, and although it is probably good

practice to vary the patient's position, so that he is not too long continuously on his back, the patient himself prefers to lie flat.

This absence of orthopnoea applies as much to those with confluent consolidation as to those who have signs of bronchitis only. It is not due to the patients being too ill to care, for the mild, the medium, and the severe are alike in this respect. The probable explanation is that the pulse remains good until quite at the very end, and there is little dilatation or failure of the right ventricle. Failure of the right heart is the commonest cause of orthopnoea in cases of dyspnoea without obstruction to the bigger air-passages, and it is a striking feature of the hearts of these cases at autopsy that its dimensions, right and left sides alike, remain practically normal. In a word, the cyanosis is not cardiac.

The patients breathe with greater rapidity than normally, silently as a rule, except in the terminal phase, and each respiration is short and shallow. When left to themselves the patients may be breathing only 28 or 30 times a minute, but the slightest exertion, such as that entailed by rolling to one side or trying to undo the buttons of the shirt, increases this rapidity to 40, 50, or 60 per minute for the time being, any liability to cyanosis being markedly increased at the same time. There is clearly very little reserve power in the respiratory system, but very few patients complain of difficulty in breathing unless the respiratory movements are interfered with by the pain of acute pleurisy. It is not a *dys-pnoea*, but rather a *tachy-pnoea* or *poly-pnoea*.

Cough is troublesome in some cases, almost absent in others.

It is apt to recur in paroxysms, and these may be very exhausting in the cases in which there is little sputum. When the latter is abundant it comes up fairly easily so long as the patient has a reserve of strength; in bad cases a time comes when the effort of coughing is too much, and the patient, whose lungs are full of what would be better expelled, neither coughs nor expectorates at all.

We have found that a persistent cough is an indication for the examination of the chest (undue examination is, of course, to be deprecated in these "pneumonic" cases) for evidence of fluid.

The pulse.—The heart does not fail as a rule, unless quite as a terminal event.

It is remarkable how often, when the general appearance of a patient shows he has only minutes to live, the pulse may still be quite regular, of good volume, and not much faster, perhaps, than 120 per minute. Earlier, the pulse-rate is generally not faster than corresponds to the degree of pyrexia; and often it is less rapid than the ordinary temperature-pulse ratio would lead one to expect. There are, of course, cases in which irregularity develops, or the pulse races towards the end; but, broadly speaking, the condition of the heart remains satisfactory throughout and the patients do not die from cardiac failure.

It is noteworthy that in no single case did we meet with pericarditis either clinically or post mortem. This, we think, will not prove the case in records from other districts, and we are surprised at not having seen one case.

In one single case typical auricular flutter developed; this appeared to be a direct result of the influenza itself and not of the pneumonic complications, for it was already present when the latter supervened during convalescence from an ordinary influenzal attack. The man made no complaint about his heart though it was beating over 250 times a minute and the pulse waves were too small to feel, and he was doing well until he contracted pneumonic complications a few days after he had seemed to have recovered. He had in fact been apyrexial for two days and had got up in the ward. Digitalis in large doses had an excellent effect upon the pulse rate, which in just 96 hours from the institution of treatment fell to 90 beats to the minute.

Herpes facialis.—Herpes of the lips or chin or *alæ nasi* has occurred in a small number of cases, roughly speaking 5 per cent.

The eruption has seldom been extensive, though sometimes the vesicles themselves and the inflamed area on which they stood have become a hæmorrhagic scab. In one case only has this hæmorrhagic tendency been extreme. In this patient the wide area of the eruption, affecting both nostrils, the upper lip, the lower lip, both cheeks near the mouth-margin, the chin and the neck for some distance below the jaw, with the accompanying hæmorrhage into the area of the eruption, was like that of severe spirochaetosis ictero-hæmorrhagica. But it was not followed by a fatal result.

Herpes of the ears.—Sometimes with, but as often without, herpes of the lips and face, herpes of both pinnae has occurred.

The vesicles were generally disseminated over the outer aspects of the pinna either singly or in groups of two or three, and not as coalescing patches. The eruption here was not associated with any other special feature in the cases, but the soreness of the ears was a trouble to the patient.

The eyes and eyelids.—Quite early in the disease the upper eyelid tends to droop, as though the patient were half asleep. This is illustrated typically in Plate I.

In the purely influenzal cases, or in the "pneumonic" cases that are not severely affected, this drooping of the upper eyelids is inconstant, and the patient opens his eyes fully when his interest is aroused; but in the severer cases the droop persists even when the man is spoken to; it is more than a mere state of being "heavy-eyed" then, and it is an unfavourable sign. The eyelids are those of a man who is very toxic or half doped, and at the same time, in bad cases, the conjunctiva is dull and the eye looks dazed. The condition supports the view that the symptoms are due less to the condition of the lungs themselves than to the extremely toxic state of the blood and tissues generally.

Delirium.—Mild degrees of delirium, especially in the early hours of the morning, have occurred even in the purely influenzal cases. In those with "pneumonic" complications there have been remarkable variations in the

degree of delirium presented by patients at different periods of the epidemic and in different areas of the Aldershot Command.

At one time hardly a single "pneumonic" patient out of hundreds presented any delirium at all worth mentioning; then we meet with a series of cases in which delirium lasting day and night, with hallucinations and a tendency to be physically and vocally violent, was pronounced. This delirium seemed unrelated to previous alcoholism, and the cases in which it was most marked were not necessarily fatal. More common than violent delirium with hallucinations was the low muttering type, with the tendency to get shakily out of bed until nurse came and put the patient quietly back again.

Upon the whole, however, delirium of either mild or violent degree was less marked a feature even of the severe and fatal cases than one would have expected. On the contrary, it has been heart-rending to see heliotrope-cyanosed lusty great men breathing 50 to the minute, and obviously bound to die within a brief hour or two, still clear-headed, able to talk connectedly, not complaining and not obviously in physical distress, yet fully conscious of what is about to happen to them by reason of what they know has happened to their fellows from the same regiment a day or two before.

On the other hand, there is a type of termination in which a restless coma precedes death by many hours or even by a day or two. The patient lies low in bed with his head thrown back, moving his limbs or his whole trunk restlessly from time to time, with partly opened mouth, a ghastly yellow pallor of the hollow sunken cheeks, pallid lavender hue of lips and ears, rapid sighing respiration, incontinence of urine and of faeces, a heavy closed-up cellular sort of smell about the bed, but complete oblivion and total absence of any suffering.

Subsultus tendinum.—Apart from delirium, a high percentage of the more serious cases, whether fatal or not, has exhibited the following condition.

This is not so much the "picking at the bedclothes" tendency as marked involuntary jerkings and twitchings, now of one leg, now of the head and neck, now of a wrist or fingers, now of a whole arm, now of one side of the abdomen or of the back—an extreme degree of subsultus tendinum. So very twitchy and jerky have some cases been that an overdose of strychnine has been the first suspicion, but the condition has been common without strychnine or any other drug having been used at all. The symptom is further evidence that the patients suffer from generalised toxæmia of severe degree, the badly oxygenated state of the blood being perhaps an added factor in the subsultus, the nervous system being starved of oxygen by reason of the anoxhæmia.

Otitis media.—Deafness of some degree has been a fairly common symptom, both in the purely influenza cases and in those with "pneumonic" complications.

Here and there a patient has become stone-deaf for the time being, even when no quinine, aspirin, or salicylate has been administered. It seems likely that the chief factor in the production of this deafness is microbial infection, perhaps pneumococcal, spreading from the nasal mucous membrane to the Eustachian tube. In further confirmation of this view is the fact that, though many of the cases have lost their deafness spontaneously after a few days or a week, some have had severe earache followed by otorrhœa. The radical mastoid operation has been required in two such cases already, and there may be others still to be similarly dealt with. In one case the bilateral ear discharge was so acute that it consisted of almost pure blood. Unfortunately we have not ourselves been able to investigate any such ear case bacteriologically.

Parotitis.—In about a dozen cases—one of the severe "pneumonic" type which ended fatally, the others of the simple influenzal type—unilateral or bilateral swelling of the parotid glands has developed when the patient was already in hospital for his influenzal attack.

The chief difficulty in these cases has been to decide whether they were examples of mumps developing during influenza or whether they were infective parotitis other than mumps arising as a complication of influenza, and this difficulty has been increased by the knowledge that an epidemic of mumps has been simultaneously present in the command. Orchitis did not occur, but even if it had done so the further difficulty of possible gonococcal orchitis would have presented itself—such orchitis is met with so often in men who fall ill with something else. None of the parotid glands involved in our cases ended in suppuration. On the whole the swelling, whatever the degree, was relatively painless, and ability to open the mouth fully was comparatively unimpaired.

Jaundice.—Jaundice has been quite uncommon in the cases in the Aldershot Command.

No case has presented more than a slightly icteric tinge of the conjunctiva. Through the courtesy of Captain Means, United States Medical Service, however, we have seen 15 cases of definite jaundice in "pneumonic" influenzal cases in United States troops; the condition of all these men was grave at the time. Full details of these and others will, we hope, be published by the United States authorities.

The smell of the patients.—Just as many typhoid fever patients have a peculiar smell which is difficult to describe, but which is none the less almost characteristic, so do many of the influenzal "pneumonic" cases exhibit a peculiar faint indefinite smell, best noticed, perhaps, when the bedclothes are first turned back for purposes of chest examination.

It is not the sour smell of perspiration, nor is it merely faecal from the coated tongue or the sordes that are apt to collect on lips and gums in spite of the most careful nursing. It could not be called pathognomonic, but it has seemed to us worth while to call attention to it. More than once it has been so pronounced that we have asked whether

the patient has had a small dose of paraldehyde or any such drug some time previously; but the smell seems to have no relation to any drug that has been given.

■ In several cases there has been quite a different smell—a real stench, not of the mouth or of the sputum, nor the result of incontinence, but of the patient's living body generally. It has no particular application to those who have died of the disease, for in no case at autopsy has the body presented any unusual odour, nor do the tissues decompose or become evil-smelling with any undue rapidity, at any rate at the temperature of the month of October.

Nephritis.—A high percentage of the "pneumonia" cases suffer from acute nephritis, but this fact would be missed if reliance were placed upon clinical evidence alone.

There is no œdema of the legs, back, or eyelids. The amount of urine passed daily is not lessened beyond what one would expect from the pyrexia. In a series of cases daily measurements of the urine passed varied between 45 and 70 ounces, with an average of 54 ounces.

It is very exceptional to find enough hæmaturia for it to be recognised by the naked eye. In the course of routine urine examination, however, albuminuria is found in some degree in nearly all the severer cases; and in quite a large number the amount of albumin present is from 1 to 5 parts per 1000, in association with renal epithelial cells, and fragmentary tube casts, generally epithelial and often ill-formed owing to the acuteness of the condition. Red blood corpuscles are seldom seen.

It is most important that absence of all œdema in this type of very acute nephritis should be realised to be the rule and not the exception, and we would urge that the routine examination of urines should be carried out with even greater zeal than usual during an epidemic of this sort lest patients should be discharged as cured when really they are still nephritic. It is from cases such as these that "Rose Bradford kidneys" arise later on—the small, white, granular kidney of "unknown" origin.

Large, red, blood-oozing kidneys of the type seen in acute scarlatinal uræmia have been almost constant at the autopsies of the fatal cases, and the occurrence of this acute nephritis is further evidence of the infecting agent, or at any rate its toxins, being widespread throughout the body, the "pneumonic" part of the disease being but a portion of the whole.

Localised abscesses.—The commonest form of localised abscess in these cases is empyema.

Acute pleurisy is the rule rather than the exception. In many cases this remains dry, but in many others it leads to the exudation of a small amount of fluid, thin but turbid, often blood-stained, not actual pus, though it contains numbers of polymorphonuclear leucocytes and organisms such as pneumococci. In fatal cases death generally occurs before there is time for this to change to true pus, and in cases that recover the fluid most often reabsorbs spontaneously, notwithstanding the presence of micro-organisms and pus cells in it. Here and there, however, we have found cases in which the fluid has gone on accumulating, and far from this proving a bad omen, the majority of such cases have ultimately done well.

We do not think it wise to resort to surgical treatment of the empyema with the same rapidity that one would adopt were the infection in the abdomen. It has seemed to us that when the infection thus shows a strong attempt at localising itself to a definite pus-focus the virulence of the general toxæmia or septicæmia has lessened, as though from the formation of a "fixation-abscess" (*vide infra*). We have come to regard it as a source for congratulation when one of these patients, very gravely ill, develops a definite empyema; our view upon the prognosis improves at once, and we have formed the impression that, unless there are strong individual reasons to the contrary, it is wiser to wait a whole day, or even longer, before resecting a rib.

Another point that has impressed us in this connexion is that simple needling of the chest has been so often followed by improvement in the patient's general condition that we would advocate such needling being done with less hesitation than is generally the case.

Subcutaneous abscesses of pyæmic nature have been seen by us in two cases only.

Although recovery was slow both these cases, very gravely ill for a long time, ultimately recovered. Painful, slightly swollen red areas, generally of small size, developed now in one part, now in another—perhaps a dozen altogether in the course of four or five days. One or two of these broke down into pus, softened, and incision was necessary, the rest resolved by themselves without forming abscesses. Very grave though the outlook had appeared at one time in both these cases, we are inclined to think the subcutaneous formation of abscesses helped these patients to recover in some obscure way. These cases may be analogous to that of the "fixation abscess" produced in the manner described below, and suggest a deflection of the toxins to one focus, converting a septicæmia into a comparatively benign focus of infection.

Hemiplegia.—This occurred in one case only, and it was preceded by auricular flutter for some days. We thought the hemiplegia most likely due to a cerebral embolus from an intra-auricular clot rather than to a cerebral hæmorrhage or to local thrombosis.

Phlebitis of one or other leg, with typical painful swelling of the whole limb, was met with in half a dozen cases.

In one or two the leg condition developed whilst the general disease was at its height; in the others it was a phenomenon of early convalescence. In none of the cases did the vein-clotting lead to any suppurative locally, and the patients recovered gradually without further complications.

Skin rashes.—We have referred above to one case of purpura of the legs associated with hæmorrhagic bullæ between knees and ankles, and to a number of cases exhibiting curious painful purple spots over the dorsum of the foot

accompanied by general œdema of one or both feet. We have also referred to the absence of any generalised purpura in our series of cases, though so many of them were so extremely toxic or septic, and we have discussed herpes of the lips and ears.

Other skin eruptions were infrequent.

In a small number there has been acute inflammatory reddening of the skin around the nose and nostrils, spreading for a variable distance over the face, and presenting the characters of facial erysipelas; these cases did not do badly.

In several there has been a widespread erythema of limbs, trunk, neck and face, resembling the rash of scarlatina at first sight, but exhibiting no characteristic puncta and differing from scarlatina in that neck and face, as well as the trunk and limbs, might be involved by the rash. This erythema could not be attributed to any drug, such as aspirin, belladonna, or salicylate in some of the cases at any rate, and it was not the result of serum injections, though serum rashes did occur in some of the cases treated with antitoxic serum.

In one case there was a generalised morbilliform rash without the coryza or other phenomena of measles.

Meningitis.—Notwithstanding the extreme severity of the general infection and the recovery of pneumococci or streptococci from the blood and viscera post mortem and even during life, meningitis has not been met with as a phenomenon of influenza-pneumonic cases.

Several patients suffering from acute meningitis have been admitted as cases of influenza, but these have all been found to be meningococcal. A certain number of cerebro-spinal fever patients come in all the year round, but the number has, on the whole, been appreciably smaller during this influenzal epidemic than it has been in general. It would not be surprising if here and there amongst the thousands an instance of simultaneous influenza and cerebro-spinal fever should occur, and we believe that this has happened, but we do not regard the meningococcal meningitis we have thus seen as essentially related to the influenza. The existence of a widespread epidemic of severe influenza, however, does make the early recognition of cerebro-spinal fever more difficult than ever.

In no case of "pneumonic" influenza seen by us post mortem has there been any obvious meningitis.

Finally, a fairly extensive investigation of severe cases of influenza with special reference to the cerebro-spinal fluid, yielded in all cases an absence of any evidence of increasing intracranial pressure; the fluid was always clear and contained no excess of albumin, very few cells, and was always sterile.

Ruptured rectus abdominis muscles.—In upwards of 20 cases we have seen spontaneous rupture of one or both rectus abdominis muscles, generally in that portion of the muscle which lies below the level of the umbilicus.

The effort of coughing is apparently the immediate cause of this rupture, but the muscle has become diseased before it breaks. Sometimes one finds the rectus extensively affected post mortem without actual rupture having occurred. In most instances, even when there has been no rupture, the affected portion of the muscle presents the same sort of appearance as does the breast of a pheasant when one skins the bird after it has been badly shot at close quarters; the muscle is dark crimson, of bruised appearance, full of diffusely extravasated dark blood, friable, readily torn by the fingers, and it may be squeezed into a pulpy mass without much force.

Why this muscle in particular should be affected in this way we do not know, unless it is the result of vessels in it giving way in consequence of violent coughing efforts. Doubtless the lesion is related to Zenker's degeneration of the muscle such as occurs in other infective maladies, enterica for example; but in ordinary Zenker's degeneration the muscle is pallid and not hæmorrhagic, whereas in the present cases the lesion has gone on to a local hæmorrhagic pulpy state even if the muscle has not been actually ruptured during life. Both rectus abdominis muscles are apt to be affected at the same time in cases in which either is affected at all; that is to say, bilateral rupture has been as common as unilateral.

Subcutaneous emphysema of the chest wall.—In about 15 cases altogether palpation has elicited the striking phenomenon of widespread subcutaneous crackling of the deep tissues of the chest and neck and back, the result of subcutaneous emphysema.

This has always started on one or other side of the thorax itself, generally in front or towards the axilla rather than behind, spreading rapidly over a variable extent of the whole thorax and even to the neck, where it may form a complete collar of crackling swelling. It is an event of very grave import, though one case at least recovered after its development.

It is generally difficult to demonstrate post mortem how the air reaches the subcutaneous tissues. One explanation is to assume its origin from the lung root via the mediastinum; but in some cases at least it results from a small acutely necrotic focus in one lung ulcerating directly through both layers of pleura into the extra-pleural tissues. Minute or small superficial abscesses in the lungs are met with in quite a number of cases; these are surrounded by sticky pleuritic exudate sufficient to prevent the development of pneumothorax when the visceral pleura is ulcerated through at a pin-hole point. The parietal pleura becomes infected by direct extension, and it only needs a pin-hole perforation in it, too, to cause the subcutaneous emphysema of the chest wall which has been so striking in certain cases in this epidemic.

That acute ulcerative or focal necrotic changes in the lung tissue are in this way the cause of the emphysema is further suggested by the way the onset of the subcutaneous crackling has not infrequently been simultaneous with acute hæmoptysis, as though the focal lung necrosis opened up an arteriole at the same time. Nearly all these patients die.

MORBID ANATOMY.

The Lungs.

Although we believe that the infection is widespread and not confined to the lungs, the patients exhibit a preponderance of chest phenomena, so that naturally the lungs attract first attention at autopsy. We would emphasise, however, the bacteriological findings in the heart blood and spleen, and the prevalence of acute nephritis, as indicating that the lung lesions are very far from being the whole basis of the so-called "pneumonic" cases. We think that the fatal disease is an influenzo-pneumococcal or influen-zo-streptococcal septicæmia with more or less marked local lesions in the lungs, but we do not think it is in the main a lung disease any more than we would regard enterica as essentially a bowel malady, notwithstanding the ulcers in the ileum being the chief lesions found post mortem in typhoid fever cases.

In the next place, although the physical signs during life may often be precisely those with which one is familiar in lobar pneumonia, it is absolutely exceptional to find the straightforward typical hepatisation—red or grey—of true croupous pneumonia.

Only in one single case have we found what appeared to be true red hepatisation—and this was in two-thirds of one lobe only, the rest of the lungs presenting broncho-pneumonia, hæmorrhage, and bronchiolitis of the type described below. In one other case a small portion of one lobe looked like grey hepatisation in contrast to the multiple and diverse lesions elsewhere in the same lung.

True lobar pneumonia is not what is found post mortem in the vast majority of the cases. Whole lobes may be consolidated and in an anatomical sense the lesion is "lobar"; but the term "lobar pneumonia" has come by common consent to be a particular and well-defined variety of lobar consolidation, and one does not use the term "lobar pneumonia" of every form of lung consolidation that happens to have a lobar distribution.

In the next place, though some variety or degree of consolidation has been the rule throughout the serious cases in the present epidemic, we would lay much stress upon the fact that here and there an autopsy reveals practically no lung consolidation at all.

The lower lobes may be dark-red, almost black-red, heavy, œdematous, congested, the upper lobes pale and distended; but no part of any lobe actually sinks in water, or, at any rate, only tiny portions, carefully searched for, found with difficulty, and cut out with fine scissors. These cases without consolidation have run almost identically the same clinical course as those with much, and it is one of the striking features of the disease that the extent of the lung consolidation is no measure whatever of the severity of the infection.

This is precisely what struck us when we wrote in 1917 about "purulent bronchitis." Fatal cases of the latter exhibited varying degrees of broncho-pneumonia associated with bronchitis or bronchiolitis or without any broncho-pneumonia at all. And we believe that the "purulent bronchitis" then described was only one type of a condition which has recently shown itself to be remarkably protean.

The next point to emphasise is the absence of thick abundant bronchiolar pus in our own cases at the present time.

In the "purulent bronchitis" cases one of the most marked phenomena post mortem was the way in which thick yellow pus welled in smaller or larger spots and dots from all the bronchioles when the lung was cut. This peculiarity has been strikingly absent in the great majority of the recent Aldershot influenza cases, only small quantities of pus being expressible from the tubes, as a rule. And yet in precisely similar "influenzo-pneumonia" cases seen in another command during the same epidemic the amount of pus expressed from the bronchioles was similar in amount to that of the "purulent bronchitis" cases. There is nothing constant about the lung lesions, and what may be true of a group of cases in one place may not hold good for another group of cases elsewhere, although the disease in general is clearly the same in both.

We will now try to indicate the kind of lesions met with, as a rule. It is not easy to depict these because they are so variable in the degrees and extent to which the following various conditions may be mingled together, namely:—

Broncho-pneumonia.	Multiple small areas of collapse.	Pleurisy.
œdema.	Massive collapse.	Compression (by fluid).
Extreme congestion.	Formation of abscesses.	Interstitial emphysema.
Diffuse hæmorrhage, not solid.	generally small, but often multiple and aggregated.	Bronchitis and peri-bronchitis.*
Solid hæmorrhage.		Gangrene.
Infarction.		

* Difficult to demonstrate macroscopically, but shown to be extensive microscopically.

One case may exhibit extreme congestion and œdema, with disseminated non-confluent broncho pneumonia, subpleural hæmorrhages, and angry-looking purulent pleuritic lymph.

The next may have complete consolidation of both lower lobes by confluent broncho-pneumonia without any pleurisy at all.

The next may have not lobar consolidation but irregular masses which are more easily felt than seen, of deep crimson consolidation due to combined broncho-pneumonia, collapse, and hæmorrhage, scattered widely through all the lobes of both lungs, with or without acute pleurisy.

The next may have one entire lung apparently healthy, the upper lobe of the other pale and over-distended, and the remaining lower lobe

heavy, nearly but often not totally airless, of a consistence to suggest spleen rather than liver, and of a dull, deep-slate colour externally, still further suggesting a post-mortem spleen.

The next may have broncho-pneumonia, more or less extensive in the lower lobes with firmer wedge-shaped areas amongst the latter strongly suggestive of infarcts; whilst the upper lobes, free from broncho-pneumonia, may present from one to half-a-dozen or more typical infarcts, generally not large, of deep red colour, contrasting with the paler hue of the rest of the upper lobes.

In another case these infarcts may not be uniformly deep red, but pale, with crimson margins, due to the breaking down of the central parts into one or more incipient small abscesses.

Again, there may be no definite infarct, and yet over a more or less circumscribed region of one lobe, and often just below the pleura, as if they were originally in an infarct, one may see 20 or 30 pale yellow, slightly prominent areas, each of which turns out to be an incipient abscess or even a definite necrotic focus from which the contents can be washed out with a medium stream of water or readily expressed with the finger. It is from such superficial abscesses as these that perforation of both layers of pleura and consequent subcutaneous emphysema may arise; and if this is the sequence of events it is easy to understand why the development of subcutaneous emphysema generally prognosticates a fatal termination.

What the pathology of the infarcts is we cannot say with certainty.

Very possibly they are thrombotic and not embolic, in which case they point to severe changes in the vessel walls and perhaps in the blood itself. On the other hand, when one considers the frequency of purulent infection of the sphenoidal air cells (see below) one feels that thrombosis of venules in the neighbourhood of the base of the skull, where they are difficult to demonstrate either clinically or post mortem, is not an improbable event, leading perhaps to small but virulent septic emboli of the lungs with infarction and the formation of abscesses in the infarcts.

Perhaps both thrombotic and embolic infarcts occur; in either case their occurrence, not by any means in all cases but none the less in many, is a reminder that the vascular route of lung infection must not be forgotten. It seems highly probable that much of the lung mischief is due to direct invasion through the respiratory passages—from main bronchus to bronchioles and from the latter to the alveoli, bronchitis preceding broncho-pneumonia. But another route may be via the blood stream, thus accounting for the great severity of the infection and its high mortality.

Apart from actual infarcts, hæmorrhage into the deep lung tissue has been very common. Sometimes it is diffuse and difficult to demonstrate, owing to the already very deep crimson colour of the congested lung; but even then one can see it in the form of very dark, almost black, patches or ill-defined diffuse network, or a bigger localised mass which can be felt and which sinks in water.

The lower lobes have been affected very much more than the upper, though apical consolidation with confluent broncho-pneumonia is met with in a few instances.

With few exceptions the colour of the lower lobes has been deep crimson from extreme congestion, and very marked œdema of the lower lobes has been the rule, frothy blood-stained serous fluid pouring from the cut lungs when they are gently squeezed. This œdema is responsible for much of the increased weight of the lower lobes, and it occurs equally whether there is much broncho-pneumonia or little.

Although we have met with many cases with multiple small areas of necrosis or abscess formation, and many in which the lungs were pulped with ease by the hand, much in the same way as a decomposing spleen may be squeezed to pulp, we have met with no case so far of actual gangrene of the lung, and there has been no other suggesting incipient gangrene. Perhaps this is due to the rapidity with which the disease progresses, so that patients have died before there has been time for true gangrene to develop.

We have met with no case of pneumothorax.

Pleurisy has been very variable in its incidence.

Quite a number of consecutive cases have exhibited acute pleurisy of the "lack-lustre" type with little or no fibrinous exudate and no free fluid, the acute pleurisy affecting one or both lower lobes, and much less often an upper lobe. Another group of cases have demonstrated no naked-eye evidence of pleurisy, although the intra-pulmonary lesions may be various and abundant. It has been exceptional to find much free fluid in the pleural cavity; one or two ounces of turbid blood-tinged fluid are present in a fair number of cases, but a large effusion has been exceptional post mortem. This is partly due to the recognition of fluid in the chest during life and its removal by aspiration, for fairly large pleuritic effusions have not been particularly uncommon in the wards. It is also partly due to the recovery of the whole of those cases in which the focalising effect of a copious effusion has been the patient's salvation.

The thin turbid fluid is clearly of the nature of an empyema, but it is not actual pus; it may become pus and need operation clinically, but we have not seen more than one or two cases of actual empyema in this disease post mortem. We think the empyema cases tend to do well for the reason stated above.

Interstitial emphysema in the form of a fine melon-rind network beneath the pleura has occurred in several cases; the condition is doubtless the result of inflamed alveolar walls giving way under the stress of coughing efforts.

Acute bronchiolitis is nearly always present.

The histological changes in the lung tissues must be postponed for a subsequent communication. We would only say here that in many sections there is an appearance in and around the bronchioles and inside the alveoli which at first makes one think that the paraffin has been imperfectly removed from the tissue. We thought at first that this was actually the cause of the appearance seen, but on further testing it seems that the appearance is due to a homogeneous structureless non-cellular exudate which fills the bronchioles and the peri-bronchiolar tissues and forms as it were a plastering round the inside of the alveoli. It is not fibrinous like the exudate of croupous pneumonia. Presumably it is an albuminous exudate, coagulated in the process of fixation, and it is very similar to that which can be seen in fatal cases of poisoning by chlorine gas.

This albuminous exudate throws much light on the nature of the dreaded cyanosis. If the oxygen in the alveoli has to traverse this albuminous layer in addition to the alveolar wall before it can get to the hæmoglobin of the blood, it is evident why there is such marked anoxæmia.

Other Post-mortem Findings.

The larynx, trachea, and bronchi.—Starting at a variable distance down the trachea, often near the top of it and sometimes in the larynx itself, there is reddening and congestion of the mucosa, the depth of crimson increasing rapidly as one passes down the trachea, until in the main bronchi the dark-red colour is extreme.

That there is tracheitis and bronchitis in addition to whatever changes there may be in the lungs suggests strongly that, even if a blood infection does occur as well in the way we suggest, invasion of the respiratory tissues by extension from above downwards is pretty constant. In addition to deep crimson congestion there is often a granular appearance of the surface of the mucosa of the lower part of the trachea and of the main bronchi, suggestive of a small amount of exudate upon the surface. This may even reach the stage of giving the appearance of a very fixed milky film over a crimson base, but we have not seen the definite membranous exudate described by others.

When viewed in an oblique light the inflamed mucosa often exhibits multiple minute depressions, very shallow but well defined. These look like extremely small surface ulcers not penetrating the whole thickness of the epithelial covering, but they may, on the other hand, be merely normal unevennesses exaggerated by the congested swollen state. As yet we have not settled this point histologically.

The bronchial glands.—The lymphatic glands below the bifurcation of the trachea have been found enlarged and crimson from injection in practically every case, and as a rule they have been not merely large but very large.

In one case only had actual suppuration occurred in a big gland below the right bronchus; in this instance it contained fully 2 drachms of pus. It had not burst to produce mediastinal suppuration, though it seemed clear that this must have been the result if the patient had survived a day or two longer.

The glandular infection is not confined to those about the main bronchi; the glands in the root of each lung, in the superior and posterior mediastina, and the deep glands up the neck even as high as the cricoid cartilage also are often enlarged and deeply crimson from inflammatory congestion. We have not noticed similar involvement of glands elsewhere—for example, in the abdomen.

The thyroid gland.—Considerable enlargement of the thyroid gland has been the rule.

In one or two cases the swelling has not been less than that seen in an average case of Graves's disease, and the isthmus was enlarged in the same proportion as the lateral lobes. Presumably this enlargement of the thyroid is the result of the general toxæmia, corresponding in this respect to its enlargement in some other forms of toxic trouble; at any rate, it has been quite pronounced and almost constant in our cases.

The heart.—The most remarkable feature about the heart is the general absence of dilatation.

In quite a large proportion of cases there has been no trace of dilatation; in a fair number of others there has been some dilatation of the right side, but this has seldom been extreme, perhaps enough to cause the apex of the heart to be formed about equally by right and left ventricles. Most often the heart has appeared of normal dimensions and the apex has been formed entirely by the left ventricle. This absence of dilatation accounts for the clinical absence of orthopnoea.

Whether or no pericarditis ever occurs, we have not met with one case of it yet; and the same applies to endocarditis.

We have also been struck by the absence of subpericardial petechiæ, such as are generally met with in very toxic conditions.

The spleen.—In many cases no enlargement of the spleen has been evident; in many others it has been slightly enlarged—half as big again as normal, or, exceptionally, twice its normal size. It has never been pronouncedly big—never big enough, for example, to have been palpable below the rib margin.

In most cases the splenic substance has looked normal. In a few there have been multiple small areas of increased firmness and darkened colour, due apparently to quite small infarcts. In two cases there have been massive and unmistakable infarcts, one of which was already softening into an abscess. Whether these were embolic or thrombotic it is difficult to say, but in the absence of endocarditis their thrombotic nature seems the more likely.

In one or two cases there have been multiple ill-defined small areas paler than the rest just beneath the capsule, not firm like infarcts, not palpable at all, and yet on close inspection seeming to be very slightly swollen above the general contour of the organ. None of these have shown any tendency to break down, but there have been granules and tags of recent fibrin on their surface, so that they would appear to be foci of localised infection in the spleen with focal acute capsulitis over them.

The liver.—The liver has been in nearly all cases of a paler brownish-red colour than normal and moderately increased in bulk, but otherwise not obviously affected. The naked-eye changes are those common to any acute febrile illness of short duration. There has been no undue congestion, still less any nutmeg change.

The stomach, intestines, and vermiform appendix.—The alimentary canal has not exhibited any particular change.

We have had no case of pneumococcal or streptococcal peritonitis. The stomach and intestines have been relatively empty, for the patients have been too ill to take food. There has been no special tendency to over-distension of either the stomach or the bowels with gas.

The vermiform appendix has not shown any notable change. We mention this because there has been a tendency elsewhere, we have been told, for certain of these influenzo-pneumonic cases to develop acute appendicitis.

The kidneys.—These, in the fatal cases, have presented uniformly, the same, or approximately the same, appearances.

They are of slightly larger size than normal, the capsules peel readily, the stellate veins upon the surface are not markedly obvious, the colour is dull purplish red but not strikingly abnormal, but on cutting each kidney open in the ordinary way and leaving it to lie for a moment, the cut surface rapidly becomes obscured by dark red blood which wells slowly but steadily from every part of the organ, particularly from the glomerular region. On close inspection one can see the reddened swollen glomeruli fairly easily, and on pressing the organ the blood oozing becomes still more pronounced.

There is no evidence of cardiac passive congestion, the pyramids are not particularly more cyanosed than is the cortex, the whole condition is reminiscent of acute scarlatinal nephritis. After scarlet fever the large red kidneys are described as "blood-dripping"; in the present cases the kidneys are rather "blood-oozing" than "dripping," though if they are held up and gently pressed they drip blood slowly in fair amount.

Histologically there is confirmatory evidence of acute nephritic changes, particularly of the "acute glomerular" type. Details of this, as of other histological appearances in these cases, must be kept for another section; but that so many, if not all, of these fatal influenzo-pneumonia cases have acute nephritis even though they have no œdema is, it seems to us, a point of much importance.

The sphenoidal and other accessory nasal sinuses.—We have examined the sphenoidal and ethmoidal air cells in 20 consecutive cases.

In one only was there no naked-eye evidence of disease of one or other or both, particularly of the sphenoidal which lends itself most easily to clear examination. In most of the 19 there was definite pale bright-yellow pus in the sphenoidal air cells: in several this pus squirted out on to the chisel used for opening the bone. When there was not thick yellow pus there was turbid serous fluid with angry red congestion of the lining membrane and adjacent parts. Doubtless this is one factor in the severe headache from which some of the patients complain, when they are not too ill to complain at all.

We did not examine the frontal sinuses or the middle ear as a routine. We are much impressed, however, by the frequency with which the sphenoidal air sinuses are infected or full of pus, and we must add in passing that we think this serves to emphasise the importance of the uppermost air passages, especially the naso-pharynx, in connexion with the disease. It is very unlikely that the sphenoidal air cells became infected secondarily to the lungs. In some cases the total length of illness had been so short that, for so much purulent fluid to have been present in the sphenoidal air cells, infection in that region must have been present from the start. When the frequency and severity of epistaxis is remembered, as well as the tendency to otitis media already commented on, the importance of the naso-pharynx as a likely site from which the whole trouble starts can hardly be exaggerated. The practical issue of this surmise should be insistence on the simple antiseptic toilet of the nose and throat—by nasal douche and gargle—once a day or oftener both by healthy individuals exposed to the danger of infection, and by the influenzal cases themselves at the earliest possible moment before they are too ill to gargle or to douche.

The bacteriology of the sinus infection is dealt with lower down.

TREATMENT.

Treatment of influenzal cases naturally divides itself into two categories—that directed to the general run of simple uncomplicated cases, and that which has been tried for the virulent septicæmic group.

Uncomplicated Cases.

The first group is readily dismissed. Although a large number of different remedies have been recommended and vaunted as "specific" for the early treatment of influenza, consideration of their application with controls upon a very large scale has encouraged us to doubt whether the course of the disease is modified or abated in the slightest degree by any one of them. And in this connexion we would like to add our gradually increasing conviction that although common sense naturally dictates the greatest reasonable precaution possible even for the mildest case, yet the virulent type appears to originate *ab initio* and to develop in spite of early treatment. We have been struck so frequently by the change in character of the mild into the virulent type in spite of every care in the early stage that the conclusion appears to us irresistible that development of the virulent type was unavoidable.

FIG. 1.—This illustrates an early case in which the facial colour is frankly red, and the patient might not appear ill were it not for the drooping of the upper eye-lids, giving a half-closed appearance to the eyes.



FIG. 2.—This illustrates a pronounced degree of the "heliotrope cyanosis." The patient is not in physical distress, but the prognosis is almost hopeless.



FIG. 3.—This illustrates another type of the cyanosis, in which the colour of the lips and ears arrests attention in contrast to the relative pallor of the face. The patient may yet live for twelve hours or more.



As a routine procedure every case was given calomel gr. iv. and mag. sulph. ʒ ii. on the following morning. As "specific" remedies we employed ol. cinnamon, aspirin, quinine, and sod. salicylate, and our ultimate conclusion has been that although drugs at this stage are of value as symptomatic remedies no value attaches to their application either in cutting short the duration of a mild attack or in preventing its development into the more serious type.

Quinine merits a word of special reference, since its advantage as a prophylactic has been loudly acclaimed. Whilst it is impossible to declare that no defence whatever is produced by this drug, we can at least publish the experience of seeing eight cases in men who had for a month previous to their admission to hospital with influenza been taking 10 grains of quinine regularly every day for malaria.

Finally, we would add a warning that the attempt to belittle the condition and allow the patient to return to his ordinary duties after a short febrile period has been poor economy. In very many cases—we are speaking of the present epidemic, as distinguished from the cases in June, which took a much milder course—a recurrence has occurred on the third day after the patient has been allowed to rise; and we consider it highly necessary to insist on at least three afebrile days before the patient gets up at all, and then three clear days up and dressed with relative inactivity before he is permitted to return to his unit even for light duties.

Treatment of the Virulent Type of Case.

In the earlier cases reliance was placed upon (1) the employment of oxygen in the orthodox fashion; (2) the administration of cardiac stimulants; and (3) venesection.

It is convenient to consider *venesection* first. Notwithstanding the absence of right-sided cardiac dilatation, the blue appearance of the patient seemed analogous to that of a typical pneumonic case in which venesection was indicated, and suggested this form of treatment. In no case has venesection produced the slightest improvement, not merely in the patient's general condition, but even in the degree of cyanosis. Apart from other considerations, the act of venesection itself is unsatisfactory. The blood flows with great difficulty, and only with prolonged perseverance has it been possible to extract the quantity likely to be of any benefit; in fact, the absolute failure to ameliorate the condition induced the conclusion that mere venosity of the blood alone was not the cause of the colour, but that some change had taken place in the blood itself which prevented its taking up oxygen, as, for example, the formation of methæmoglobin or even of some other pigment which had destroyed its capacity for carrying oxygen. Such a conclusion has, however, been completely disproved by the absence of any characteristic bands in the spectrum, and also by our experiments upon the oxygen-carrying capacity of the blood, which showed in all cases a condition fully equal to the normal, and in a few cases, presumably owing to polycythæmia, actually surpassed normal controls. Similarly, the employment of oxygen in the routine fashion 10–15 minutes at a time failed to produce even temporary relief. Reference will be made later to the continuous administration of oxygen.

With the failure of venesection, *saline infusions* were next adopted as a routine procedure in all "blue" cases. Subcutaneous, or rather intramammary, introduction was found, with one curious exception (*vide infra*), to produce no improvement. On the principle that a more immediate effect might be produced by intravenous medication, this route was substituted for the subcutaneous method, but with no greater success. And, again, no more favourable report is possible in the case of the simultaneous processes of venesection and intravenous injections, which other observers have claimed to employ with satisfactory results.

With the failure of saline infusions, addition of various substances to the saline solution was instituted on more or less empirical lines. On the principle that "acidosis" was playing a part in the production of cyanosis sodium bicarbonate in various quantities was used, and later glucose in 1, 2, and even 4½ per cent. strengths of solution.

The specific treatment by Mulford's antipneumococcal serum, administered intravenously, was tried in a few cases only owing to the comparative difficulty of obtaining large quantities, but no results accrued to encourage its employment on a large scale.

And, indeed, however lamentable such an admission must be, we must place on record the conclusion that not one

single line of treatment can be credited with the capacity of saving one of the virulent cases. Certainly desperate cases recovered though few in number, and in not one of these cases was any special line of treatment adopted.

A striking instance was afforded by one particular case whose condition was so extremely grave as to appear hopeless, so much so that it was felt to be unfair to adopt any of the special methods of treatment which were on trial, for failure in this case could hardly be a reflection upon the adequacy of the treatment. And yet this case was one of the very few extreme cases which recovered.

Other Forms of Treatment.

It has been mentioned that one curious exception occurred in the treatment by subcutaneous saline injection. In this instance suppuration occurred at the site of inoculation with sloughing of the tissues and the formation of an abscess, in the pus of which were identified *Staphylococcus aureus* and a streptococcus morphologically resembling the organism recovered from the heart's blood in some of the fatal cases. The patient made a complete recovery, although a week previously his condition had appeared hopeless. On the principle of forming other "fixation abscesses" of this kind, intramammary saline infusions were then resumed in another series of cases, the idea being that injury to the tissues by distension with the fluid might lead to the same happy result as in the case referred to. Not a single case, however, responded in similar fashion, nor was any improvement otherwise obtained. In a more heroic attempt to encourage abscess formation, a live culture of streptococci obtained from the heart's blood of a fatal case were injected in a dozen cases, the dose administered being estimated at 15 millions. In not a single case did any suggestion of suppuration appear at the site of inoculation, and of the 12 cases upon whom this treatment was tried 8 died. It only remains to be added that the four who recovered were severe but not desperate cases, and it cannot be supposed that the culture contributed in any way to their recovery, as dozens of similar cases recovered without such treatment. Injections of turpentine were also employed, but without any advantage.

On the presumption that want of oxygen was the cause of the cyanosis and presumably of death, the continuous administration of oxygen by the Haldane apparatus, similar to that employed in "gassed" cases, was then undertaken. It must be added that only a certain percentage of cases are suitable for this treatment which, as recommended by Professor Haldane, must be practically continuous for many hours. The patient must be sufficiently intelligent and *compos mentis* to understand the persuasion that it is necessary for him to tolerate any slight discomfort for the sake of the ultimate gain, and the application is impossible in the case of patients with pulmonary secretions which soon foul the apparatus. We cannot state that any real advantage arose from this method of treatment. A few patients admitted a certain temporary gain in comfort at the end of several hours, although ultimately death ensued; the majority resented its application altogether.

The stimulant employed as a routine procedure was brandy, 4 oz. in 24 hours being administered. Strychnine was found to be unsuitable. It appeared to excite the patients unnecessarily and increased delirium; and whilst of no value to the sufferer was the cause of much annoyance and distress to other patients by the noise produced.

Sedatives were also employed, principally bromide, bromide and chloral, tinct. opii and morphine hypodermically, but the last named alone appeared to have any value in producing sleep or quietening delirium. Paraldehyde has been more recently tried, but at the time of writing no definite conclusion in its favour can be stated.

Emetics were administered in a few cases in which, from the chest signs, expulsion of purulent material might have been expected. Large doses of vinum ipecac. and vinum antimoniales proved useless; emesis was induced by apomorphine hypodermically, but no relief could be noted.

We may perhaps anticipate one criticism of our attempts to treat the virulent cases under consideration. It may be argued that the value or otherwise of no line of treatment can be estimated by its application to moribund or desperate cases. This, of course, is perfectly true, but, as we have found reason elsewhere to mention, it is impossible to estimate the severity or the probable development of severity of a case; and to apply any line of treatment indiscriminately to all cases on the principle that some might be

prevented from developing into the virulent type would be a useless method of estimating the value of the treatment, since the large majority of cases which spontaneously recover would have to be credited to the particular treatment under consideration. It cannot be argued that any time was lost once the suspicion arose that a desperate case was to be anticipated, and since it is obviously impossible to quote actual statistics under this head, we can only express a conviction that so far as our observation extended nothing prevents the development of the serious case from one apparently trivial, and nothing can claim to avert the course of its virulence once it has developed.

PROGNOSIS.

This leads us to say a few words on the question of prognosis. The great majority of cases of influenza, of course, recover. What particular percentage comes into this category it is not possible to decide, since the 3800 or so cases admitted to the Connaught Hospital during the recent epidemic afford no indication as to the total number of cases in the Command, and the difficulty of obtaining figures sufficiently reliable to be of value has been insuperable. The comparatively mild cases are treated in large numbers at their own units, only those who are clearly from the outset of comparative severity or those in whom pyrexia has persisted for 48 hours are sent into hospital. We would once again indulge in the consolatory reflection that we are convinced that no untoward results must be attributed to the deprivation of early hospital treatment in all cases; neglect of any case is of course to be condemned, but again we would add that the virulent case appears to be something *sui generis*.

As regards the prognosis of the admittedly serious case, we must confess to having found difficulties in the establishment of criteria, even after an experience of many hundred cases. Early in the epidemic we were persuaded that the cyanosed cases invariably succumbed. Later we were fortunately able to record that a certain, even if a small, number of these recovered; and yet the latter have been quite indistinguishable from the majority of the cyanosed cases who died. No criteria as to temperature, pulse-rate, or respiration-rate, and not even of general condition, can be absolutely determined. It is true that a rapid fall in temperature without any amelioration of symptoms was in a "blue" case almost always a precursor of death within 24 hours, and that the case with blue colour, when accompanied by a cold, clammy skin, might be considered to be beyond hope of recovery. And yet cases whom earlier in the epidemic we considered to be beyond redemption certainly recovered, encouraging the determination not to abandon hope entirely until the patient was unmistakably moribund.

An even more painful indication of one's prognostic deficiency was afforded by cases who, not only at their admission but even for several days of treatment in hospital appeared to run a comparatively trivial course and to give rise to no legitimate anxiety, suddenly took a turn for the worse, rapidly developed cyanosis, and died within a few hours of being only trivially ill.

PROPHYLAXIS.

A few final words may be added on the question of prophylaxis. We cannot refer to the greater question of dealing with the prevention of the epidemic or of limiting its spread once it has appeared, for these are matters for the consideration of sanitary officers, both relating to troops and the general public. The precautions taken in the hospital itself were the ordering of a gargle as a routine procedure twice daily for all in attendance upon the patients and for those patients who had exhibited the disease to a comparatively mild degree. The solutions utilised were either pot. permanganate 1:4000 or tinct. iodine 1 drachm to the pint. In addition all medical officers, nurses, and orderlies were instructed to use a gauze mask around the nose and mouth whenever they were in attendance upon patients.

It may be added that not a single case developed in five special wards of the hospital devoted to tuberculous and neurasthenic cases, although these patients were from force of circumstances being visited by medical officers who were in attendance elsewhere upon influenza patients, and that in the large venereal division of the hospital only two or three sporadic cases appeared—these had apparently entered the hospital with the disease—who were immediately segregated,

and no instance of infection of other patients occurred. In the Detention Barracks at Aldershot, in which every patient occupies a separate cell in which he takes his meals, only coming into contact with his fellow inmates when he parades in the open air, not a single case developed. Incidentally, to complete the story, it must be added that the medical officer who visits these barracks daily is attached to the Connaught Hospital, and in addition to other duties has been in charge of influenza patients.

PATHOLOGY.

This investigation was carried out with a view to establishing, if possible, the identity of the causal organism or organisms and their distribution in the body in cases of influenza. Furthermore, the work appeared profitable if it were only to establish or disprove the connexion between the present epidemic and what had previously been described under the term "purulent bronchitis."

The most striking feature of the results obtained is the frequency with which streptococci were isolated, while the *Bacillus influenzae* could not be demonstrated with equal constancy. These streptococci fell into two groups: (1) a long-chained streptococcus; (2) a small short-chained streptococcus exhibiting a preponderance of diplococcal forces. This latter organism appeared to have some claim to individuality and will be referred to as a "diplostreptococcus."

Before describing the organisms in detail the pathological and bacteriological findings will be considered.

Throat swabs.—The material was taken from the nasopharynx with a West swab and inoculated on to blood-agar.

	Mild cases.						Severe cases.				Total.
	1	2	3	4	5	6	7	8	9	10	
Pneumococcus ...	+	-	-	-	+	-	-	-	+	-	3
<i>M. catarrh</i> group	+	-	+	+	+	+	+	+	+	-	7
<i>Strept. longus</i> ...	-	+	+	-	-	+	+	+	+	+	7
Diplostreptococcus	+	+	-	+	+	+	+	+	-	+	7
<i>B. influenzae</i> ...	-	+	+	+	-	-	-	-	+	+	5

Profuse expectoration in these cases was uncommon, so that it was not possible to draw any conclusion from the small number of sputa examined.

Blood cultures.—Blood cultures were made in glucose broth in 10 cases shortly before death, but although several dilutions were tried only 1 case gave a positive result; the organism in this instance was the *Streptococcus longus*.

Urines.—Examinations gave the following results:—

Cases.	Albumin %	Deposit.	Culture.
1. Moribund ...	0.02	Granular and cellular casts.	No growth.
2. " ...	0.1	No casts. Transitional epithelial cells.	"
3. Severe ...	0.5	Transitional epithelial cells.	"
4. " ...	0.1	Cellular casts and leucocytes.	"
5. " ...	0.4	No casts. Transitional epithelial cells.	"

It is remarkable that although in some cases casts were abundant, red blood-cells were not identified in the urinary deposit. Examination of the kidneys from these cases furnished no evidence of old-standing renal disease.

Leucocyte counts.—The following are the total leucocytes per c.mm. and the differential counts (P., polymorphonuclears; L., lymphocytes; L.M., large monocytes; E., eosinophiles):—

Case.	Total.	P.	L.	L.M.	E.
1. Severe ...	6200	54%	39%	6%	1%
2. Moribund ...	5890	68%	26%	5%	1%
3. Slight cyanosis...	4650	44%	47%	7%	2%
4. Mild ...	4960	66%	30%	3%	1%
5. Moribund ...	4960	70%	26%	2%	2%
6. Bronchitis. Slight cyanosis.	6820	86%	11%	2%	1%

In the last case bronchitis with purulent expectoration was present, which may account for the higher polymorphonuclear value, as compared with the other cases.

Cerebro-spinal fluid.—In two severe cases the fluid was clear, pressure normal; albumin (1) 0.006 per cent., (2) 0.0009 per cent.; cells normal; organisms negative; culture, no growth. In the absence of signs of meningitis or meningism this examination was not pursued to any

length, and the above results are typical of the total number investigated.

Oxygen capacity of blood.—This was in control case and four severe cases as follows (oxygen per 100 c.cm. of blood):—

Control.	1	2	3	4
18.5 c.cm. ...	17.0 c.cm. ...	20.5 c.cm. ...	18.5 c.cm. ...	18.0 c.cm.
Hæmoglobin = 105 per cent.				

These results were obtained by using Haldane's potassium ferricyanide method. It was not possible in the circumstances to estimate the blood carbon dioxide or alkali reserve. The absorption bands of methæmoglobin were not detected in the samples of blood examined.

Apparently the cyanosis in these cases may be attributed to the inadequate functioning of the pulmonary epithelium.

Bacteriological findings in post-mortem material.—The following organisms were found:—

Material.	Number of cases.	Pneumococcus.	Diplo-streptococcus.	Strept. longus.	B. influenza.
Heart blood... ..	28	2	9	3	2
Spleen	28	1	2	3	0
Lungs	28	8	11	10	7
Sphenoidal sinus.	12	6	4	6	3
Ethmoidal sinus..	5	3	2	0	2

Description of the Organisms Isolated.

The characteristics of the organisms isolated are given below.

The long-chained streptococcus grew well on all ordinary media, and on agar formed discrete pin-point colonies. On blood agar hæmolysis occurred in all cases. No clot was formed in milk during three days' incubation, but acid was produced in lactose and glucose media.

The "diplostreptococcus" also grew well on all ordinary media. On agar the colonies were larger than those of the long-chained streptococcus and showed flattening of the surface and a spreading margin, which did not appear raised. Confluence of the colonies was seen in some cases. Hæmolysis occurs to a slight extent.

Ancillary action of the *Staphylococcus pyogenes aureus* was very marked, resulting in increased size of the diplostreptococcal colonies.

A turbidity was usually formed in broth during the first 24 hours of incubation, but within three days flocculi settled to the bottom of the tube, leaving the supernatant fluid clear. The organism is Gram-positive, but in a few instances some members of a chain have failed to retain the Gram stain. Involution forms appeared in old cultures. A capsule was not demonstrated by Muir's staining method.

The pleomorphism exhibited by this organism is a striking feature; in 24 hours' pure culture on agar many diplococcal forms appear, together with short chains of coccoid individuals. After repeated subculture the streptococcal forms preponderate. The formation of chains does not appear to occur more readily in broth or other fluid media than on agar.

This organism has been found in pleural exudates during life and showed diplococcal and streptococcal forms, while pure cultures obtained from these fluids again gave evidence of pleomorphism.

The action on carbohydrate media has been uniform: acid is produced in glucose and a dense clot is formed in milk; there is no action on lactose, mannite, saccharose, or inulin, nor has gas been formed in any of the media used. The organism is not bile soluble. Agglutination reactions with antipneumococcus sera Types I., II., and III. were negative.

Four cultures from heart blood and two from the lung were inoculated subcutaneously into mice, but in no instance did death occur, nor was a local suppurative lesion produced.

In one case following subcutaneous saline injection abscess formation occurred, and it is interesting to record that the organisms isolated were the "diplostreptococcus" and the *Staphylococcus pyogenes aureus*.

The "diplostreptococcus" appears to resemble the *Streptococcus brevis*, although the latter is not usually regarded as pathogenic to man. Perhaps it would be best to use the name *Streptococcus brevis* generically; the "diplostreptococcus" could then be regarded as a species if its consistency of action and conformity of type could be established. In some respects the diplostreptococcus resembles the *Streptococcus viridans*, but the characteristic greenish hue of the colonies was not observed.

Gruber and Schädel, and also Bernhardt and Meyer, have recently described a diplostreptococcus which occurred in the internal organs of cases examined post mortem. They regard this organism of decisive importance in the causation of acute pulmonary conditions and fatal complications of influenza.

Histology.

The histological findings in the lungs, kidneys, and liver are now briefly described.

The lungs.—In the majority of cases congestion and œdema were the most marked changes recognised in the post-mortem room, while a definite broncho-pneumonia was of less frequent occurrence.

In the former type of lung the alveoli contained a scanty fibrinous exudate with erythrocytes and polymorphonuclear leucocytes. The bronchial epithelium was thickened and proliferating, and leucocytic infiltration of the peribronchial tissue was present. Dilatation and

engorgement of the peribronchial blood-vessels was a marked feature. These appearances correspond with those seen at an early stage of broncho-pneumonia.

Sections examined from lungs at a later stage showed a confluent broncho-pneumonia. The alveoli were completely filled with sero-fibrinous material, in which numerous polymorphonuclear leucocytes and pigmented catarrhal cells were seen. The smaller bronchi contained masses of leucocytes and epithelial cells embedded in a sero-fibrinous matrix. In the more congested areas the alveolar septa in many places had given way and the exudate had become confluent.

The kidneys.—Cloudy swelling of the tubular epithelium was seen in some areas. The glomeruli were engorged with blood, and Bowman's capsule was thickened in most of the specimens examined. In a few instances a clear exudate was seen within the Malpighian bodies. There was no evidence of interstitial changes or endarteritis.

The liver.—The liver cells in the portal areas showed cloudy swelling and fatty degeneration. No cellular infiltration was evident in the tissues surrounding the portal vein. Amyloid change was not seen in the arterial zones.

SUMMARY.

1. The recent pandemic of influenza has included a large number of cases of septicæmia or toxæmia with a high degree of mortality.

2. These severe cases appear definitely related to the cases of "purulent bronchitis" which have been described as occurring in various parts of the country and in France. The essential feature is an infection by the *Bacillus influenza* with a secondary infection by some other organism. The existence of copious purulent expectoration is only an incident which may or may not be present and which has been singularly absent in the recent pandemic.

3. The secondary organism in question is the pneumococcus, *Streptococcus pyogenes longus*, or a "diplostreptococcus," the virulence of which appears to be exalted by the initial influenzal infection.

4. The characteristic features of the septicæmic type of case are variable lung symptoms, ranging from slight bronchitis to lobar pneumonia, very characteristic heliotrope lividity, dyspnœa, or rather polypnœa, and very rarely orthopnœa. These, with other so-called complications of influenza, such as pleurisy, nephritis, and others of lesser import, are evidence of the septicæmia or toxæmia referred to.

5. The relative frequency of the septicæmic type of case cannot be estimated with any degree of accuracy. The mortality of the septicæmic cases would appear to be as high as 90 per cent. at the beginning of an epidemic, falling to 50 per cent. at its termination.

6. Infection takes place in the upper respiratory passages, and involves the accessory nasal sinuses, where a septic sinusitis develops. From this and possibly other foci as yet undetermined, the toxæmia or septicæmia originates.

7. In view of the large number of instances in which the diplostreptococcus has been isolated in pure culture from the heart's blood and internal organs immediately after death, it is concluded that this organism plays an important rôle in the fatal cases.

8. The very large majority of cases of influenza run an uncomplicated course, terminating in from 3 to 14 days. No treatment has been found to be of any value in aborting an attack, or in preventing its development into the virulent type.

9. The large majority of cases of septicæmic type die in spite of any form of treatment. Cases have recovered who have been given no specific treatment of any kind.

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