The intraocular levels are higher still and persist up to 36 hours if adrenaline 1:1,000 is the solvent.

In the experimental animal a destructive *Ps. pyocyanea* infection of the cornea is fully controlled by one subconjunctival injection of 0.5 g. of streptomycin in 1 ml. of adrenaline 1:1,000.

For clinical purposes streptomycin to be injected subconjunctivally should be dissolved in 10 min. (0.6 ml.) of water to which 5 min. (0.3 ml.) of adrenaline 1:1,000 is freshly added.

Clinically, streptomycin is effective when used subconjunctivally in infections of the cornea due to Gram-negative bacilli. As these lesions are highly destructive, early treatment is essential, and the characteristic clinical appearance of such infections facilitates early diagnosis. Streptomycin locally is also invaluable in acute conjunctivitis due to Gram-negative bacilli.

Systemic streptomycin therapy has proved helpful in tuberculous keratitis. It has given poor results in presumably tuberculous iridocyclitis and in periphlebitis. In phlyctenular ophthalmia it tends to cut short severe attacks, and probably reduces the frequency and severity of relapses.

Our thanks are due to Dr. P. D'Arcy Hart and the Medical Research Council for liberal supplies of streptomycin during the earlier stages of this investigation, when the material was not readily available. We are obliged to Sister Thorogood and her staff of the Royal Eye Hospital unit at Lambeth Hospital and to Sister Condon, formerly of White Oak Hospital, for their help in the treatment of patients. To Dr. P. Muggleton and Mr. B. I. Helliwell, of Glaxo Research Laboratories, we are indebted for technical assistance.

THE CLINICAL FEATURES OF THE PNEUMONIAS UNDERGOING VIRUS TESTS

BY

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The response of the pneumonias to sulphonamides and penicillin has broadened rather than solved the problem of the differential diagnosis and treatment of lung consolidations. Since such treatment has been introduced, a wide group of non-bacterial pneumonias caused by viruses and rickettsias has been revealed. American authorities have stressed the increasing incidence of virus pneumonias, Goodrich and Bradford (1942) finding them almost as frequent as pneumococcal pneumonias, and Reimann (1943) computed figures of 70% of all pneumonias for this group. The process of sorting out the various non-bacterial pneumonias is not yet far advanced, and while influenzal pneumonias and the pneumonias of psittacosis, lymphocytic choriomeningitis, glandular fever, lymphogranuloma venereum, and Q fever have emerged as definite entities other similar pneumonias await identification.

The group of "primary atypical pneumonia, aetiology unknown," has been considered by some as an entity (Joules, 1950), but this has been denied elsewhere (Scadding, 1948). In the last-named condition the non-specific cold agglutination reaction has been used as a diagnostic test; in the other pneumonias mentioned the diagnosis is confirmed by the detection of specific antibodies by complement-fixation and neutralization tests. A rise in antibody titre in these tests is diagnostic and is

particularly valuable in influenza, in which it is often impossible to obtain the virus from the patient's nose or throat and so to isolate it by ferret inoculation.

The complement-fixation test was the one employed in the series of cases described below, and most of the cases were also examined for complement-fixing antibodies of *Rickettsia burneti*, psittacosis-ornithosis and lymphogranuloma viruses, and by *Streptococcus M.G.* agglutination. Where possible the tests were done on acute and convalescent phase sera, but in some cases only convalescent sera were obtainable. These tests were performed by Dr. B. P. Marmion, Dr. A. D. Macrae, and Dr. A. P. Goffe, of the Colindale Group Laboratory. Cold haemagglutination tests were also done on many of the cases at the Edgware General Hospital by Dr. E. D. Hoare. Nearly every case was questioned and examined by me so as to obtain a uniform approach to the clinical aspects of these cases of pneumonia. This paper is a review of the clinical findings in 159 of such cases seen in the Edgware General Hospital between the beginning of January, 1949, and the end of May, 1950.

Clinical Investigation

It soon became apparent that clinical methods did not readily distinguish the various forms of pneumonia, so all cases of suspected lung consolidation seen during the investigation were serologically tested. The cases are divided into two groups, the first being seen between January 1 and September 1, 1949, and the second group between early November, 1949, and the end of May, 1950. A fairly severe outbreak of influenza (mainly of the A type) is included in the first group, and the second group covers a lesser outbreak of influenza B in March and April, 1950. While the patients were being submitted to the tests just mentioned special consideration was also given to certain features: the history and symptoms of the illness; a past history of chest infection; the signs of the illness; the duration of the fever; the x-ray findings; the white cell counts; the sputum examinations; and the nature of any complications.

The two groups showed very similar numbers of cases, 88 being examined in the 1949 group, and 71 in the 1949-50 group. The cases were all of severe respiratory disorder, and either showed clear pneumonic signs or had such symptoms of lung involvement that pneumonia was immediately suspected. The patients had all been active till the onset of the illness, even though some had old respiratory or cardiac disease, and the rapid development of severe symptoms, often of sudden onset, was a feature in all. The composition of the two groups as determined by the special tests is shown in Table I, the

TABLE I

	Group 1 (1949)	Group 2 (1949-50)
Influenza (confirmed)	16	18
(probable)	22	—
Primary atypical pneumonia	11	11
Psittacosis-ornithosis	—	2
Unclassified	39	40
Total	88	71

"primary atypical pneumonias" being the cases in which a cold agglutinin titre of 1 in 16 or over was reached. The cases classified as definitely positive influenzas were those which showed a rise of influenza antibody titre between the acute and convalescent phases; if a signifi-

cantly high titre was found only in the convalescent phase the case was listed as "probable positive." Neither of the psittacosis-ornithosis cases appeared to have been exposed to avian infection. No case of Q fever was detected during the whole investigation.

The age distribution in the two groups is shown in Table II, and a remarkable similarity is noticeable. Thus

TABLE II.—Age Distribution

Age Groups (Years)	Group 1					Group 2		
	Infl. (Confirmed)	Prob. Infl.	Total Infl.	Primary Atypical Pneumonia	Uncl.	Infl.	Primary Atypical Pneumonia	Uncl.
0-9 ..	1	1	2	0	2	0	0	1
10-19 ..	1	5	6	1	2	0	0	3
20-29 ..	1	1	2	3	2	2	2	4
30-39 ..	3	0	3	2	7	3	3	5
40-49 ..	3	5	8	3	4	4	3	4
50-59 ..	6	5	11	1	10	2	1	13
60-69 ..	1	4	5	0	8	7	1	9
70+ ..	0	1	1	1	4	0	1	1
Totals	16	22	38	11	39	18	11	40

25 (65.8%) of the influenza cases of group 1 were over 40, and 13 (72.2%) of those in the second group were over 40. Of the unclassified cases 26 (66.6%) in group 1 and 27 (67.5%) in group 2 came in this age category. The primary atypical cases were fewer and also on the average younger than those in the other groups; thus 8 (72.7%) in each group were between 20 and 50. The influenza figures correspond with the observations of Stuart-Harris *et al.* (1950) on influenzal cases in Sheffield, many of his cases being in the older age groups.

During the investigation five patients died in group 1 and three in group 2. These figures, which are a striking testimonial to modern treatment, become even more remarkable when the ages of the patients and other associated conditions are considered. Thus in group 1 four patients with "probable" influenza (high complement-fixation titre at the only reading available) died; one of these was 75 and another 60; the third had a contracted horseshoe kidney and uraemia; and the fourth, a boy of 12, an old case of poliomyelitis, had widely paralysed respiratory muscles. One unclassified patient aged 63 died during the first half of the investigation. Of the three fatal cases in group 2 one aged 68 had probable psittacosis-ornithosis; another, a chronic bronchitic with emphysema, aged 52, had a suprarenal haemorrhage, and the third was admitted after six weeks' illness with organizing suppurative pneumonitis.

During the influenza B epidemic period four serologically uninvestigated patients (not included in Table I) died within a few hours of their admission, and three of them, aged respectively 21, 46, and 65 years, had sudden illnesses of influenzal type. All three failed to show influenza virus from lung culture on fertile hen's egg, but all showed a free growth of *Staph. aureus*—a possibly significant finding. The husband of the youngest of these was said to have had influenza a short time previously. The fourth, aged 69, proved to be a long-standing chronic bronchitic with a large area of grey hepatization. Thus among 159 patients with pneumonia who lived long enough to have some treatment and investigation there were eight deaths, usually facilitated by some disease other than the pneumonia, and there were four other deaths of patients in whose case there was no time for effective therapy.

Onset

A comparison between the influenzal cases and the various non-influenzal cases was attempted on the lines mentioned above. Stuart-Harris *et al.* (1938) had underlined the significance of a sudden onset as a feature of the influenzal infections; but in our investigation, which was mainly concerned with ill pneumonic cases, it was possible that this feature might be somewhat obscured. The figures given in Table III, however, show that this

TABLE III

	Sudden Onset	Possibly Sudden	Gradual
Group 1:			
Influenza	14	2*	0
Probable influenza	17	3	2
Primary atypical pneumonia	6	2	3
Unclassified	15	5	19
Group 2:			
Influenza	11	3	4
Primary atypical pneumonia	7	1	3
Unclassified	13	5	22
Psittacosis	1	0	1

* Both bronchitic cases.

observation holds good, particularly amongst the influenzal cases of group 1. (These were mainly due to the A type of infection, only six B type infections being found.) Only in two of the "probable" cases of this year did the illness appear to have a gradual onset, and in one of these, a girl of 21, recent tuberculosis was also found; the other was an old bronchitic case. Many of this first series were admitted within a week of the onset of the illness. All the cases in group 2 found to be influenzal were of the B type; they were admitted on the average later in the illness, but, even so, only four had symptoms of seemingly gradual onset, and of these one was a case of gross mitral stenosis and two had illnesses of two and six weeks' duration. Thus in only one of the four was the true onset of the infection clearly discernible.

But sudden onset is not confined to influenzal pneumonias, as is clearly shown in Table III. It is noteworthy that over one-third of the "negative" unclassified cases in the two years should have had onsets very difficult to distinguish from influenza. This finding is one of those which encourage the belief that there are other respiratory viral infections yet to be identified. Of the two psittacosis-ornithosis cases the more strongly positive also showed a sudden onset.

Severe headache is regarded as a distinguishing feature of "primary atypical pneumonia," but only half our cases in this group showed this symptom, while headaches of varying severity were seen in just over a quarter of the influenzal and in nearly a third of the unclassified cases.

The frequent occurrence of two phases of onset of the illness is also remarkable in all the groups of cases, 28 of the 1949 cases and 27 of the 1949-50 cases showing this feature. In them, after a beginning usually "influenzal" and sudden, there was a period of malaise followed by partial improvement; then, sometimes after the patient had been active, the illness returned with redoubled force and usually with symptoms suggestive of lung involvement, such as chest pain, dyspnoea, and severe cough. The interval between the two phases ranged from two days to three weeks, but in many cases was about one week. The average length of the interval

was slightly more in the unclassified cases (ten days) than in the influenzal and primary atypical pneumonic cases (seven or eight days). The expected evidence of a bacterial invasion to account for the second phase was not forthcoming in more than two-thirds of these cases, and in them the progressing invasion by the viruses, facilitated by inadequate rest, probably explains the advance of infection.

It is also noteworthy that no influenza-positive case showed cold agglutinins and no case with cold agglutinins showed a positive influenza complement-fixation reaction.

Respiratory Symptoms

Stuart-Harris *et al.* (1938) also emphasized the greater preponderance of malaise and general symptoms over respiratory symptoms in the influenzal cases, though he also seemed to imply that coryzal and non-exudative pharyngitis were common features in influenza. But we found pharyngitis in only 5 to 10% and coryza in less than 20% of all our cases, and laryngitis was conspicuous by its absence. The fact that the cases had usually passed to a pulmonary phase in the disease, and that mental hebetude may have caused some of the patients to forget such early symptoms, does not account entirely for the lack of prominence of these symptoms. On the other hand, our influenzal pneumonias were like those of Scadding (1937) in not being prominently dyspnoeic—except in the rare fulminating cases—but they often showed light cyanosis and a very great deal of toxic apathy and asthenia. And the non-influenzal cases in many instances gave a clinical picture indistinguishable from this.

Before considering the other respiratory symptoms, the effect of preceding respiratory disorders in these cases cannot be overlooked. Thus an old bronchitic case developing influenza naturally soon tended to show an exacerbation of bronchitic symptoms, while an asthmatic was liable to show in addition marked bronchial spasm and wheezing. In such cases dyspnoea was often severe and cyanosis pronounced, and in them the sudden type of onset was less in evidence. The proportion of cases with preceding chronic bronchitis was as great amongst the influenzal cases during the two outbreaks as amongst the other pneumonic cases investigated. The only group in which chronic bronchitis was not a marked feature was the "primary atypical pneumonic" group, and, as has already been pointed out, the average age was lower in this group than in the others. Pleuritic pain was an early feature in from one-half to two-thirds of the cases in each category.

Generally speaking, the symptoms failed to distinguish the influenzal cases from non-influenzal pneumonic cases, an observation in line with those of Francis (1941) and other observers in the United States (Horsfall *et al.*, 1940; Sulkin *et al.*, 1941). Dingle and Abernethy and their co-workers (1948) in the U.S. Commission on Respiratory Diseases worked in two U.S. Army camps and failed to distinguish influenzal cases from other acute respiratory diseases by ordinary clinical methods. While they found sore throat and sputum commoner earlier symptoms in acute respiratory diseases, and sudden onset, muscular aching, and prostration commoner in influenza, such differences were not consistent enough to permit a clear separation. A survey of the results of our case symptoms showed that despite treatment there was a greater tendency to prolonged fever of over one week in the influenzal and "primary atypical pneumo-

nic" cases. As all cases on admission were given full therapy with sulphonamides, and often with penicillin as well, and as resistant bacteria were rarely encountered, this tendency to prolonged fever may in these cases well have been a sign of viral infection.

Analysis of Physical Signs

Before making a comparison of physical signs in the two groups it is interesting to recall the old anatomical division of pneumonias into bronchopneumonias and lobar pneumonias. If an influenzal outbreak occurs the affected cases are likely to be further infected with the prevailing bacteria of the locality, and if these are pneumococci, lobar pneumonic manifestations are likely to be frequent. While a pure pneumococcal lobar pneumonia was once of apparently common occurrence, this is not so to-day, and in our series of 159 cases only one case without evidence of recent viral infection fulfilled all the criteria of lobar pneumonia as regards history, signs, radiological appearance, leucocytosis, and pneumococcal sputum. It is not improbable that pneumococci have been rendered less pathogenic and less widespread by the effective therapy of recent years, but it is also probable that "lobar pneumonias" could on past occasions have been viral pneumonias secondarily infected by pneumococci.

In our cases of the first group seven of those which were an established recent infection with influenza and ten with a probable recent infection showed large areas of dullness, bronchial breath sounds, and rales, and so might have been classified as lobar pneumonia. The signs were unilateral or bilateral and were usually basal; similar findings were made in 15—a similar proportion—of the unclassified cases. The findings in the second group of cases were very similar, and in both years there was one influenzal case in which the lung consolidation had broken down under the influence of *Staph. aureus* and had produced cavernous signs, apical in one instance and basal in another. Scadding (1937) has mentioned the cases in which the dullness to percussion is associated with an absence of breath sounds sufficient to suggest fluid. These cases were fewer in the Edgware series: only one among the influenzas, three among the probable influenzas, and seven among the unclassified cases. In a small proportion of these early cases pleural fluid, usually in small quantities, was actually present, but more usually it appeared later, masking previous typical pneumonic signs.

Scadding has also commented on a stage of influenzal lung infection where patches of slight percussion impairment, weak breath sounds, and adventitia unassociated with x-ray changes are found. In these he considers lung oedema to be present, and of those in group 1 we found nine among the established and probable influenzas—one cold-agglutinin positive and eight among the unclassified cases. Nine of the influenzal cases (including the "probables") and ten of the unclassified cases in group 1 showed merely bronchitic signs, unilateral or bilateral rales or rhonchi, or both, without percussion impairment. These cases included a number of chronic bronchitics, but it also must be emphasized that radiological evidence of consolidation occurred more often than could be elicited by physical signs.

The figures for group 2 were largely similar in all instances, and it is evident that influenzal cases cannot be separated from non-influenzal by mere consideration of physical signs.

Scadding (1937) has classified the lung involvement in influenzal pneumonia as follows: (a) Cases without clinical signs of lung involvement; (b) cases with lung signs but without consolidation; and (c) cases with demonstrable consolidation. The last two groups he has further subdivided according to their extent and severity. By use of his criteria, and making allowance for the presence of a number of borderline cases, the extent of lung involvement in our cases is shown in Table IV. It should be explained that, whereas C1 and C2 represent respectively consolidation and more extensive consolidation of patchy nature, C3 cases are those with much bronchitis as well as lobar consolidation, and C4 are cases of purely lobar type.

Table IV further shows the impossibility of separating the cases of the various categories on the basis of clinical signs. As will be seen, this difficulty extends to the so-

TABLE IV.—Extent of Lung Involvement (Scadding's Classification)

	1949				1949-50		
	Infl.	Prob. Infl.	Cold Agglut. Positive	Unclassified	Infl.	Cold Agglut. Positive	Unclassified
A ..	0	0	1	1	0	0	0
B1 ..	1	1	0	1	1	1	3
B2 ..	6	3	1	8	3	0	7
C1 ..	6	12	7	21	9	10	19
C2 ..	3	6	2	6	5	0	10
C3 ..	0	0	0	0	0	0	0
C4 ..	0	0	0	2	0	0	1
	16	22	11	39	18	11	40

called primary atypical pneumonias, though, as often noted in the past, these tended to show signs disproportionately small for the amount of consolidation. They also twice showed an extrapulmonary feature peculiar to them in this investigation—namely, conjunctival injection.

An approximate correlation of the physical signs with the radiological findings is discussed in the next section.

Radiological Appearances Correlated with Physical Signs

In all groups these varied greatly, and it can be said at the outset that they did not have any conclusive power in separating cases in the various groups. As might have been expected, prominent bronchial shadows of a linear and branching type were a feature of the bronchitic cases (B1 and B2 of Scadding's classification). A closer-knit reticulation and a very fine mottling in the more affected areas—often basal—was the next degree. These cases and the more definite pneumonias with larger areas of mottling (C1 of Scadding) usually produced a variable degree of percussion-note change with weakened breath sounds and rales at one or both bases. The reticular and mottled appearances were found in all classes of the pneumonias investigated.

A curious dense haze in the lungs, sometimes referred to as a "ground-glass" shadow or "partial" consolidation, was also seen in cases in all groups. The bronchial markings could often be seen through it, and even when extensive it usually spared the lung periphery. There was often with it a history strongly suggestive of viral pneumonia, and it occurred noticeably in the "primary atypical pneumonia" series. The signs were often those of moderate percussion-note change, distant tubular breath sounds, and fine rales, but, like all the other

radiological appearances of pneumonia, this partial consolidation was associated with variable signs, the breath sounds over it being sometimes much diminished, at times frankly bronchial, and at others a patchy mixture of the two. The same range of signs was noted both where there were large woolly, partly confluent areas, and also where the consolidation was fully confluent and dense. For example, in one of the "primary atypical pneumonias" a comparable partly confluent consolidation in one lower lobe was associated with bronchial breath sounds and in the other lower lobe with very weak breath sounds.

Where there was marked percussion impairment the x-ray shadows were usually dense, but smaller shadows were found in resonant zones, particularly where emphysema had a masking effect. Many cases with chest pain showed pleural friction, and a number of these went on to develop pleural effusions, usually small, clear, and sterile. Pleural effusions always showed typical signs, but these at times suggested rather more fluid than was present—a not surprising fact when one remembered that in other cases consolidation mimicked the presence of fluid.

Two influenzal cases which developed staphylococcal abscesses in the consolidated areas showed clear cavernous breath sounds in the dull area near the cavitation. One non-influenzal case with an abscess cavity associated with little consolidation of the near-by lung showed the usual paucity of signs manifested by lung abscesses.

The slowness with which severe influenzal pneumonias cleared has been previously mentioned, and our cases were no exception. One extensive case took almost five months to become clear, and periods of two months from the outset were not uncommon. The heavy consolidations were naturally the most persistent; the "ground-glass" shadows usually cleared within three weeks, and the fine mottling even more rapidly.

Our findings accord with those of Ackermann (1941), who did not observe any specific form of influenzal consolidation. He found lobular consolidations, peribronchial consolidations, and "miliary" consolidations all in varying combinations. He also found that the appearances suggested pulmonary tuberculosis in some of his cases; but, apart from one case actually complicated by pulmonary tuberculosis and another with small upper-zone abscess cavities, this difficulty did not arise in our cases. The consolidations were usually in the lower zones, and as the shadows were of such varied character tuberculosis was not strongly suggested.

Bacteriology and Blood Examinations

Investigations of the sputum and blood are considered in the same section because a relationship between them might be expected. Scadding (1937) has mentioned that as a general rule his groups A and B (influenzal pharyngitis, tracheitis, laryngitis, and bronchitis) show neither significant organisms nor initial leucocytosis, and he believed that when leucocytosis occurs later in group B it is probably due to secondary infection. Similarly, he considered that in his group C the consolidations were due to secondary invaders which also caused leucocytosis, and in his "lobar" groups C3 and C4 pneumococci predominated in every case.

The question whether influenza or other respiratory viruses can alone cause consolidation is not fully decided. Goodpasture (1919) has described two cases of probable

pure influenzal pneumonia, but the main bulk of the consolidations seen are due to secondary invaders. Scadding refers to the basal pulmonary oedema and alveolitis which occurs when the virus passes into and beyond the terminal bronchioles, but implies that such involvement produces no striking consolidation.

Our cases were admitted usually with at least several days' history of illness and were investigated because of symptoms or signs that were frankly pneumonic; only a few of them had received sulphonamides or penicillin before admission, but all subsequently received one or both of these treatments to lessen the effects of secondary invaders. The first sputum results were therefore rarely modified by treatment. The initial leucocyte counts were considered in relationship to the bacteria of the sputum, to the patient's age, to the duration of the illness, and to a rough assessment of the amount of consolidation in the various groups.

The great majority of cases in all the groups showed some consolidation, but many had no sputum, the coughs being occasional, dry, and harsh, and this lack of sputum was not to be accounted for by treatment before admission. It seemed that in all groups there were those who had no marked bacterial infection, and it is thus not unreasonable to suggest that quite often the suspicion of a largely viral infection of the lungs was supported. Very rarely a patient was too weak to expectorate, and one influenzal patient without sputum who later developed an empyema was such a case. Among the cases with previous chest infections there was, as might be expected, a very large proportion in all groups with a bacterial sputum.

Where the probability of virus participation was great—namely, in those cases with positive influenza complement-fixation or positive cold agglutination reactions—certain facts emerged. Only 9 of the 22 cases of the latter type ("primary atypical pneumonia") showed some evidence of secondary infection, and of these only three showed much consolidation—one of these a very old subject, another a chronic bronchitic, and the third having a heavy *Staph. aureus* infection. But of the influenzal cases, probable and confirmed together, 29 of the 56 had purulent or mucopurulent sputum, and four of the others died before sputum could be obtained.

TABLE V.—Incidence of Bacillary Infection in the Various Groups

Infecting Organism, Alone or Mixed	1949			1949-50		
	Infl.	Cold Agglut. Positive	Uncl.	Infl.	Cold Agglut. Positive	Uncl.
<i>Staph. aureus</i> ..	7	0	3	4	1	2
Pneumococci ..	5	0	7	4	1	6
Haem. str. ..	2	1	1	1	0	3
<i>H. influenzae</i> ..	0	0	1	1	0	2
<i>Bact. coli</i> and <i>Proteus</i> <i>vulgaris</i> ..	1	0	3	1	0	0
M.U.R.F.* (including <i>Str. viridans</i>) ..	6	3	5	3	3	6
Total cases in group	38	11	39	18	11	40

* Normal mixed upper respiratory organisms in pus-containing sputum and unmixd with other organisms listed.

As can be seen from Table V, *Staph. aureus* was found alone or in mixed infections in the sputum of 11 of the influenza cases; in 7 this was a heavy infection. Among these cases were the severest influenzal pneumonias, with most consolidation, two showing abscess formation. As against this, *Staph. aureus* was found in

only 5 of the 79 unclassified cases, while pneumococci were found only 9 times among the influenzas and as many as 13 times among the unclassified groups. Two other cases of probable fulminating influenzal pneumonia in which death occurred soon after admission showed heavy *Staph. aureus* infection, and the predilection of *Staph. aureus* for influenzal pneumonias (Wollenman and Finland, 1943; Stuart-Harris *et al.*, 1950) is thus confirmed to some extent in our cases. Blood occurred in the sputum in these cases only with heavy secondary infections. There were many cases tested (26 in all) in which *Streptococcus viridans* alone or together with *Micrococcus catarrhalis* (M.U.R.F., or mixed upper respiratory flora) were predominant in purulent or mucopurulent sputa. It may be that these organisms can become pathogenic where previous damage has been inflicted on the respiratory tract by virus infection.

The initial leucocyte counts seemed to bear little general relationship to the nature or extent of the infection, to the patient's age, or to the previous duration of the illness. The one partial exception to this fact is found amongst the influenzal cases in which a greater degree of consolidation did correspond in a number to a greater leucocytosis and apparently also, as Scadding (1937) has observed, to appreciable secondary infection of the lung. There was also a general tendency for the cases with little or no consolidation or secondary infection to be the cases without leucocytosis. But even here there are exceptions—for example, one case of *Staph. aureus* infection with lung abscesses whose white cell count was only 6,000. It was evident that the individual variation to infection, so well seen in the general appearance and reactions of patients, extends to the leucocyte counts, and it is evident that, while greater in bacterial diseases, this variation also occurs in viral infections, there extending from moderate leucopenia to moderate leucocytosis. It is thus not surprising that where these two types of infection are associated, as in so many of our cases, the leucocyte count is not a reliable guide to the nature of the pneumonia under consideration.

Complications

As the aim of this paper has been to evaluate the clinical approach to the pneumonias as an aid to distinguishing between the various types, the complications are also considered in this light. The commonest complication is the pleural effusion, and here no great difference between the influenzas and the unclassified groups was found, though the effusion was less common in the cold-agglutinin-positive cases. Only one empyema occurred in the whole 159 cases, and that, in an influenzal patient, contained sterile pus—a striking testimony to the efficacy of penicillin and the sulphonamides. There were in all 24 clear sterile pleural effusions. No cases of incomplete resolution were detected among all the cases who recovered. One only—that with the upper zone abscesses—showed a little residual fibrosis. As already mentioned, one case first showed an acute tuberculous focus during influenzal pneumonia.

A possible point of distinction between cases in the cold-agglutinin-positive group and those in the other groups is the occasional occurrence of severe haemolytic anaemia amongst the former. The case with the highest recorded titre of cold agglutinins (1 in 2,048) showed the

most marked haemolysis, the haemoglobin falling from 70% to 40% in eight days, the red blood cells being uncountable during this period, when slight icterus developed. But there was no correlation between the agglutinin titre and the degree of haemolysis, one case with a titre of 1 in 256 showing a fall of haemoglobin level to 60% (Haldane), though no anaemia developed in others with a similar titre seen at the same time of year. Two other cases with titres of 1 in 32 and 1 in 256 showed haemoglobin levels of 68% and 74%, but an emphysematous subject with a titre of 1 in 1,024 showed no apparent anaemia. The severely anaemic case first mentioned showed a fall of titre to 1 in 128 by the 39th day of her illness. At the end of the seventh week her haemoglobin level was 94% and the red cell count 4,740,000 per c.mm. Of the 137 cases in the other groups only two showed anaemia, and one of these was a toxic influenza B pneumonia with heavy secondary infection with *Staph. aureus*; in this case the haemoglobin level fell at first to 60%, but was back to 90% four weeks later. The other case was that of a patient with severe bronchitis and marked "influenzal" symptoms in whom all influenza complement-fixation tests and cold-agglutination tests were negative.

Stuart-Harris *et al.* (1938) have doubted the liability of influenzal cases to nervous complications, but Hollander (1947) has described 23 cases of post-influenzal "sensory polyneuritis," and Laha and Mitter (1945) have described a case of transient flaccid paralysis of the lower limbs which they attributed to influenza. In neither of these investigations was the diagnosis of influenza serologically verified. Nor does Leigh (1946) claim more for his two cases of polyneuritis than that they occurred during an influenza B epidemic and that some of them had respiratory symptoms. Holmes (1947) described six cases of viral pneumonia possibly of primary atypical type which showed evidence variously of infective polyneuritis, lymphocytic meningitis, and encephalitis.

One of our established influenza A cases, a girl aged 10 with slight basal pneumonia, showed immediate neck rigidity and a positive Kernig's sign; her cerebrospinal fluid (C.S.F.) at first contained 30 lymphocytes per c.mm. Her influenza antibody titre rose from less than 1 in 4 on the third day of the illness to 1 in 64 on the 21st day. Another probable influenza A case (titre 1 in 128) showed exaggerated tendon-jerks in the legs and one indefinite and definite extensor plantar response for a few days early in the illness. Two cases showed symptoms of polyneuritis of the greatest severity. One of these was a woman of 56 with probable influenza A (titre 1 in 16), the other, a man of 41, had a primary atypical pneumonia (cold-agglutinin titre 1 in 64). The former, who had complete ophthalmoplegia and inco-ordination of the arms and legs, also showed marked general flaccid paralysis of the face and moderate flaccid weakness in all four limbs, with slight peripheral sensory loss in all four limbs. Tendon-jerks were persistently absent. C.S.F. protein was raised to 90 mg. per 100 ml., with normal cytology. Over a period of five months she made an almost full recovery. The man was less severely affected, but had complete bilateral facial palsy and a severe flaccid paralysis of both lower limbs with loss of tendon-jerks and slight sensory loss. C.S.F. protein was 270 mg. per 100 ml.; cytology was normal. Limb power recovered well, and he was able to leave hospital walking after two months, but the facial weakness has been very persistent.

Discussion

This account is more concerned with diagnostic than with therapeutic problems, and because "aureomycin" and chloramphenicol were not easily available throughout a great part of the period of observation they were not tried. Despite this, out of 159 cases of severe respiratory disease, mainly pneumonic and often in subjects past the prime of life, only eight (5%) died. Only in this 5% group where the dice were very heavily loaded against recovery did the sulphonamides, penicillin, oxygen, and good nursing fail to cure. In all other cases there was recovery without noticeable residuum, and only one recovery was delayed by the formation of an empyema. Secondary invasion with bacteria, and particularly with *Staph. aureus*, was seen both in the observations in this paper and elsewhere (Wollenman and Finland, 1943) to be the main cause of complications and death in viral pneumonias. This fact is well attested by the efficacy of the remedies just mentioned both in prophylaxis and in curative therapy. The liability to secondary infection seemed less marked in "primary atypical pneumonias" than in the influenzal groups, but, even so, the former tended to have a fairly prolonged febrile course, which newer antibiotics might well have curtailed.

It is evident that the viral pneumonias are still a largely uncharted country for these groups of cases, which were tested for various viruses yet showed at the last a majority of unclassified cases without significant bacterial infection. It is also evident from the uniformity of the clinical findings within the various groups that only with the help of the virus expert, and the wider employment of complement-fixation tests such as those for influenza and other virus infections used during this investigation, will the whole obscure problem be elucidated.

Summary

During 1949 and 1950 one observer saw 159 cases of pneumonia, many of them with symptoms suggestive of virus infection. They have been examined from the clinical, radiological, and viral aspects.

The virus tests have separated a group of influenza A cases and a few influenza B cases in one year, and a number of influenza B cases in the second year. These cases could not certainly have been detected by any other means, although their occurrence during influenza epidemics made them especially suspect. Their tendency to be secondarily infected with *Staph. aureus* was once again evident. Other probable cases of viral pneumonia indistinguishable from the influenza cases in symptoms, signs, x-ray appearances, blood counts, and bacteriology were seen during the epidemics and at other times.

A sudden onset of illness was a usual feature in these cases. Two of these were proved to be due to psittacosis-ornithosis infection, and 22 had cold-agglutinin-positive tests and are tentatively grouped together as "primary atypical pneumonia, aetiology unknown." None of these cases had antibodies to influenza viruses A and B, but this group may still prove to be a mixed one. They showed no tendency to occur in epidemics, but were sporadic throughout the whole year. Some of them had a marked tendency to haemolytic anaemia, though this may also occur in other viral pneumonias.

No cases of Q fever were found throughout the investigation.

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ROLE OF STATISTICS IN REGIONAL HOSPITAL PLANNING

WITH SPECIAL REFERENCE TO THE BIRMINGHAM HOSPITAL REGION

BY

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Before the inception of the National Health Service on July 5, 1948, there was no unification of the organization of the hospital services in this country. The main types of hospitals were those supported by voluntary contributions and those maintained by local authorities. Within any one area the development of each type was independent of that of another except so far as both were reliant upon contributions extracted either voluntarily or compulsorily from the residents of the area in which they were situated. The inauguration of the National Health Service led to new methods of financing the hospital service—namely, the collection of funds (in the form of National Health stamps and taxation) by the State from a large proportion of the population. It is now possible, therefore, to plan an overall health service without reference to regional differences in the distribution of the nation's wealth.

Many estimates of the desired ratio of beds to population have been given both by Government-sponsored committees and by independent workers, as cited in Table I, which shows considerable variation with respect to a putatively adequate bed/population ratio. All these estimates are much higher than any actual ratios referable to the Birmingham Region, overall figures for which are included in the same table.

The region encompasses five counties—Herefordshire, Shropshire, Staffordshire, Warwickshire, and Worcestershire. Its total population on December 31, 1947, was

TABLE I.—Estimates of Number of Hospital Beds Required for Each 1,000 Persons

Estimate	Type of Bed				
	General	Chronic Sick	Isolation	Tuberculosis	Maternity
Surrey plan	6.0		0.75	1.0	
Berks, Bucks, and Oxon scheme	5.5	2.5	0.60	0.7	
Scottish survey	4.8	1.5	1.50	1.71	0.96 ^a
Consultant services (M.O.H.)	Approx. 6.5	1.5	0.60	Not shown	1.00 ^a
Hospital survey U.S.A.	4.5-5.5	2.0	Not shown	1.77	
Birmingham Region:					
Total bed complement	2.85	1.44	0.47	0.52	0.39
Available complement	2.53	1.34	0.24	0.24	0.38

Approximate requirements in Birmingham Region based on: ^a 12 beds per death per annum. ^b 2.5 beds per death per annum. ^c 4-5 beds per 100 births. ^d Including antenatal beds.

4,259,500, of which some 60% are resident in the Birmingham-Wolverhampton conurbation, while Herefordshire and Shropshire are rural counties with a low density of population. The distribution of hospital beds within the region varies considerably from district to district, but not necessarily in accordance with their needs (Table II). In one rural area the overall ratio of

TABLE II.—Numbers of Beds per 1,000 Persons in Various Areas in Birmingham Region (June 30, 1949)

Bed	Rural Area		Suburban and Dense Rural Area		Dense Urban Area			
					1		2	
	Total	Available	Total	Available	Total	Available	Total	Available
General	3.66	3.46	2.65	2.57	3.36	2.49	2.76	2.62
Chronic sick	1.90	1.60	2.26	1.87	0.34	0.32	1.26	1.20
Fever	0.66	0.28	0.87	0.44	0.58	0.14	0.52	0.28
Tuberculosis	0.70	0.70	0.55	0.55	0.22	0.17	0.59	0.57
Maternity	0.53	0.53	0.46	0.46	0.42	0.38	0.42	0.42
Total	7.45	6.57	6.79	5.89	4.92	3.50	5.55	5.09

beds (excluding mental) to population is 6.64 per 1,000, while in an area of high population density the ratio is as low as 3.35.

As yet most of the estimates of the requisite bed ratios are but inspired guesses, and until further information is available about the work done in hospitals it is not possible to provide more reliable figures. At present our problem is to remedy gross deficiencies in the hospital service; and a reasonable target for the immediate future is the provision of sufficient beds, so that the bed/population ratio of every locality is at least equal to the present average for the country as a whole. This done, it would be time enough to estimate future requirements on the basis of predicted changes in the age structure of the population (Enid Charles, 1935, 1948).

It is here pertinent to recall the words of Florence Nightingale, herself one of the early advocates for hospital statistics. Writing in 1860, she remarks: "I am fain to sum up with an urgent appeal for adopting this or some uniform system of publishing the statistical records of hospitals. . . . I have applied everywhere for information, but in scarcely an instance have I been able to obtain hospital records fit for any purpose of comparison." It is chastening to realize that she would find little improvement if she were alive to-day. It should be recognized that regional authorities have far too little available information as a basis for day-to-day administrative decisions. A single example brings this deficiency into focus. There is at present a serious shortage of