PNEUMONIA IN WEST LONDON, 1949-1950

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In the autumn of 1949 a study of the "pneumonias" admitted to Hammersmith Hospital, London, was begun. It was designed to determine in as many cases as possible the specific aetiological groups to which they could be assigned, and thus to enable the clinical pictures of the groups so defined to be compared. Virus investigations were undertaken at the Central Public Health Laboratory; details of the methods will be published elsewhere. Other pathological investigations were carried out in the Department of Pathology, Postgraduate Medical School of London. In the latter part of 1950 a therapeutic trial of antibiotics in pneumonia, under the auspices of the Medical Research Council (see p. 1361 of this issue), was begun at this and other hospitals and was added to the aetiological study already in being. The present paper, however, is concerned only with the aetiological and clinical studies of the first year of the investigations.

The year covered by this investigation presented a few features of interest in relation to the incidence of pneumonias. There was a prolonged fine autumn in 1949 which led to a delay in the seasonal winter increase in pneumonia incidence. In the early months of 1950 there was an outbreak of influenza B; no influenza A was recorded in our area. The total number of cases of pneumonia treated in the hospital during the year was similar to that of previous years.

Material.—The survey covered the period from October 1, 1949, to September 30, 1950, and included all cases which were diagnosed as pneumonia in the general medical wards. The only exceptions were those in which the pneumonia was thought to be secondary to cardiac failure or was subsequently proved to be due to carcinoma of the bronchus (six cases). The patients were treated by accepted methods, as outlined by one of us (Scadding, 1949).

Methods

A full history was taken on admission, including inquiry into contact with birds and possible sources of Q fever, such as farm animals or their products. Sputum or, failing sputum, a nasopharyngeal swab, was obtained for culture aerobically on blood agar before chemotherapy was begun. From August, 1950, sputum was also injected intraperitoneally into mice for isolation of pneumococci. A white blood count was done, and blood was taken for culture and for serology. A radiograph of the chest was obtained as soon as possible after admission, and usually repeated at weekly intervals. From a number of cases sputum, garglings, or necropsy material were preserved at about −70° C. for later virus studies if indicated.

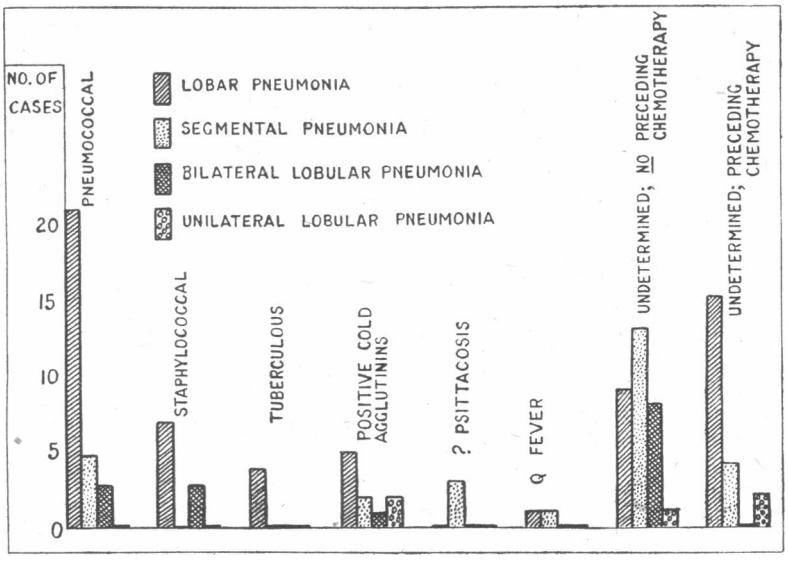
As soon as possible after admission the blood serum was examined for cold haemagglutinins and for immune bodies to *Streptococcus MG*, influenza viruses A and B, *Rickettsia burneti* (Q fever), and the psittacosis group of viruses. These examinations were repeated between the 10th and 14th and between the 14th and 21st days after the onset of the illness.

A total of 110 cases was included in the series. Their ages ranged from 8 to 86 years (mean 45.5, median 45). There were 61 males and 49 females.

In all cases we tried to make both an anatomical and an aetiological diagnosis. The results are summarized in Table I and the Chart.

TABLE I.—*Aetiological and Anatomical Diagnosis in 110 Cases of Pneumonia*

	Pneumococcal	Staphylococcal	Tuberculous	Cold Agglutinins >1:64	? Psittacosis	Q Fever	No Aetiology Determined: No Chemotherapy before Admission	No Aetiology Determined: Chemotherapy before Admission	Total
Lobar ..	21	7	4	5	0	1	9	15	62
Influenza B	3	2	0	0	0	0	0	1	6
Segmental ..	5	0	0	2	3	1	13	4	28
Influenza B	0	0	0	0	0	0	4	0	4
Lobular ..	3	3	0	3	0	0	9	2	20
Unilateral	0	0	0	2	0	0	1	2	5
Bilateral ..	3	3	0	1	0	0	8	0	15
Influenza B	0	0	0	0	0	0	0	1	1
Totals ..	29	10	4	10	3	2	31	21	110
Influenza B	3	2	0	0	0	0	4	2	11



Aetiological and anatomical diagnosis in 110 cases of pneumonia.

Anatomical Diagnosis

Definitions.—The anatomical diagnosis, defining the distribution of the pneumonia, was made mainly on radiographic evidence obtained as soon after admission as possible. The cases were divided into three main groups—lobar pneumonia, lobular pneumonia, and segmental pneumonia. The term "lobar pneumonia" was used when the pneumonic process occupied the whole of one lobe. Lobular pneumonia was used to indicate a pneumonia producing a patchy opacity on the radiograph, which might be in one or both lungs; it was preferred as an anatomical diagnosis to "bronchopneumonia," as the latter term carried certain aetiological implications. Cases in which the radiographic opacity was uniform rather than mottled, but which occupied less than a complete lobe, were called "segmental pneumonia." In many of these a lateral radiograph indicated that the lesion did in fact correspond to one or more of the anatomical segments of the lung, but in others it was not possible to obtain a lateral film early in the illness and a segmental lesion was assumed on the strength of the appearances on the postero-anterior film. Although the anatomical categories may have been determined partly by the stage of the disease at which the patient was first examined, in practice it was very rarely that the radiographic appearance changed before the stage of resolution sufficiently to alter the anatomical category.

Results.—Of the 110 cases, 62 were lobar in distribution. In fact, the pneumonia was lobar in a high proportion of cases, whether bacterial or non-bacterial. The 28 segmental pneumonias were distributed through all aetiological groups, with the exception of staphylococcal and tuberculous. These exceptions are probably fortuitous; segmental lesions are certainly seen both in pulmonary tuberculosis and in staphylococcal pneumonia. In 11 of the 20 cases of lobular pneumonia no aetiological agent was identified; pneumococci and staphylococci were each isolated from three and a significant titre of cold agglutinins was found in three. There was a contrast in age distribution between the lobular and the segmental pneumonias. Among the 20 patients with lobular pneumonia all except three were over 40 years of age, and 15 were over 50. The three exceptions consisted of one patient with fulminating staphylococcal pneumonia and two with significant titres of cold agglutinins. On the other hand, all except 9 of the 28 patients with segmental pneumonia were under 40.

Aetiological Diagnosis

Some preliminary explanation of the principles on which cases were classified in the various aetiological groups is required; more detailed consideration will be given below to each group individually. In general, the diagnosis of bacterial pneumonias depended upon the combination of a compatible clinical picture with isolation of the organism from sputum, blood culture, or the lung post mortem. The diagnosis of virus and rickettsial pneumonias, and of influenzal infection, depended upon serological reactions, either specific (psittacosis group, Q fever, influenza), or non-specific (cold agglutinins, *Str. MG* agglutination), and was thus always retrospective; in no case was a virus isolated. The large group classified as of indeterminate aetiology consists of all cases in which no positive evidence of aetiology was obtained; probably it includes some cases which really belong to one of the already mentioned groups, but in which the methods used failed to indicate the aetiology.

In Table I the cases in which there was evidence of influenzal infection are tabulated horizontally, rather than vertically, like those of the psittacosis, Q fever, and "cold-agglutinin-positive" groups, because it is well recognized that the influenzal pneumonias of man, even those of the fulminating type, are due to mixed influenzal and bacterial infections (Scadding, 1937).

Pneumococcal Pneumonia

There was laboratory evidence that pneumococci were responsible for the pneumonia in 29 cases. It is probable that this is an underestimate, as mouse inoculation was employed only in the last two months of the survey. The organism was isolated from the sputum in 28 out of the 29 cases, and from the blood culture alone in the remaining case. Typing sera were not at first available, so that few comments can be made on incidence of the different types of pneumonia. Blood culture was done in 21 cases and was positive in 11.

In 21 of the pneumococcal cases the distribution was lobar, in five it was segmental and in three lobular. There is therefore a clear bias towards a lobar distribution. Blood culture was done in 14 of these lobar cases and was positive in nine.

Clinically the pneumococcal lobar pneumonias did not differ significantly from the classical description, although most of them were cut short by chemotherapy. Two-thirds were of sudden onset and just under half had an initial rigor. Over half had rusty sputum. In all the percussion note was impaired over a lobe and in nearly all there was bronchial breathing. Only 3 out of 21 had white blood cell counts under 10,000 per c.mm., and two of these had had chemotherapy before admission. Three had serological evidence of preceding influenza B infection. They did not seem particularly severe; one of them responded rather slowly to chemotherapy but had a large pleural effusion in addition to the pneumonia.

Five of the pneumococcal pneumonias were segmental in distribution. They occurred at all ages. One of the patients had a preceding upper respiratory infection and two had chronic bronchitis. Three had initial rigors, one had rusty sputum, and the blood culture was positive in two out of the four cases in which it was done. The white blood cell count was over 10,000 per c.mm. in all cases and over 20,000 in two. These facts would suggest that the organism was normally virulent. Three of the patients were afebrile on admission, or became so without chemotherapy, and in the other two the fever subsided on the first and second days after starting chemotherapy.

The three pneumococcal lobular pneumonias did not appear to differ from other cases of similar distribution. In two of them there was a profuse growth of pneumococci from the sputum; in the third the pneumococci were scanty. All had negative blood cultures.

Staphylococcal Pneumonias

Ten cases of pneumonia were ascribed to coagulase-positive *Staphylococcus aureus.* Seven were lobar in distribution, with one death. The remaining three were lobular and all three were fatal. Staphylococci were isolated from the sputum in 8 of the 10 cases, and from the lung post mortem in the other two. They were

penicillin-sensitive in five cases, penicillin-resistant in two, partly penicillin-resistant in one, and not tested in two. In one of the patients with a resistant strain the temperature subsided rapidly while under treatment with penicillin, though the physical and radiographic signs cleared very slowly. The other patient with a resistant strain and the one with a partly resistant strain both died.

It was of interest to determine whether the staphylococci causing pneumonia in this series belonged to related strains. Phage typing of the staphylococci was kindly carried out by Dr. R. E. O. Williams, of the Central Public Health Laboratories. The penicillin-sensitive staphylococci were of assorted types. The two highly resistant staphylococci were related (47/47B/53 and 47/47B/53/54+). The partly resistant strain was not typed. Further details of these studies will be published by Dr. Williams and his colleagues.

Two of the patients with staphylococcal lobar pneumonia had serological evidence of preceding influenza B; neither was very ill and both made a satisfactory recovery.

Clinically there was nothing particularly characteristic of the group except the high mortality, which will be discussed later. Several patients had preceding upper respiratory infections or bronchitis, and in most cases the onset was gradual. Five out of the seven patients with lobar consolidation had rusty sputum, but in only three was bronchial breathing heard. In most of those who recovered the fever subsided rapidly, but in the older patients radiographic clearance was much delayed. In no case was there evidence during life or at necropsy of gross abscess formation.

Apart from the 10 cases in which the staphylococcus appeared to be the dominating agent, there were several in which staphylococci were isolated in addition to other important organisms. Two patients were admitted with an acute pneumonia, and staphylococci were isolated from the sputum; but tubercle bacilli were also found and pulmonary tuberculosis became the dominating condition. In both it seemed probable that the staphylococcal pneumonia was responsible for lighting up a latent tuberculous infection, but the cases have been classified as tuberculous pneumonia.

In two other cases both staphylococci and pneumococci were isolated from the sputum, but the blood culture grew pneumococci only. These cases have been grouped with the pneumococcal pneumonias.

In one other case there was a minor growth of *Staph. aureus* from the sputum; but there was no response to penicillin, a good response to "aureomycin," and the serum later showed a high titre of cold agglutinins. This case has been classified in the "cold-agglutinin-positive" group.

Tuberculous Pneumonias

Tubercle bacilli were isolated from the sputum of four patients. Two of these cases have been discussed above. They presented as staphylococcal pneumonias; the temperature responded initially to treatment, but began to rise again almost immediately and tubercle bacilli were found in the sputum. The radiographic changes cleared partially, leaving substantial residua which were attributed to tuberculosis.

The third patient was admitted with unexplained fever. There was initially no cough, and no localizing sign in the chest; within a day or two she had started to cough, and abnormal physical signs and radiographic consolidation were detected at the left apex. A diagnosis of pneumonia was made, but a few days later tubercle bacilli were found in the sputum. The fourth patient was admitted with the signs of lobar pneumonia at the left base; her temperature failed to respond to penicillin, and tubercle bacilli were eventually found in the sputum.

Q Fever

There were two cases of Q fever. A woman aged 39 was probably infected in the South of France. She was admitted with an illness which had begun with febrile symptoms only, followed by dry cough and pleural pain. The temperature was 103.8° F. (39.9° C.) on admission, but she did not seem very ill. There was a segmental pneumonia of the right upper lobe, and the total white cell count was 8,000, with 86% neutrophils. The temperature failed to respond to penicillin but fell rapidly when aureomycin was added. The complement-fixing antibody for *Rickettsia burneti* rose from less than 1:8 on the eighth day of illness to 1:512 on the 35th. The second case was in a woman aged 63. She had been in the country near Windsor six days before the onset, but the source of the infection could not be traced. She was admitted on the sixth day of her illness, which had started with severe headache followed by dry cough. She was found to have pneumonia in both lower lobes, with a right basal pleural effusion, which on tapping yielded a greenish-yellow, thin, non-purulent fluid. The white cell count was 8,000, with 81% neutrophils. A minor growth of pneumococci was found in the sputum, but the serum showed a titre for *Rickettsia burneti* rising from 1:128 to 1:512.

Psittacosis

The sera of three patients showed high titres of complement-fixing antibody to the psittacosis group of viruses. In the first case the first serum was obtained only on the 45th day of the illness; the titre was 1:80 on three occasions and fell gradually over the next few months. In the second case the titre on the sixth day was 1:160 and fell slowly later. In the third case there was a rise from 1:80 on the fifth day to 1:160 on the 21st and higher than 1:160 on the 60th.

Skin tests varied from case to case. In the first, tests with both the Frei and heat-treated psittacosis antigens were negative; in the second the Frei alone was positive; and in the third the psittacosis alone.

The clinical picture in the three cases was not uniform, and in none was particularly suggestive of psittacosis. Nor was there epidemiological evidence to support the diagnosis. It is known that serologically there may be a cross-reaction between psittacosis and lymphogranuloma venereum and that titres for either may remain raised for long periods. In two of the patients there was a previous history perhaps consistent with lymphogranuloma venereum. Therefore, in the absence of a fourfold rise in titre, we think it doubtful that the illness we observed in any of the patients was in fact psittacosis.

Pneumonia with Cold Agglutinins

The discovery that among the large number of cases of apparently non-bacterial pneumonia of undetermined aetiology some, either sporadic or in local outbreaks, show auto-agglutination of the red cells by the serum at low temperature, encouraged the hope that this phenomenon, usually briefly described as "cold agglu-

tination," might serve to define an aetiologically distinct group. Cold agglutinins, however, are occasionally found in cases of pneumonia due to pneumococci and, very rarely, in those due to recognized viruses or to rickettsiae. It is to the group of cases of indeterminate aetiology showing cold agglutinins that the term "primary atypical pneumonia" has been most often applied. This term is illogical and has been used in several different senses; it should therefore be abandoned (Scadding, 1948). It can advantageously be replaced, in the contexts in which it has been most legitimately used, by "pneumonia, presumed due to an unidentified virus." The group characterized by cold agglutinins is generally assumed to be due to one aetiological agent, but there is no positive evidence that this is so. Eaton *et al.* (1944, 1945a, 1945b) claimed to have isolated a virus from cases of "primary atypical pneumonia" with cold agglutinins and to have demonstrated antibodies to the virus in the sera of convalescents. This work is not yet generally accepted (Horsfall, 1949). The Commission on Acute Respiratory Diseases in the United States has done transmission experiments in man and has also claimed to have demonstrated a virus responsible for pneumonia with cold agglutinins (Dingle, 1945).

There is confusion in the literature about the method by which the titre of the cold agglutinins is expressed. We use a 0.5% suspension of red cells. We express our results in terms of the final dilution of the serum, including that effected by the red-cell suspension. Even if allowance is made for discrepancies introduced by this confusion there is great divergence of opinion about the titre of cold agglutinins which is to be regarded as helpful in defining a distinct group among the pneumonias. Finland and Barnes (1951) accept a titre of 1:20 as specifically significant, though by this criterion positive titres were present in a number of their cases in which other aetiological agents were identified. We have found that titres as high as 1:64 have occurred in one or two cases in each of our aetiological groups except the tuberculous and staphylococcal pneumonias. Thus, with our technique, a titre up to that level cannot be regarded as specific. In our specific group, with titres of 1:128 or above, it was significant that in 5 out of the 10 cases there was at least a fourfold rise in titre while under observation. In all cases the highest titre was observed between the tenth and twentieth days of the illness.

Thomas *et al.* (1945) found specific agglutinins for a streptococcus—*Str. MG*—in pneumonias with cold agglutinins. In two of our cases in this group *Str. MG* titres of 1:80 or above were observed. In three cases in other aetiological groups titres of 1:20 were recorded.

In 3 of our 10 cases with what we regarded as significant titres of cold agglutinins the titres rose only to 1:128. Their ages (45, 64, and 77 years) were higher than those of the rest of the group; and two of them had pleural pain, which did not occur in the other eight. All three were very dyspnoeic. Two had lobar pneumonia and one had lobular pneumonia, and all presented a clinical picture indistinguishable from that of the bacterial pneumonias.

The seven patients with cold agglutinin titres of 1:256 or higher were aged 10 to 31 years; as a group they were thus much younger than the whole series or than any of the groups defined within it on aetiological grounds. Only one, a child of 10, had a history of recurrent bronchitis; one had had a sore throat before admission, but none of the others had any history to suggest a preceding upper respiratory infection. There was nothing characteristic about the anatomical distribution of the pneumonia; three had a lobar, two a segmental, and two a lobular distribution. Constitutional and febrile symptoms were severe in all seven. Initial headache was present in all and prominent in three. None had pleural pain. The sputum was mucoid in all. There was impressive dullness to percussion in only one, and the same case was the only one in which bronchial breathing was heard. Only two patients were dyspnoeic, and these both showed widespread fine rales in both lungs. The leucocyte count was 12,000 per c.mm. or less in five cases, but the other two had counts of 17,000 and 28,000 per c.mm. respectively, with 81% and 90% neutrophils; both these high counts were observed late in the disease. Penicillin, sulphonamides, or both were given in five cases with no convincing evidence of response. Aureomycin was given in three with prompt defervescence; two of these had previously received penicillin.

This account is consistent with the accepted picture of a "virus pneumonia" characterized by general rather than respiratory symptoms, absence of rusty sputum, no pleural pain, few localizing signs in the chest, a normal or low white cell count, and a poor response to penicillin and sulphonamides.

Pneumonias of Indeterminate Aetiology

Of the 52 patients whose pneumonia could not be classified in a specific aetiological group, 21 had received chemotherapy before admission. In 15 of the 21 the pneumonia was lobar in distribution and may therefore have been pneumococcal, the organisms having been masked by the chemotherapy.

In 31 other cases which could not be classified aetiologically no chemotherapy had been given before admission. Nine were lobar. In these the clinical characteristics, leucocyte counts, and response to therapy were consistent with the suggestion that they were bacterial pneumonias in which the causative organism was not isolated. As mouse inoculation was used only in the last two months of the investigation, it is probable that we missed laboratory confirmation of some cases of pneumococcal origin. Humphrey *et al.* (1948) have pointed out that the proportion of cases in which pneumococci are isolated can be increased by about a third by using mouse inoculation.

Thirteen of the 31 cases were of segmental distribution. In 11 of these 13 there had been some preceding abnormality of the respiratory tract; in four there was serological evidence of influenza B infection, in four a history of preceding upper respiratory tract infection, and in three of chronic bronchitis. In all except one the white cell count was 11,000 or more per c.mm. These facts suggest that in most of these cases the pneumonia was of the "aspiration" type (Ramsay and Scadding, 1939; Scadding, 1948, 1951).

Of the nine patients with lobular pneumonia for which no specific aetiology was determined, one was admitted late in the illness with involvement of one lung only and recovered rapidly. Several of the remaining eight patients with both lungs involved had had a recent upper respiratory tract infection or had chronic bronchitis. Their ages varied from 49 to 68 years, their illnesses occurred between October and March, and all seven in whom blood counts were done early in the illness showed a

high leucocytosis. It is reasonable to suggest that these were lobular aspiration pneumonias in elderly bronchitic subjects in which the severity of the illness varied according to the organisms incidentally present and the patient's resistance, local and general.

In summary there seems little evidence that our "indeterminate" group of pneumonias included any significant number due to a specific but as yet unidentified organism. Most of the cases can be accounted for by assuming either that they were "missed" specific bacterial pneumonias or that they were pneumonias associated with organisms derived from the upper respiratory tract and normally of low pathogenicity. These organisms had been enabled to gain access to the lower part of the broncho-pulmonary tree and there give rise to an inflammatory reaction, because of impairment of the host's defences, especially the local mechanical defences of the respiratory tract and possibly those of the body in general. The evidence for this view is indirect and incomplete, but it seems to provide a reasonable working hypothesis.

Seasonal Incidence and Complications

The seasonal incidence of the different aetiological types among our cases cannot have great significance owing to the small numbers. The pneumococcal cases mainly occurred between October and March, though there were a few cases in the summer months. All the staphylococcal cases were seen between October and April. Both the Q fever cases were admitted in June. Cases with cold agglutinin titres above 1:128 were scattered between October and June. All the cases with serological evidence of influenza B infection were seen between January and April.

A pleural effusion large enough to be aspirated occurred in 10 cases. In all 10 the pneumonia was lobar in distribution. Three were caused by pneumococci; in the remaining seven no aetiology was determined and cultures of the fluid were sterile, six out of the seven having had chemotherapy before admission. Only two of these cases developed a frank empyema; both recovered after surgical treatment.

Apart from pleural effusion there were few complications. One patient developed acute nephritis three weeks after the onset of a pneumococcal lobar pneumonia. A second had a thrombophlebitis of the leg while convalescent from a pneumococcal segmental pneumonia.

Deaths

There were 10 deaths. Details of these are given in Table II. The single death from pneumococcal pneumonia was in a man aged 69 who had had chronic bronchitis for many years. He was admitted exceedingly ill on the seventh day of his pneumonia and died in a few hours.

There were four deaths among the 10 cases of staphylococcal pneumonia. One out of the seven patients with staphylococcal lobar pneumonia died, but all three cases of staphylococcal lobular pneumonia were fatal. The death from staphylococcal lobar pneumonia was in a previously fit man aged 63 years who was admitted on the ninth day of a left upper lobe pneumonia which had been unsuccessfully treated with sulphonamides. He was desperately ill and had auricular fibrillation. There was no sputum, and blood culture was sterile. He was treated with sulphonamides and with penicillin 300,000 units six-hourly. His temperature fell and he appeared to improve for three days, but on the fourth day his temperature rose again and he became very weak. Consolidation was detected in his right lower lobe. The blood urea was 296 mg. per 100 ml. and he died the same day. Necropsy revealed purulent bronchitis and red hepatization of the left upper and right lower lobes; microscopically the affected lobes showed confluent bronchopneumonia. The kidneys were substantially normal. Penicillin-resistant staphylococci were isolated post mortem from his nose and from both the affected lobes. The case occurred in October, 1949, when there was no evidence of an epidemic of influenza B.

Two of the three fatal cases of staphylococcal lobular pneumonia were in women aged 80 and 86 years who became steadily worse in spite of chemotherapy. The third case was a fulminating one in a woman aged 33. Following an upper respiratory catarrh for four days she became very ill and was admitted on what was presumably the third day of the pneumonia. She was then desperately ill, and was given 250,000 units of penicillin.

TABLE II.—*Summary of Data on 10 Fatal Cases*

Case No.	Sex	Age	Aetiology	Anatomy	Leucocyte Count		Day Admitted	Day Died	Previous Chronic Bronchitis	Chemotherapy before Admission	Chemotherapy in Hospital
					Total per c.mm.	% Neutrophils					
69	M	69	Pneumococcal	Lobar	—	—	7	8	Yes	No	Aureomycin, 2 g., then 1 g. 4-hourly. Total 5 g.
7	M	63	Staphylococcal	,,	17,000	93	9	13	No	Yes	Sulphonamides and penicillin, 300,000 units 6-hourly
17	F	86	,,	Lobular	37,000	90	2	8	Yes	No	Penicillin, 60,000 units 3-hourly
110	F	80	,,	,,	11,000	90	14	34	N.R.	Yes	Penicillin 300,000 units twice daily. Later streptomycin, 0·5 g. twice daily
72	F	33	,,	,,	—	—	3	3	No	No	Penicillin, 1 dose of 250,000 units
99	F	76	Indeterminate	Lobar	27,000	95	30	39	N.R.	No	Penicillin, 500,000 units 6-hourly
13	M	64	,,	Lobular	16,000	68	18	21	Yes	No	Penicillin, 100,000 units 6-hourly
16	F	64	,,	,,	29,000	82	19	23	Yes	No	Sulphonamides and penicillin, 200,000 units 3-hourly
85	M	68	,,	,,	20,000	89	10	77	Yes	No	Penicillin, 250,000 units 4-hourly. Later streptomycin, 0·5 g. 6-hourly
62	F	49	,,	,,	30,000	89	8	11	No	No	Penicillin, 200,000 units 3-hourly

N.R. = Not recorded.

She died within a few hours. Penicillin-sensitive staphylococci were obtained from the lungs post mortem. Efforts to recover influenza virus were unsuccessful, although the case occurred when influenza B infection was prevalent and presented clinical and pathological features suggestive of a fulminating influenzo-staphylococcal pneumonia.

Of the five fatal cases of pneumonia of indeterminate aetiology, four were lobular and one was lobar. All the patients except one were over 60 years old and had other complicating factors such as long-standing bronchitis, bronchiectasis, or cerebral softening. The exception, a woman aged 49, had no sputum, the blood culture was negative, and permission for post-mortem examination was refused. She may well have had a specific bacterial pneumonia which was not diagnosed. Two patients died after long illnesses, partly as a result of disease elsewhere, though lung consolidation was still present at the time of death. No bacteriological studies were made post mortem. Two others died earlier in the course of the pneumonia, and, in these, cultures from the lungs and bronchi were sterile, with the exception of a growth of *Staph. albus* from the bronchial wall in one; both had received large doses of penicillin up to the time of death.

Discussion

Full investigation of a series of cases of pneumonia, including thorough bacteriology and virus serology, is now a formidable undertaking, and not many such surveys have been published. The cases studied in the Medical Research Council (1951) therapeutic trial of antibiotics in pneumonia, of which part was conducted at Hammersmith Hospital, were investigated aetiologically, but that series is not comparable with the one studied in the aetiological survey which forms the subject of the present report. The therapeutic trial was restricted to patients who were admitted with an initial diagnosis of "pneumonia"; the present aetiological survey included not only these patients, but also those admitted with another provisional diagnosis—for example, "bronchitis" or "unexplained pyrexia"—and who later developed symptoms and signs on which a diagnosis of pneumonia was made after admission. Moreover, the therapeutic trial excluded patients who had received specific treatment before admission. On these criteria, the Q fever cases, some of those with significant titres of cold agglutinins, all those in the group "indeterminate aetiology, with chemotherapy before admission," and some of those in the specific groups would have been excluded.

The most important comparable aetiological survey in Great Britain is that of 351 cases of "primary pneumonia" admitted to the Central Middlesex Hospital in 1942–4, published by Humphrey *et al.* (1948) and Glover *et al.* (1948). Since the area from which these cases came adjoins that served by Hammersmith Hospital, a comparison of the findings is of special interest. The criteria adopted for inclusion in the two series were on the whole similar; the only important difference was that patients over the age of 70 years were excluded from the Central Middlesex Hospital series. The most obvious difference is the smaller proportion of pneumococcal pneumonias in our series. In the Central Middlesex series 79% of the cases were diagnosed as pneumococcal, but this diagnosis was made in some cases on clinical grounds, even though no pneumococci had been isolated. An attempt may be made to adopt comparable standards of diagnosis by comparing the percentage of cases in the two series from which pneumococci were isolated. This amounts to 56% for the Central Middlesex series and 26% in ours. Alternatively, if all the cases classified in our series as lobar pneumonia of indeterminate aetiology are added to those from which pneumococci were isolated, the total amounts to only 48% of all pneumonias. Positive blood cultures were obtained in 21% of our pneumococcal cases, so defined, compared with 5% of the Central Middlesex cases. In 1938–9 at Hammersmith Hospital, pneumococci were isolated from 67–68% of all pneumonias of lobar distribution, compared with 33% in the present series; the addition of all pneumonias of indeterminate aetiology treated before admission with antibacterial drugs increases the latter figure only to just under 50%.

It is possible that the fall in hospital cases of pneumococcal pneumonia in this area suggested by these figures is partly due to the successful home treatment of the less severe cases. That our cases were selected for severity, as compared with those treated at the Central Middlesex Hospital in 1942–4, is suggested by the percentages of cases with positive blood cultures given above. Wingfield (1951), also in London, saw only seven cases of what he regarded as typical lobar pneumonia among a series of 109 patients with pneumonia. He gives no detailed information, and it is difficult to make a useful comparison with our series. But it seems likely that the use of sulphonamides and penicillin by general practitioners has led to a fall in the proportion of patients with pneumococcal pneumonia admitted to hospital.

The numbers of cases due to bacteria other than pneumococci in the Central Middlesex Hospital series and in our own were comparatively small. They do not call for further comment except to point out the gravity of staphylococcal lobular pneumonia in both. The literature of staphylococcal pneumonia has recently been well reviewed by Gibson and Belcher (1951). Although they record the high mortality of staphylococcal pneumonia in published series, they themselves had no deaths among their 10 cases. But Stuart-Harris *et al.* (1950) have drawn attention once more to the fulminating type of staphylococcal pneumonia which may accompany acute influenza and prove fatal within a few hours. One of our cases seemed likely to have been of this type, but no influenza virus was recovered from the lung.

It is worth emphasizing that cases of tuberculosis may be admitted with acute pneumonia and may be missed unless tubercle bacilli are sought in the sputum in all cases. If a case of pneumonia does not respond to conventional treatment, tuberculosis should always be kept in mind and further sputa examined.

There was some serological evidence of rickettsial or virus infection in 26 out of 110, or nearly a quarter, of our cases. In 11 of these the virus was influenza B. In the Central Middlesex Hospital series in 1942–4 serological tests for influenza were not carried out and Q fever was not then recognized as a possible cause of pneumonia in London. Six cases of probable psittacosis were identified among 45 cases tested, and the virus was isolated in one of these. On the other hand, what were regarded as significant titres of cold agglutinins were found in only 2 of 95 cases tested at the Central Middlesex; one of these had myeloid leukaemia and the other later developed a pneumococcal empyema. We found 10 cases among 110 tested. It is possible

that this type of pneumonia was introduced to Great Britain during the war and that its incidence has increased since 1944.

Finally it must be remembered that serological diagnoses in pneumonia are made retrospectively. The results are not available in time to assist in immediate diagnosis or to act as a therapeutic guide. Decisions about the management of a case will often have to be made on clinical grounds alone, bearing in mind, of course, that other factors besides a virus cause may account for failure to respond to penicillin or sulphonamides.

Summary

110 cases of pneumonia admitted to Hammersmith Hospital between October, 1949, and September, 1950, were fully investigated from the aetiological point of view.

In 58 cases laboratory investigations provided specific aetiological evidence—29 were pneumococcal, 10 staphylococcal, 4 tuberculous, and 10 associated with significant titres of cold agglutinins. There were two cases of Q fever and three doubtful cases of psittacosis. Eleven cases, scattered among the other aetiological groups, showed serological evidence of recent infection with the virus of influenza B.

In 52 cases no specific aetiological agent was identified, but 21 of these had had chemotherapy before admission. Reasons are given for suggesting that in these 52 cases there were few, if any, attributable to any specific but as yet unidentified aetiological agent.

The clinical aspects of the various aetiological groups are discussed.

The bacteriological investigations, on which so much depended in this work, were carried out successively by Dr. Hilda Boffa, Dr. D. R. Barry, Dr. M. Millard, and Dr. O. G. Jones. We are most grateful to them and to Dr. W. Hayes, Dr. D. A. Mitchison, and Dr. G. M. Ross, of the Department of Bacteriology, Postgraduate Medical School of London, who have taken a keen interest in the study. We are glad to acknowledge the help of Dr. J. V. Dacie with the cold agglutinin estimations. We also record our gratitude to our colleagues in the Department of Medicine, who have allowed us to investigate their patients, and to the nursing staff and laboratory technicians who have done so much to assist our work.

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In its *Annual Report, 1951,* the National Institute for the Deaf (105, Gower Street, London, W.C.1) notes that many of the larger cinemas, including 300 on the Gaumont and Odeon circuits, have now had hearing-aids installed to help partially deaf members of the audience. These aids are not yet being fully used, and the Institute is arranging social evenings in collaboration with Circuits Management Association, Ltd., to popularize their use among the hard of hearing.

LUNG INVOLVEMENT IN INFLUENZA

BY

JOHN FRY, M.B., F.R.C.S.

(From a General Practice)

This is a report on a group of cases seen in a general practice during last winter's influenza epidemic. This practice, a single-handed one, is situated on the south-eastern urban outskirts of London, and consists of approximately 4,000 patients, who belong sociologically to the "lower middle classes."

During a period of seven weeks, from the end of December, 1950, until mid-February, 1951, 223 cases were diagnosed as epidemic influenza, and it is these cases which are reported. This figure represents 6% of the total population of the practice. It should be pointed out that there must at the same time have been quite a considerable number of other cases of mild influenza, for which medical advice was not sought.

Diagnosis

The word "influenza" has unfortunately become a byword in clinical medicine for the description of almost any vague clinical short-term febrile condition without any localizing signs. Influenza can be definitely diagnosed only by isolating the virus from a suspected case. This, however, is a costly and impracticable procedure in general practice. The diagnosis is much more accurate during an epidemic than when dealing with sporadic interepidemic cases. It is thus probable that the diagnosis was correct in these cases. Epidemic influenza is a specific disease, both aetiologically and clinically.

The clinical features on which the diagnosis of influenza was based in this series correspond exactly with those reported in previous epidemics (French, 1920; Stuart-Harris *et al.*, 1937). Most patients presented a remarkably uniform picture, case after case exhibiting features which differed from one another only in grades of severity.

The patient, usually in good health, is suddenly taken ill. This sudden onset is characteristic. The most frequent early symptoms, apart from general malaise and fever, were frontal headache, pains in limbs and back, pain behind the eyes, and symptoms of irritation of the respiratory tract—that is, cough and coryza. Gastro-intestinal symptoms were not common. In 12 patients vomiting occurred during the early phase, but diarrhoea was not noted in any case. If "gastric influenza" is a clinical entity one would expect to see a good number of cases with vomiting, abdominal pain, and diarrhoea during this period of the epidemic. Such cases were not seen. It is therefore probable that "gastric influenza" is a loose and inaccurate term for gastro-intestinal upsets of unknown aetiology, and its use is deprecated.

On examination at this early stage there were no localizing signs. There was marked constitutional upset, the patient being drowsy, heavy-eyed, feverish, and ill-looking. The fever varied from 99 to 105° F. (37.2 to 40.6° C.), and the pulse rate was correspondingly rapid. The fauces were injected, but no exudate was seen. The normal course of the uncomplicated case was persistence of symptoms and fever for two to five days. The