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## ACUTE INFECTIONS OF THE CHEST IN GENERAL PRACTICE

BY

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Disorders of the respiratory tract account for the largest group of organic conditions encountered in general practice to-day. In analyses of general practice, they have been shown to account for 33% of the attendances in eight Yorkshire practices (Pemberton, 1949), 24% in ten practices from different parts of the country (Logan, 1953), and in south-east England figures of 20% from a rural practice (Taylor, 1954) and 25% from a suburban practice (Fry, 1955) have been reported. Infections of the upper respiratory tract account for 60% and, of the lower respiratory disorders, acute infections account for more than half the attendances.

Many studies of acute chest infections have been made in hospitals and among Service communities, but in this country they have seldom been undertaken in general practice. It was therefore decided to make such a study, with the aid of the full diagnostic facilities that are normally only practicable in hospital, during the winter of 1954-5. This was achieved by a co-operative study between a group of practitioners and their local hospitals, one of us (A. B. S.) acting as intermediary for the collection of specimens and the clinical co-ordination of the work.

The main aims of the investigation were fourfold: (1) a clinical study of acute infections of the lower respiratory tract in general practice; (2) a detailed investigation of these infections; (3) to make observations on treatment though no controlled therapeutic trial was attempted; and (4) to correlate the clinical and investigative data, noting which of the latter were of most practical value under the conditions of general practice.

### Materials and Methods

**Patients.**—The cases of acute infective chest disease occurred in the practices of eight practitioners\* in south-east London between October 1, 1954, and May 1, 1955 (see Fig. 1). A total of 80 cases were studied (44 males and 36 females). The ages of the adult males ranged from 16 to 76 (average 44.9 years) and of the adult females from 16 to 88 (average 38.3 years). Children under the age of 16 were excluded, though an exception was made with five children who formed part of family outbreaks of influenza. The object of the tests was

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explained to each patient, emphasizing that, in addition to this being an investigation of a general problem, the results would be of immediate value in their personal management.

**Area and Weather.**—The patients were derived from a residential suburban district in the south-east outskirts of London. They were from social classes IV and III, with some from class II. They were principally employed in local light industries and in clerical and administrative duties in central London. In October and November, 1954, there was a dry period of weather, which was followed by a cold spell, with snow in January, 1955. Slight fog was present for three days in February. It was an "average winter" so far as illness in general practice was concerned.

**Clinical Criteria of Cases for Study.**—The patients studied were those with clinical features of an acute infection of the lower respiratory tract, severe enough to confine them to bed at home. We excluded mild relapses of chronic bronchitis, as the numbers of these which would have occurred would have been too great for our facilities to investigate, but severe infective relapses were included. The cases we set out to investigate were those which are included by such diagnostic labels as acute pleurisy, bronchopneumonia, influenza with chest complications, lobar pneumonia, and others.

**Method of Study.**—Each practitioner participating in the scheme was responsible for the clinical care of his patients throughout the investigation and managed them in his normal way, but keeping details of the clinical data on a form. When first called to a case of acute infective chest disease, he informed one of us (A. B. S.), who visited the patient in his home within the next twenty-four hours, repeated the clinical examination, and took specimens for examination to a local hospital

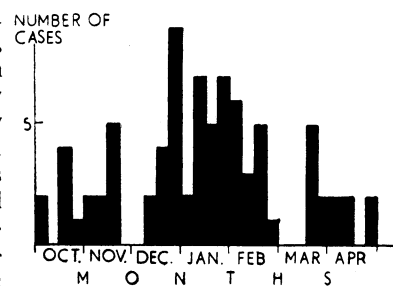


FIG. 1.—Time of onset of 80 cases of acute chest infection, October, 1954, to May, 1955.

laboratory. If practicable, the initiation of specific treatment was delayed until the specimens had been taken, but this could not always be achieved. Each patient was visited a second time by A. B. S. during the third week of illness for the collection of a second sample of blood. We were anxious to investigate patients early in the course of their disease, and that this was achieved is

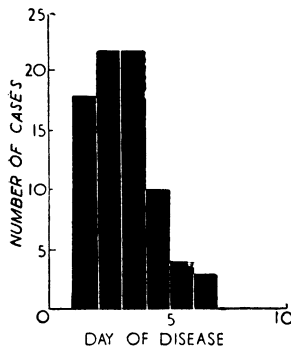


FIG. 2.—Day of disease when bacteriological and other samples were collected from 79 cases of acute chest infection. The eightieth case was seen in the first week of clinical illness, but initial specimens were not taken until the fourteenth day (Table V, Case 62).

shown by Fig. 2. It will be seen that 72 out of the 79 patients (91%) were first seen for the collection of bacteriological and other specimens within five days of the onset of symptoms.

### INVESTIGATIONS

The investigations included a full examination of the blood taken at the first visit (haemoglobin, white blood cell count, and erythrocyte sedimentation rate) and estimation of cold agglutinins in the first and second samples.

Throat swabs and per-nasal swabs were taken at the time of the first visit,

and if the temperature was above 100° F. (37.8° C.) blood was taken for culture. Sputum was collected for examination if available and, if not, a wax carton was left with the patient for later use and delivery to the local hospital laboratory by a friend or relative.

Gargles for virus study were collected in a vacuum flask of ice if the patient was seen within five days of the onset of illness. Paired specimens of blood were examined for serological evidence of infection by influenza, Q fever, the psittacosis/lymphogranuloma venereum group of viruses, and against the streptococcus M.G.

Chest radiographs were arranged by the practitioner of each case. If he thought that there was clinical justification arrangements were made for a domiciliary chest radiograph during the acute stage of illness: if not, the patients were radiographed as soon as they were fit to attend a local hospital. Lateral radiographs were taken in cases when abnormality was shown on the postero-anterior chest film, but for practical reasons they were not performed in every case. Abnormal pulmonary changes were followed up by serial radiography.

### Clinical Classification

The most satisfactory classification of disease is on an aetiological basis, but the acute infections of the lower respiratory tract are difficult to differentiate in this way in general practice and are the subject of much terminological confusion.

Among the reasons for difficulty in their differentiation are: (1) the special features of the pathology of acute infections of the lower respiratory tract, which has only a limited response to attacks by pathogenic bacteria and viruses: the same clinical picture may be produced by different infective agents, and, conversely, the same infection may cause varying clinical syndromes; (2) even when full investigations are carried out, the aetiology cannot always be determined with the tests at present available; and (3) the tests which are available for their investigation are either difficult or time-consuming to carry out in general practice and there may even be no local facilities to have them undertaken.

As a result of such difficulties, the practitioner has to adopt a practical classification of his cases, based primarily on a clinical assessment of the patient, in which descriptive

rather than aetiological terms form the basis. There is no generally agreed classification of these cases, but we divided them by their mode of clinical presentation into three main groups: (1) influenza with chest complications, (2) bronchitis, and (3) pneumonia. Table I shows the number of patients in the three clinical groups and their age and sex distribution.

TABLE I.—Age and Sex Distribution of the Cases of Influenza with Chest Complications, Bronchitis, and Pneumonia

Group	Sex	Age in Years							Total		
		10-	20-	30-	40-	50-	60-	70-		80+	
1	M	4	1	3	1	1	—	—	—	10 12	27.5%
	F	4	4	—	2	1	1	—	—		
2	M	1	1	1	2	1	6	1	—	13 3	20%
	F	—	—	—	1	—	—	1	—		
3	M	2	2	3	5	3	3	2	—	20 22	52.5%
	F	2	5	3	5	3	2	2	—		
Total		13	13	11	16	9	12	5	1	80	

#### Group 1. Influenza with Chest Complications (22 Cases, 27.5%)

The diagnosis of influenza is often inaccurate when applied to the true sporadic case, but this is not so during times of epidemic. During the investigation there was a proved outbreak of influenza B in the area and there was therefore justification for diagnosing influenza in those with its clinical features, but only cases whose respiratory-tract symptoms were a prominent feature of their illness were included.

Of the 22 cases, none had clinical consolidation, eight had a local area of moist sounds, and in nine there were widespread and bilateral rhonchi and rales. In five cases no abnormal signs were elicited.

The clinical course of these cases showed nothing worthy of remark—none was severely ill and all recovered rapidly without any serious complications.

#### Group 2. Bronchitis (16 Cases, 20%)

Bronchitis was diagnosed in those cases in which the infection appeared to be predominantly bronchial; their differentiation from "pneumonia" was at times extremely difficult and was made from two main clinical criteria: First, in those cases with diffuse rhonchi and rales over both lung fields, the cases of "bronchitis" were distinguished from the "pneumonias" only by the degree of clinical severity of the illness; second, any case with predominantly localized signs, irrespective of the degree of illness, was classified as "pneumonia." As a consequence of adopting these definitions for the diagnosis of "bronchitis," none of the patients in this group was severely ill, the temperature was never above 100° F. (37.8° C.) in any case, and all exhibited signs of scattered diffuse and bilateral rales and rhonchi in varying degrees. Cases were divided into two subgroups: those with acute bronchitis and no previous pulmonary disease, and those with acute relapse and who were subject to chronic bronchitis. Seven patients were included in the first and nine in the second subgroup. In six of the seven cases included in the former subgroup bronchitis was preceded by an infection of the upper respiratory tract and in only one of the latter.

#### Group 3. Pneumonia (42 Cases, 52.5%)

The classification of pneumonia has undergone radical alteration in recent years, but many different systems are still used by the authors of standard textbooks of medicine. We are in full agreement with the current trend that pneumonia is best classified on an aetiological basis, but it is often difficult or even impossible to find an aetiological label for many of these cases, even with full ancillary investigations in hospital, and the difficulties are even greater in general practice, where fewer facilities for investigation are available.

Of the many classifications of pneumonia, that proposed by Scadding (1952) is the most acceptable, and in this paper we applied his classification to cases of "pneumonia" when encountered in the home, and observed the correlation that was obtained when the cases were fully investigated. Scadding has classified pneumonia into three main groups—bacterial, viral, and aspiration. The first two groups are self-explanatory; the aspiration pneumonias he defines as "those due to failure of the normal defences of the respiratory tract, allowing organisms not specifically pathogenic to gain access to the pulmonary acini . . . their later course being influenced by the bacterial flora." Among those included in this group are patients whose pneumonia follows acute or chronic catarrh of the upper respiratory tract, and those who are the subjects of long-standing pulmonary disease, such as chronic bronchitis. These two groups can readily be recognized by the practitioner, and we found that 29 of our 42 cases of "pneumonia" fell within this definition.

The remaining 13 cases were provisionally classified as bacterial pneumonia; for the diagnosis of virus pneumonia, Scadding's third group, is seldom made by a practitioner when he first encounters a case, unless in the presence of a known epidemic (Table II).

It is of greater immediate concern to a practitioner to know whether pneumonia is present than its exact aetiology, and, although much has been written on the treatment of pneumonia in general practice, little work has been done on methods of diagnosis. In general practice pneumonia usually presents as an illness of fairly sudden onset, and the diagnosis has to be made in the first place on clinical grounds. In the next section we discuss the great help which a practitioner may derive from radiography in a suspected case, but this is not always necessary nor is it always available. In this section the clinical diagnosis is discussed.

TABLE II.—*Clinical Distribution of 42 Patients with "Pneumonia"*

Previous History. Physical Signs	Possible Aetiology			Total
	Bacterial Pneumonia	Aspiration Pneumonia		
		No Previous History of Chronic Lung Disease or U.R.I.	Preceding U.R.I.	
Consolidation . . . .	2	1	1	4
Local rales . . . . .	9	8	2	19
Diffuse rales and rhonchi	2	2	9	13
Pleural rub . . . . .		2		2
No abnormality . . . .		4		4
Total . . . . .	13	17	12	42

The clinical criteria on which the diagnosis of "pneumonia" was made in 42 cases were the severity of the respiratory illness and the presence of local signs of pulmonary inflammation. By adopting the first criteria many patients with generalized rales and rhonchi were diagnosed as "pneumonia" who might have been classified by others as cases of "severe bronchitis," but the diagnosis of "pneumonia" was made because of the severity of their constitutional disturbance. The second group included those who had varying degrees of clinical illness other than suspected influenza. It is in the clinical diagnosis of suspected pneumonia that the practitioner may have to place greater reliance on physical signs than his hospital colleagues, to whom radiology is so more readily available. The cases have therefore been divided into five groups on the basis of the abnormal physical signs which were elicited when the patients were first seen or within the first few days of illness.

The results are shown in Table II. It will be seen that an area of localized rales (one of the criteria for the diagnosis of "pneumonia") and diffuse rales and rhonchi were the

two sets of signs most often encountered. Signs of consolidation were detected in only four cases suspected of having "pneumonia" (9.5%).

The cases of "pneumonia" included the most severely ill patients in the series, and the only four cases, out of the total of 80, who required admission to hospital all presented in this way. One was admitted because he was too ill to be nursed at home, two because of inadequate home facilities, and one because of failure to respond to specific therapy at home.

### Radiography

Seventy-three patients were radiographed during the course of their illness, five refused a radiograph, and in two the investigation was overlooked.

Relevant pulmonary abnormalities were detected in 35 of the 73 cases (48%). The earlier the radiograph was taken the higher was the percentage of abnormalities revealed. Table III shows the number of cases radiographed

TABLE III.—*Week of Illness in which the First Radiograph was Taken (73 Cases) and the Number and Percentage with Abnormalities*

Week:	1	2	3	4	Total
No. of cases . . . . .	32	21	17	3	73
No. with radiological abnormalities . . . . .	25	7	2	1	35
Abnormalities . . . . .	78%	24%			

in the different weeks of illness and the percentage of abnormalities. In the 32 patients who were radiographed in the first week, 25 had pulmonary abnormalities (78%); 22 of these were radiographed on a domiciliary visit, of which 18 showed abnormalities (82%). Only 10 out of the 41 who were radiographed after the first week at local hospitals showed significant pulmonary changes (24%).

These two sets of cases are not comparable, because the group who were radiographed early in their illness contained more patients who were severely ill and who would normally have a chest radiograph, and the second group included the milder cases which might not have had a radiograph had they not been included in the investigation.

The abnormalities detected in the 35 patients included one with unsuspected evidence of bronchial obstruction which was later proved to be due to a bronchial carcinoma, and one who developed a spontaneous pneumothorax. The remaining 33 radiographs showed evidence of pneumonic change. These have been divided on an anatomical basis into lobar, lobular, and segmental changes, after Crofton *et al.* (1951). Lobar pneumonia denotes a pneumonic process involving the whole of one lobe. Cases in which there is a patchy opacity in the radiograph, which might be in one or both lungs, were called lobular pneumonias. Segmental pneumonias were those in which there was a uniform rather than mottled shadowing, but which occupied less than a complete lobe, and in most of these the segmental distribution was confirmed by a lateral film. Segmental pneumonias (19 cases) formed the largest group, of which three were bacterial in origin and 16 were aspiration pneumonias.

There were 10 lobular pneumonias. Four were due to virus infection, three to bacteria, and three were aspiration pneumonias. Lobar pneumonia was diagnosed in only four cases, of which three were bacterial and the fourth was an aspiration pneumonia of the middle lobe.

Radiography was the most helpful of the investigations that were undertaken. It enabled a correlation to be made with the clinical findings, and it also served to exclude other types of disease such as tuberculosis, of which we found no case, and bronchial neoplasm, of which there was one. The earlier that the radiograph was taken the higher was the proportion of abnormalities, but of greater importance were the films taken after clinical recovery to ensure that resolution was complete.

### Bacteriology

In the hospital investigation of cases of acute infective chest disease, negative bacteriological results are frequently attributed to previous domiciliary treatment with antibacterial agents; the present investigation gave an opportunity to study the bacteriology early in the course of illness. In 62 patients specimens were obtained before the start of antibacterial treatment and in 18 therapy had been started within the previous twenty-four hours.

In spite of this early collection of specimens, pathogenic bacteria were isolated from only 25 of the 80 cases (31%). The number of positive isolations from the different sources is shown in Table IV. It will be seen that the highest percentage of positive isolations was from the sputum (25%), followed by throat swabs (18%), and pernasal swabs (11%). No isolations were made from 18 blood cultures taken when there was a fever of over 100° F. (37.8° C.).

TABLE IV.—Results of Positive Bacteriological Tests

Source	Bacteria						No. of Positive Tests*	Total No. Tests	Positive Tests
	<i>Str. pneumoniae</i>	<i>Staph. aureus</i>	<i>Str. pyogenes</i>	<i>E. coli</i>	<i>B. proteus</i>	<i>H. influenzae</i>			
Throat swab	6	2	—	1	1	4	13	72	18%
Nasal swab	2	4	—	1	1	2	8	71	11%
Sputum	5	2	1	—	—	5	13	51	25%
Blood culture	—	—	—	—	—	—	—	18	—
Total	13	8	1	2	2	11	34	212	16%

\* Where more than one organism was isolated from the same specimen it is shown as one positive result in this column. Further details in other columns.

The organisms most frequently isolated were *Streptococcus pneumoniae* (13), *Haemophilus influenzae* (11), and *Staphylococcus aureus* (coagulase-positive) (8). In 26 instances the sputum was cultured on Löwenstein's medium but no tubercle bacilli were grown. Sensitivity tests to antibiotics were not performed as a routine.

The isolation of a pathogenic organism, especially from a throat or pernasal swab, was not necessarily regarded as the cause of the concurrent respiratory illness. In analysing the bacteriological results we considered them in relation to the clinical, radiological, and other pathological findings, to the source of their isolation, and to the profuseness of their growth. In 14 of the 25 patients (17.5% of the total, 80) from whom pathogenic organisms were isolated, they were regarded as the cause of the infection, and in 11 their presence was not thought to be of primary aetiological significance.

The low percentage of positive bacteriological isolations, even from sputum, was disappointing. Seventeen patients claimed to have no sputum, and 12, who reported sputum at some stage, failed to send specimens for examination; therefore sputum was examined from only 51 of the patients and only one specimen was examined from each case. Of the sputum specimens received by the laboratory, some consisted of saliva, and the desiccated state of a few indicated the time they had been in transit; it was not surprising that these often gave negative results, and it was concluded that the only method of ensuring that the laboratory received a fresh and adequate specimen was for a practitioner to collect and deliver the sputum personally. It was not our intention to adopt special bacteriological techniques, but merely to have the specimens examined in the standard way that was used by the local hospitals. The results would undoubtedly have been different if we had employed special techniques, but there is no point in commenting on these unless proper specimens are first received by the laboratory. But, using simple and commonly accepted techniques, and with better facilities for collection than

normally attain in practice, we had a small reward for a considerable amount of labour in collecting and culturing the specimens.

### Virus Studies

Investigations for evidence of virus infection gave positive results in 15 of the 80 cases (18.8%). Two tests were used: an attempted isolation of viruses from throat garglings and the examination of paired sera for a change in the antibody titre.

Garglings were collected from 67 cases seen within five days of the onset of the illness, but in no instance was a virus grown.

Paired sera were examined from 70 cases, of which 50 gave negative results. In six the results were equivocal and in 14 the titres were considered to be diagnostic of recent virus infection—that is, they showed either a fourfold rise in titre or a high titre which subsequently fell. Of the positive cases, eight showed evidence of influenza B, one of influenza A, and two of psittacosis; three showed titres against streptococcus MG which are acceptable for the diagnosis of virus pneumonia, and these also showed a significant elevation of cold agglutinins. A fourth case, with a negative streptococcus MG titre, was also diagnosed as a virus pneumonia on the basis of a fourfold rise in cold agglutinins, leucopenia, and the clinical features (Table V).

TABLE V.—Investigations in Four Cases of Virus Pneumonia and Two Cases of Psittacosis

Case No.	Day of Disease*	Complement-fixation Tests		Cold Agglutinins	W.B.C.	Radiograph
		Psitt. L.G.V.	Aggl. Strep. MG			
<i>Virus Pneumonia</i>						
12	7/14 24/31	0 0	1/80 1/10	1/128 1/64	6,000	Lobular shadows right upper and lower lobes
24	4 16	N.T. 1/8	N.T. 1/10	1/8 1/32	3,000	Lobular shadow left upper lobe
34	3/11 17/25	0 0	1/10 1/80	1/1000 1/128	9,000	Diffuse lobular opacities in right lung
40	3 16	0 0	1/40 1/160	0 1/128	6,000	N.A.D.
<i>Psittacosis</i>						
61	5 16 32	— 1/256 1/128	— 0 0	0 1/16 —	10,000	N.A.D.
62	14 30	1/1024 1/512	0 0	— —	12,000	Lobular shadow right lower lobe

\* Days of preliminary and main clinical illness; sera taken on days shown to right of oblique line.

Our results in testing for virus infection were shown to be of limited practical value. We met with no success in isolating viruses from garglings in spite of the great care that was taken in collecting and transporting the specimens. The serological tests had two practical limitations: (1) there was an inevitable delay of at least four weeks from the onset of illness before the results were known, and (2) they required two venepunctures—a procedure unwelcome both to a busy practitioner and to the patient, who has usually recovered by the time the second specimen has to be taken, although in urgent cases a result could be obtained in 10–20 days. But the positive results in 18.8% of cases were of great clinical interest, especially in confirming the diagnosis of influenza and revealing two unsuspected cases of psittacosis.

### Haematology

The white-cell counts excluded such general conditions as glandular fever, and of a total of 75 counts 54 (72%) were within the normal range. Three, with virus infections, showed a leucopenia of below 4,000 per c.mm., and 18 had a leucocytosis above 15,000 per c.mm., the highest figure being 42,000 per c.mm. in a case of pneumococcal pneumonia.

The E.S.R. was carried out in 66 cases; it was normal in 11 and raised in 55, the highest figure being 113 mm. per hour in a virus pneumonia.

No cases of anaemia were discovered by performing a routine haemoglobin estimation, for which the levels ranged from 76% (11.2 g.) to 108% (16 g.), with an average of 88% (13 g.).

Cold agglutinin estimations were carried out in 63 cases. Four cases showed a significant rise in titre, all of which had other evidence of virus pneumonia.

The full investigation of acute pulmonary infection includes an examination of the blood, but the results obtained in this survey were of no great practical value to the practitioners. Leucopenia favours a virus infection, and a leucocytosis is against such a diagnosis, but in most of our cases, including three of virus pneumonia and nine of influenza, the count was within normal limits and did not help in establishing the diagnosis. The E.S.R. is a simple ancillary test in assessing a pneumonia that is slow in clearing, and, if raised, may lead to recognition of previously unsuspected carcinoma or tuberculosis. Apart from this, it was not found of great value, and we believe that all cases in which the practitioner is suspicious enough of tuberculosis or carcinoma to investigate the serial sedimentation rates are better referred to the appropriate consultant at the first opportunity.

### Correlation of the Clinical Findings and Investigations

One of the aims of our investigation was to determine the aetiology of a representative series of acute infections of the chest in general practice. As a result of our studies we were able to prove a specific bacterial or viral aetiology only in 26 of the 80 cases (32.5%). The limitations of our methods of investigation and of the tests themselves have been referred to, but from the results obtained it had to be concluded that most of our cases (67.5%) were non-specific respiratory infections with an at present unknown aetiology. This being the case, it was apparent that our investigations would be of limited help in giving guidance in attempting an aetiological diagnosis of acute respiratory disease. On the other hand, our largely negative results have revealed the limitations of our methods of investigation and our knowledge of aetiological agents. The 26 cases of proved aetiology consisted of 11 cases of bacterial aetiology and 15 cases of viral aetiology (influenza, 9; psittacosis, 2; "virus" pneumonia, 4). (There was also one bronchial carcinoma.)

### Influenza (22 Cases)

The clinical diagnosis of influenza was confirmed serologically in seven cases and there was good reason for believing that the diagnosis was correct in at least four other cases. These four cases occurred in two family outbreaks of influenza, in which all members were ill, either concurrently or simultaneously, and in each of which there was one member whose influenza was proved serologically.

Although the serological test for influenza gives a positive result in a greater proportion of cases than isolation of the virus from gargling, it is not necessarily positive in all cases. In institutional outbreaks, when a large number of persons are infected with influenza, a varying percentage will have negative titres, and instances are on record where the virus has been isolated from garglings but the serology remains negative (Stuart-Harris, 1953). As well as the four clinical but non-proved cases referred to, there were others in which the circumstantial evidence was not so strong, but which also may have been true influenza.

As influenza symptoms may be mimicked so closely by other infections of the respiratory tract it was expected that more diverse diagnoses would be revealed by investigation than was in fact the case. Two patients in the group had evidence of virus pneumonia, though one settled within a few days with only the non-specific therapy for influenza.

and two were non-specific respiratory aspiration pneumonias. In 12 cases, including the four of clinical but not proved influenza, all investigations were negative.

Though only a third of the suspected cases of influenza were proved, the correlation between the clinical and investigative findings was satisfactory. However, the results reaffirmed our belief that the diagnosis of influenza should be limited to times of known epidemic, when it can then be made with a reasonable chance of being correct.

### "Bronchitis" (16 Cases)

The cases of "bronchitis," which formed the smallest of the three groups, were divided into those without pre-existing pulmonary disease and those with a history of chronic bronchitis or other chronic pulmonary disease.

Of the seven cases diagnosed as bronchitis without previous pulmonary disease, all investigations were negative in four; the remaining three had a previous history of nasal catarrh and two were of non-specific aspiration pneumonia. The third, a man with upper respiratory catarrh, mild general malaise, and a presumed area of aspiration pneumonia in his right lower lobe, had a titre against psittacosis which rose to 1/1024 (see Table V). This man's illness was so mild that he was never given specific therapy, and he recovered spontaneously within two weeks, before the results of serological tests were known.

Of the nine patients with a past history of chest disease, eight had chronic bronchitis and one bronchial asthma. All had a normal radiograph, pathogenic bacteria were recovered from the sputum of four, and all virus tests were negative except in one patient, diagnosed originally as a case of infective relapse of bronchial asthma, who later had evidence of psittacosis. This patient was the wife of the other case of psittacosis, but although her illness ran a more severe course than that of her husband, she was at no time more than moderately ill and her chest radiograph was normal.

The diagnosis of "bronchitis," like "influenza," may be made erroneously when almost any pulmonary disease may be the cause, and it was not surprising that three patients had an area of aspiration pneumonia, in particular as the illness in all three was preceded by upper respiratory catarrh. The only result of note was the detection of two cases of previously unsuspected psittacosis. Neither of them had had anything but minor respiratory illnesses, and both had recovered by the time the results of serum tests were known. Their infections occurred during a spell of very dry weather, and, in the absence of any other obvious source, was thought to have been contracted from the birds they fed in large numbers in their garden. Their illnesses were of interest for two reasons: (1) as a reminder of how mild the course of psittacosis may be (Bedson, 1955), and (2) to demonstrate how unusual diseases may go undetected in the guise of non-specific infections of the respiratory tract.

### "Pneumonia" (42 Cases)

The results of the investigations in the 42 cases of "pneumonia" are considered in relation to the clinical diagnosis of "bacterial or aspiration pneumonia" and to the presenting physical signs.

#### Relation of Investigations to Possible Clinical Diagnosis of the Aetiology

A practical difficulty of applying Scadding's classification of pneumonia is that two of his groups are aetiological—namely, bacterial and virus—and the third, aspiration pneumonia, is a descriptive designation. There is therefore no reason why a given case of pneumonia may not logically belong to one of the first two groups and also to the third. Thus specific bacteria may be isolated from a case of aspiration pneumonia, and we have decided, after obtaining Dr. Scadding's advice, that such cases are properly transferred to the bacterial group in discussing the cases on an aetiological basis.

Of the 29 cases diagnosed as aspiration pneumonia, a specific bacterial aetiology was established in three, and one had evidence of virus pneumonia. A fifth case demonstrated the complexity of classification and clinical presentation.

A man presented with "pneumonia" and a history of a cough for five months. His radiograph showed an opacity in the right upper lobe, he had lost weight, and the clinical picture was suggestive of bronchial carcinoma. Arrangements were therefore made for him to be seen at Brompton Hospital for an opinion regarding bronchoscopy. In the five days that elapsed before his appointment his chest had cleared radiologically and he returned home. Pathogenic bacteria had been isolated from his throat swab, and he was therefore regarded as a case of uncomplicated aspiration pneumonia from a chronic sinus infection, which had now been detected. The results of virus studies were then received, which showed that at the time of his acute illness he had been suffering from influenza A.

A sixth case, presenting as an aspiration pneumonia in a man with chronic bronchitis, failed to respond to treatment, and the breath sounds over the right lung became diminished. Radiography revealed changes suggestive of a bronchial obstruction, which later proved to be due to a carcinoma.

Of the remaining 23 cases, where bacterial and virus tests were negative, the chest radiograph showed an area of pneumonia, usually segmental, in 14, and the final diagnosis was aspiration pneumonia. The radiograph was normal in nine, most of which were "pneumonic" exacerbations of chronic bronchitis. They were not all radiographed early in the course of illness, but even had their early radiographs been normal the diagnosis of pneumonia appeared justified on clinical grounds. All were acutely ill, with an average fever of above 103° F. (39.4° C.), marked constitutional disturbance, and purulent sputum. In these severe infective relapses of bronchitis it is reasonable to believe that the bronchial inflammation had spread to peribronchial alveoli. This view is supported by the careful morbid anatomical study of chronic bronchitis by Reid (1954), who demonstrated abscesses in small bronchioles and pneumonic changes in alveoli, which not only might have been too small for radiological demonstration, but could readily have been missed in routine inspection of the specimens.

Of the 13 cases diagnosed as "bacterial pneumonia" in the absence of past or present respiratory catarrh, four had normal radiographs and negative virus and bacteriological tests. Of the nine with abnormal radiographs, six were pneumonias of bacterial origin, and one was a virus pneumonia. In two, all the ancillary investigations were negative, and, while they may have been mild virus pneumonias, they were classified as aspiration pneumonias.

Thus of the 42 cases of clinically suspected "pneumonia," the diagnosis was confirmed in 29 (69%), and reasons have been given for believing that the diagnosis was justifiable in a number of the 13 cases where the radiograph was normal. It was to be expected that the number of abnormal radiographs would be largest in this group, and it was inevitable that not all the suspected cases of pneumonia would have the diagnosis confirmed radiologically.

#### Relation of the Investigations to the Presenting Clinical Signs

When the abnormal physical signs were correlated with the results of the investigations, the main finding was that the more definite the signs of "pneumonia" the greater was the percentage of abnormal radiological and pathological investigations.

The diagnosis was confirmed radiologically in all four cases with signs of pulmonary consolidation. One was a bacterial pneumonia, one an aspiration pneumonia, and the other two were virus pneumonias. It is of interest to note that two of the four cases were virus pneumonias, for it has been traditional to regard these cases as presenting with minimal or even absent physical signs.

Of the 19 cases with an *area of localized rales* and varying degrees of clinical illness, 14 had an abnormal radio-

graph (74%)—they were aspiration pneumonias (6), bacterial pneumonias (5), or pneumonias of viral or uncertain origin (3). Of the five patients with normal radiographs, one had influenza and in the remainder all investigations were negative.

A woman aged 23, with an area of localized rales, a normal radiograph, and negative investigations, fell ill some days after her husband, who had been the victim of, clinically, the same disease. He also had an area of rales at one base, and his investigations were likewise negative except for the radiograph, which showed a lobular opacity at the site where the rales had been heard. The fever of both patients settled without antibacterial therapy, and both were fit to return to work within two weeks. But, although the husband was by then symptom-free, it was some months before his radiograph returned to normal. It was thought that both had suffered from the same disease, possibly viral in origin, which had produced radiological changes in one and not in the other.

Only 7 of the 13 patients who presented with *bilateral and diffuse rales and rhonchi* and were diagnosed as cases of "pneumonia" had abnormal radiographs (54%), but this group includes the majority of patients with chronic bronchitis for whom reasons have been given for considering that the diagnosis of pneumonia was usually justifiable even though not radiologically proved. Of the seven patients with abnormal radiographs, six had aspiration pneumonias and one was a bronchial carcinoma.

The two patients with a *pleural rub* as the only physical sign both had developed aspiration pneumonias following infections of the upper respiratory tract, one proceeding to abscess formation and a spontaneous pneumothorax.

The three cases suspected on the basis of the clinical picture to have pneumonia, even though *no abnormal physical signs* were elicited, were all confirmed radiologically to have pneumonia (bacterial and aspiration).

The results of our investigations showed a fair correlation between the initial clinical classification and that finally revealed. Seven out of the nine cases of proved influenza were so diagnosed clinically, and the diagnosis of pneumonia was correct in 29 of the 37 cases where it was radiologically proved (78%).

In 63.7% of our cases no specific aetiological diagnosis could be established. The proportion of cases in which a specific diagnosis was made varied in the three clinical groups; it was highest in the "influenzas with chest complications" (36%), followed by the "pneumonias" (31%), and was lowest in "bronchitis" (13%). Of the 34 radiologically proved pneumonias from all three groups, the majority (61.7%) were non-specific aspiration pneumonias, 26.5% were bacterial, and 11.8% were virus pneumonias. A definite aetiological diagnosis was made in only 36.3% of the 80 cases, and was achieved by elaborate pathological investigations, but it was of interest to note that in only a few cases were the results of real practical value as a guide to management. The majority of patients recovered with the treatment that was given on clinical criteria, though the investigations suggested that some who were given antibacterial therapy might have recovered as quickly without it.

## DISCUSSION

The investigation concerned the detailed clinical and pathological study of 80 cases of acute infective chest disease in the practice of eight practitioners on the outskirts of south-east London. It is appreciated that the number of cases was small, that the experiences are not representative of practice throughout the country, and that there were limitations in the investigations.

The subject provides many problems for discussion, but this is confined to those aspects to which especial consideration was given.

### Aetiology

The importance of age in the aetiology of acute chest infections is shown in Fig. 3, which gives the age of 270 patients with acute chest infections in the practice of one

of us (J. F.) over the previous five years, and shows that 80% occurred in patients under 10 and over 50 years of age. The exclusion of children, who accounted for 40% of the 270 cases, from the present study, naturally limited the number of acute chest cases that were investigated from the practices concerned.

The study was made in a suburban community, where it is more difficult to trace the source of infective illness than in the country. Not only could infection be contracted locally, but, in most households, at least one member travelled daily to central London, and it was thought that

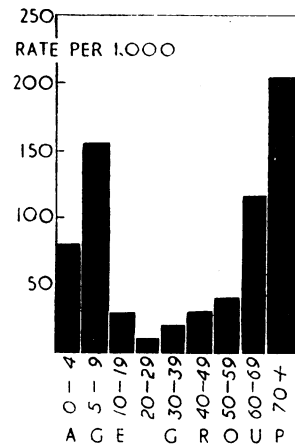


FIG. 3.—Incidence of acute chest infections in different age groups, shown as rate per thousand attendances. Figures from the practice of J. F., 1949-54.

many infections were contracted in this way or from contacts at work. Six patients, including two teachers, appeared to have been infected at school, and in 18 cases (20%) the probable source of infection was another member of the family. The close association between upper and lower respiratory infections was confirmed, for 55 of the patients (68.8%) gave a history of an upper respiratory infection, either in the two weeks prior to the onset of their chest infection (43.8%) or occurring concurrently (25%). From the investigations undertaken, it was possible to demonstrate a specific bacterial aetiology in only 17.5%, and a viral aetiology in 18.8%. In most cases the cause was a non-specific catarrhal infection. Some cases may have been secondary to primary infection with the virus of the common cold, and others may have been febrile catarrh (Stuart-Harris *et al.*, 1938) or acute respiratory disease, A.R.D. (Commission on Acute Respiratory Diseases, 1947). These two names describe a similar condition which is caused by the R1-67 virus (Hilleman and Werner, 1954), type 4 of the adenoid-pharyngeal-conjunctival (A.P.C.) group of viruses (Huebner *et al.*, 1954). Although primarily a cause of upper respiratory catarrhs, these viruses may cause bronchitis and pneumonia, and when the tests for their presence are more widely available it will be of interest to investigate the frequency with which they cause respiratory infections in this country.

That many of the cases should prove to be non-specific catarrhal infections was not surprising. Even in a series of pneumonias studied at Hammersmith Hospital, Crofton *et al.* (1951) were unable to demonstrate a specific aetiology in 45%, of which 59.5% had received no chemotherapy before admission. Prompt chemotherapy, which is given in the majority of acute chest infections, may eliminate bacteria before they appear in sufficient numbers for detection by the methods available, or may suppress the secondary infection of catarrhal conditions. But, whatever the explanation, the results of this study showed that, even with careful investigation, a specific aetiology can be demonstrated only for the minority of acute respiratory infections encountered in general practice to-day, and that the majority are non-specific catarrhal infections of largely unknown aetiology.

**Clinical Classification**

Established practitioners evolve their own terminologies for describing the acute respiratory infections with which they deal, but the new entrant will certainly experience "perplexity . . . in trying to take the nomenclature of the laboratory and classroom into the maze of undiagnosed respiratory disease in his practice" (Spence *et al.*, 1954). In

view of the difficulties of clinical terminology, we classified our cases into one of three groups—"influenza with chest complications," "bronchitis," and "pneumonia"—and have given the criteria by which they were recognized. However, any such classification is certain to produce difficulties in deciding into which group a given case will fall, and this is paralleled by clinical practice, where a case which presents as one condition may by the following morning be clearly an example of another. But in the main there was a reasonable correlation between the separation of cases into three groups and the results of the investigations, and it appeared to be as simple and practical as any classification that we have seen proposed.

In the clinical classification, the importance and value of physical signs in the chest have been emphasized, although in recent years these have been subjected to criticism by the statistical studies of Fletcher (1952) and Schilling *et al.* (1955), who have shown the wide discrepancies which even expert physicians may make in their interpretation. The valuable work of these authors has emphasized the false claims or unwarranted deductions which a single observer may inadvertently make, and have shown that the discrepancy between two observers is greatest when assessing signs which lack clear definition. Our observations on physical signs were therefore all made by two observers, one of whom examined all the cases in the study, and we limited our records of abnormal signs to those that were definite.

The frequency and importance of abnormal physical signs were shown by their occurrence in 92% of the patients. Their distribution into the five groups already mentioned is shown in Table VI, where the relative incidence is com-

TABLE VI.—Analysis of Abnormal Physical Signs in Chest in 80 Cases of Acute Chest Infections Studied in the Winter of 1954-5 Compared with those in 270 Cases Seen Between 1950 and 1955

	80 Cases 1954-5, Adults Only	270 Cases 1950-5, All Ages
Consolidation . . . . .	5%	8%
Localized rales . . . . .	33.7%	52%
Diffuse bilateral adventitia . . . . .	47.5%	39%
Pleural rub only . . . . .	2.5%	1%
None . . . . .	11.3%	—*

\* This series was confined to cases with abnormal pulmonary signs.

pared with those found in the larger series of 270 cases observed by one of us (J. F.) over a five-year period. The figures from the two series are closely comparable and demonstrate the rarity of the signs of pulmonary consolidation in general practice to-day. These were present in only 5% and 8% of the two series, and in 11% of the radiologically proved pneumonias in the present study. The two most frequent groups of signs were an area of localized rales (33.7% and 52%) or generalized diffuse and bilateral adventitia of varying intensity (47.5% and 39%). The localized rales were persistent and usually maximal in one area only. The percussion note was sometimes impaired at the same site, and local radiological changes were present in 74%.

It is not as easy to elicit abnormal physical signs in a bedroom of traditional English winter temperature as in a well-heated hospital ward, but physical signs are a valuable aid to the practitioner in his diagnosis and management of acute chest infections. They may confirm his suspicion of pulmonary disease, though their absence does not exclude it, and they may give an indication of whether the inflammation is localized or diffuse. Their exact interpretation may be difficult without radiography, but in conditions such as pleurisy, bronchitis, and asthma physical signs may reveal more than a radiograph.

**Value of Investigations**

Investigations were primarily undertaken in this study to determine the aetiology of a random series of acute chest infections, and these results have been discussed. A

secondary aim was to observe which of the investigations were of greatest help to the practitioner in the management of these cases and any special problems related to their performance in general practice. The three basic investigations of an acute chest infection are a radiograph, sputum examination, and blood picture, all of which can be carried out, if necessary, by a practitioner who has access to pathological and radiological services at his local hospitals. In the present study a blood count proved to be of least practical value, since 72% had normal white-cell counts. Leucopenia is suggestive but not conclusive of virus infection, and in the proved virus infections studied was less common than a normal white count. A leucocytosis suggests a bacterial infection, and therefore antibacterial therapy will be helpful; but our numbers were not sufficient to show whether the acute chest infections with leucocytosis recovered more quickly if given antibacterial therapy than if they were not.

It is often preached but seldom practised that sputum should be examined from all cases of pneumonia in general practice, but in spite of attempts to obtain samples early in the course of disease, from all cases, our results were disappointing, and the results of attempted bacteriological isolations from other sources even less so. Sputum examination is among the easier examinations for a practitioner to undertake, but our findings emphasize that satisfactory samples will be received by the laboratory only if the practitioner collects and delivers them himself. But in busy winter months or in rural practice it is obviously impracticable for him to do this in all cases. Furthermore, the present results show that, even if adequate samples of sputum are examined, the results will often be negative for significant pathogens.

Radiographs of the chest were the most helpful of the investigations. In acutely ill patients, or where diagnostic doubt existed, a domiciliary radiograph was of great value and saved ill patients from journeys to hospital for either admission or out-patient radiography. But in most cases it is possible to defer radiography until the acute phase of illness has been passed and then arrange for a radiograph at a local hospital or chest clinic during convalescence. The percentage of cases in this study which had a domiciliary radiograph was higher than is normally necessary, but that measure was undertaken as part of the investigation. The importance and value of the practitioner's access to local radiological facilities is well shown in the field of acute infections of the chest, for it enables him to improve his standards of diagnosis and treatment, it reduces the need for hospital beds, and is a means for detecting early cases of tuberculosis and carcinoma. It was also apparent during the study that a more economical use of films is made than when comparable cases are treated in hospital.

Our conclusion was that a practitioner must rely on clinical judgment to decide which of his cases of acute infective chest disease merit careful investigation, for it is clearly impracticable and impossible for him to investigate them all. Of the investigations, radiography is the most informative, and there should be good reason for not arranging for a radiograph at some stage of illness in the type of case with which this paper is concerned.

### Treatment

The core of the problem of treatment of acute infective chest disease in general practice is deciding when antibacterial therapy should be given and, if so, in which form. It is not necessary or desirable to treat minor catarrhal infections which will recover without antibacterial agents, but a practitioner does not wish to prejudice his patient's recovery by failing to institute such treatment when necessary. It is therefore natural that the practitioner will err on the side of over-prescribing rather than under-prescribing, but the excess should not be an unreasonable one.

In most instances patients with acute infective chest diseases are treated at home. Of the present series only 5%, and in the larger series of 270 cases only 3.6%, were admitted

to hospital. The proportion of cases admitted in different areas will depend on the facilities for home care, local investigative facilities, and the medical needs for hospital treatment, but in the area of study the proportion is small. Examination of the cases of "pneumonia" admitted to local hospitals during 1954-5 revealed that failure to respond to initial chemotherapy in the home, or the need for special hospital care in severely ill patients, were the two chief reasons for which their admission to hospital had been requested.

Of the main therapeutic problems which confront a practitioner, the decision whether or not an antibacterial agent is required is more difficult to make than which particular antibacterial agent should be used. Once it has been decided to give antibacterial treatment, we believe that there are only a few exceptions to the principle that all should initially be treated with penicillin or sulphonamides, or sometimes a combination of both. Exceptions include those patients who are so severely ill when first seen that a tetracycline drug seems to be indicated and patients who have a previous history of sensitivity to penicillin or sulphonamides. It is difficult to give exact indications for administering antibacterial agents, and when doubt exists it is probable that a practitioner will administer rather than withhold them. In general, the decision has to be made in the first instance on clinical evidence, and it is for this reason that we have stressed here the clinical presentation of the cases. The severity of the illness is the factor which most often influences a practitioner in deciding whether to give antibacterial therapy, but the physical signs, nature of the sputum, etc., provide useful guides to its need. In only a small proportion of cases in this series was treatment influenced by the investigations, and among the reasons was that the results were not known to practitioners for at least three days, except in the case of domiciliary radiography, where an answer could be obtained within twenty-four hours or less of the patient's first being seen. In only two cases was the sputum examination of value in the decision upon treatment, and these were *H. influenzae* infections which had not responded to initial penicillin. In most cases either no pathogenic organisms were isolated or the patient was improving satisfactorily on treatment already instituted by the time a positive result was received.

The therapy given to the patients in this study was in no way controlled or modified for the purposes of the investigation, and each practitioner gave to his cases the treatment which he would normally have considered appropriate. When the results were analysed, the finding of greatest interest was that almost half of the cases (45%) had recovered satisfactorily with symptomatic treatment only (Table VII);

TABLE VII.—Treatment Given in 80 Cases of Acute Chest Infections in General Practice

Therapy	No.	%
Non-specific (symptomatic treatment only) .. .. .	36	45
Penicillin .. .. .	22	28
Sulphonamides .. .. .	9	11
Penicillin and sulphonamides .. .. .	1	1
Tetracyclines (first choice) .. .. .	4	5
.. (second " ) .. .. .	8	10
	80	100

40% had been given penicillin or sulphonamides, and one of the tetracycline group was administered in 15%. Of those given a tetracycline, this was the original choice in 5%, one of whom was a man with chronic bronchitis already on another member of the same group of drugs as a long-term prophylactic, and the second refused injections; in 10% tetracyclines were prescribed because of a failure to respond to penicillin or sulphonamides. Of the 36 patients given only symptomatic treatment, the majority were "influenza with chest complications" (15) or "bronchitis" (13), but the group included some of the mild "pneumonias" (8).

The use and abuse of antibacterial agents in general practice is a much-discussed topic of the present day, and their



role in the treatment of acute respiratory infections often arises. We have no evidence to show whether the recovery of those patients given symptomatic treatment only would have been hastened with antibacterial treatment, nor whether some of the treated patients would have recovered as quickly without. Such a decision could have been reached only by studying a larger number of patients with a planned therapeutic trial, an undertaking which would be difficult to carry out under the conditions of general practice.

### SUMMARY AND CONCLUSIONS

An account is presented of an investigation of 80 cases of acute infections of the chest, severe enough to confine the patients to bed at home, during the winter of 1954-5. The patients remained under the care of their practitioners and were investigated in their homes.

The difficulties of clinical nomenclature of acute chest infections are discussed and a simple classification, applicable to general practice, has been used to divide the cases into three clinical groups: "influenza with chest complications" (28%), "bronchitis" (20%), and "pneumonia" (52%). "Influenza with chest complications" was diagnosed only at times of known epidemic, and the main clinical distinction between "bronchitis" and "pneumonia" was the degree of constitutional disturbance, though cases with localized abnormal signs, irrespective of the degree of illness, were diagnosed as "pneumonia." Abnormal physical signs were present in 92% of the cases and their value in diagnosis and management is discussed.

As a result of detailed investigation, a specific bacterial aetiology was revealed for 17.5% and a viral aetiology for 18.8%, but the majority appeared to be non-specific catarrhal infections.

Radiography showed significant abnormalities in 45% of the cases, being highest (75%) in those with clinical "pneumonia."

Attempted bacteriological isolations were made from throat and pernasal swabs, sputum, and blood cultures, but, in spite of their collection early in the course of disease, positive isolations were made in only 16% of 212 samples, and in only 17.5% of the total number of cases were the results considered of aetiological significance. The pathogenic organisms most often isolated were *Str. pneumoniae*, *H. influenzae*, and *Staph. aureus* (coagulase-positive). No virus isolations were made from 67 gargles; examination of 70 pairs of sera showed diagnostic evidence of influenza B (8), influenza A (1), psittacosis (2), and elevation of the streptococcus MG titre in three cases with other evidence of virus pneumonia.

Routine haemoglobin estimations disclosed no cases of anaemia. Elevation of cold agglutinins to a significant titre was found only in patients with other evidence of virus pneumonia (though it is known that they may be raised in bacterial and other infections). Of 75 white-cell counts, 54 were normal, 3 were low, and 18 were raised. The three cases with leucopenia were all virus infections, but 12 other virus infections had normal white-cell counts.

No planned therapeutic trial was attempted, and each practitioner gave that treatment which he would normally have considered appropriate. It was found more difficult to decide which cases should be given antibacterial therapy than which antibacterial agent should be prescribed; once it had been decided to give antibacterial therapy there were few exceptions to the prac-

tice that all should first be given penicillin or sulphonamides. Symptomatic treatment only was given to 45% of the cases, 40% were given penicillin or sulphonamides, 5% had a tetracycline drug as the initial choice, and 10% were given a tetracycline drug after failure to respond to penicillin or sulphonamides. Of the cases 95% were treated at home.

There was a reasonable correlation between the initial clinical separation of the cases into the three main groups and the final diagnosis revealed by the investigations. Seven out of the nine proved cases of influenza were diagnosed clinically and the initial diagnosis of pneumonia was correct in 75% of those in whom it was radiologically proved. Of the proved pneumonias, 67.1% were non-specific aspiration pneumonias, the majority of which had been so diagnosed on clinical grounds.

The practical value of the investigations was small in comparison with the work involved in their execution. The most helpful measure was radiography, and the special value of domiciliary radiography in cases of diagnostic doubt or severe chest illness is stressed. Bacteriology was the second most helpful of the measures, although a high percentage of negative results were obtained. Although it involves extra labour for the practitioner, the only way to ensure that the laboratory receives a fresh and adequate sample of sputum for examination is for him to collect and deliver it himself. In those cases where pathogenic bacteria were isolated the patients were usually better from the treatment already given by the time the results were known; in only two instances, of *H. influenzae* infection, were the results of practical value as a guide to specific therapy. In a number of cases where the clinical response to antibacterial therapy appeared to be significant, the negative bacterial results might be considered to have indicated that that form of treatment was unnecessary; this may have been so in some instances, but in others it may have been due to a failure of technique in collecting and culturing the samples by routine methods.

The white-cell counts were of limited value, as 75% were within the normal range. The three cases with a leucopenia were all proved to have virus infections, but it was more common to find a normal count in those in whom the diagnosis of virus infection was later proved. Leucocytosis suggested a bacterial infection, but this was not always confirmed bacteriologically; it also suggested the cases which would benefit from antibacterial therapy, but our numbers were not sufficient to show whether the cases with leucocytosis recovered more quickly with antibacterial therapy than without it. The main value of the E.S.R., based on previous experience, rather than the results obtained in this investigation, was that persistent elevation after clinical recovery from an acute chest illness may be a useful pointer that the case requires careful investigation.

Virus tests were of the least practical value, mainly because the results are not known to a practitioner for at least four weeks from the start of the illness. They were, however, of clinical interest in the present investigation in proving the diagnosis of influenza in nine cases, revealing two unsuspected cases of psittacosis, and providing supportive evidence for the diagnosis of virus pneumonia.

We wish to express our thanks to the many people who made this investigation possible, particularly to the patients for their co-operation, and to their doctors, whose names have been given,

for the help they gave us and the detailed case records which they kept. To Dr. L. L. Griffiths and Dr. J. Keall and their technical staffs, especially Mr. W. J. Hatcher, we are indebted for the pathological investigations that were carried out at Farnborough, Bromley, and Beckenham Hospitals; and to Dr. A. C. Glendenning and his staffs at Bromley and Beckenham Hospitals for the radiology. We are grateful to Dr. E. R. Mitchell for help with the transport of the garglings and to Dr. L. A. Hatch, of the Virus Reference Laboratory, Central Public Health Laboratory, Colindale Avenue, for the virus studies. For help with the preparation of the manuscript we wish to thank Dr. N. S. Plummer. The work was carried out while one of us (A. B. S.) held the appointment of senior medical registrar in the Bromley Group, made jointly by Guy's Hospital and the South-east Metropolitan Regional Hospital Board.

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## ARGENTAFFIN CARCINOMA OF ILEUM WITH RAISED SERUM 5-HYDROXYTRYPTAMINE

### REPORT OF A CASE

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Gastro-intestinal argentaffin carcinoma has lately been recognized as an endocrine growth which may cause flushing attacks and cyanosis, and perhaps stenosis of the pulmonary valve of the heart. The existence of this syndrome was suggested by Biörck *et al.* (1952), who described the post-mortem discovery of argentaffin carcinoma of the ileum in a patient who had complained of cyanosis, flushing attacks, dyspnoea, abdominal pain, and diarrhoea, and who had a pulmonary valvular stenosis. In the same year similar features were recognized by Waldenström and Ljungberg in a patient who had had an argentaffin carcinoma excised in 1944, and by Björkman in another case at necropsy. The observation of changes in skin colour and of flushing attacks led to laparotomy in two further patients, and argentaffin carcinoma was found. To a

detailed description of these five cases Thorson *et al.* (1954) have added one from their hospital records and have considered three described by Isler and Hedinger (1953), two by Rosenbaum *et al.* (1953), and five reports from earlier literature. Other probable cases have been described after death by Ratzenhofer and Lembeck (1954), Branwood and Bain (1954), Jenkins and Butcher (1955), and Fraser (1955), while Page *et al.* (1955) mention a patient with characteristics of the same syndrome.

We have recently encountered a patient in whom, following resection of a stenosing tumour of the ileum, the probable histological diagnosis was postulated on the basis of the reddish-blue colour of the patient's skin. Affinity of the tumour cells for silver was not demonstrated, but we believe that the finding of raised levels of serum 5-hydroxytryptamine (5-H.T.) and urinary 5-hydroxyindoleacetic acid (5-H.I.A.A.) confirms that the tumour originated from argentaffin cells.

### Case Report

A man aged 23 was admitted to hospital in January, 1955, with intestinal obstruction and a history of flushing attacks and cyanosis.

*Skin Colour.*—Since the age of 18 years his face had become red. It felt warm during almost every meal, and this flushed feeling usually subsided in about half an hour. In the past year there had also been some blueness of the face and hands out of doors, and he attributed this to the cold. He had become used to his colour, which caused him no concern. On examination at rest the face was red with a bluish tinge. Dilated capillaries were easily seen with the aid of a loupe. There was no clubbing of the fingers.

*Abdominal Condition.*—For ten months he had suffered repeated bouts of spasmodic central abdominal pain lasting about 24 hours, and accompanied by vomiting. At these times he could palpate a swelling in the lower abdomen and could feel it move. The attacks would often subside after a series of loose black stools, but there was no diarrhoea at other times. There had been some flatulence and borborygmi, and heartburn had been troublesome. His appetite was fair and he was not aware of any change in weight. For two weeks before admission he had suffered pain every day, and in the last 36 hours he had vomited repeatedly. On examination there was no abdominal distension. During a spasm of pain a tender, mobile, sausage-shaped swelling was palpated in the hypogastric region, and there was transient visible peristalsis in the same area. When the spasm had subsided the abdomen appeared normal.

Laparotomy revealed a stricture of the ileum 60 cm. from the ileo-caecal valve, associated with contracted mesentery containing two enlarged lymph nodes. In the liver were numerous hard nodules up to 2 cm. in diameter. The thickened mesentery and glands were excised with the stricture, and continuity of the ileum was restored by side-to-side anastomosis.

### Investigations

*Pathology.*—The specimen consisted of a segment of small intestine with obstruction caused by a ring stricture. Above this there was distended loop of hypertrophied ileum, and below was a segment of collapsed bowel. In the adjacent mesentery the lymph nodes were enlarged and had obviously been invaded by secondary tumour. Microscopically the muscle wall was invaded by sheets of eosinophilic cells with poorly demarcated outlines and pale-staining nuclei with a well-marked membrane. In some areas a pseudo-adenomatous arrangement was present (see Fig.). The sections resembled Kultschitzky-cell carcinoma more closely than adenocarcinoma, but affinity of the cells