Thorax (1968), **23**, 451.

Farmer's lung

A clinical, radiographic, functional, and serological correlation of acute and chronic stages

E. J. HAPKE, R. M. E. SEAL, AND G. O. THOMAS, WITH M. HAYES AND J. C. MEEK

From Sully and Machynlleth Chest Hospitals

In assessing patients suffering from farmer's lung, the acute stage must be distinguished from the chronic stage of the disease. The conspicuous radiographic signs in the acute farmer's lung episode and the often dramatic clearing make an important contribution to the diagnosis. The radiographic changes in chronic farmer's lung are not specific and cover a wide range of appearances. Even minor nodular changes are significant. Farmer's lung, acute and chronic, is not a disease predominantly characterized by a defect in gas exchange. During the acute illness the reduction in diffusing capacity is often accompanied by a decrease in lung volumes; the pulmonary function profile of the chronic stage is variable. In only a relatively small proportion of chronic farmer's lung patients does a defect in gas exchange predominate, and in some it may be manifest only during exercise. Airway obstruction is a feature of chronic farmer's lung. In chronic farmer's lung patients discrepancies between the severity of complaints and results of pulmonary function tests are not infrequent. In some patients with considerable disability conventional pulmonary function studies may demonstrate little or no impairment of the functions measured. In patients suffering from an acute farmer's lung episode, serological tests should be positive, possibly in high titre. In the chronic stage of the disease the chance of finding positive serology in a patient diminishes with the length of time elapsed since the last acute episode. The period of serological transition appears to be the third year.

Farmer's lung is now a well-recognized clinico-pathological entity. In 1964 it was, in the United Kingdom, recommended for prescription as an occupational disease under the National Insurance (Industrial Injuries) Act, 1946, and this was put into effect in June 1965. For this purpose farmer's lung is defined as: 'pulmonary disease due to inhalation of the dust of mouldy hay or of other mouldy vegetable produce, and characterized by symptoms and signs attributable to a reaction in the peripheral part of the bronchopulmonary system and giving rise to a defect in gas exchange' (Ministry of Pensions and National Insurance, 1964).

This definition is clearly intended to cover the chronic as well as the acute stage of farmer's lung. Though the chronic stage was mentioned as early as 1932 by Campbell, and by Fuller in 1953, most of the publications on farmer's lung are concerned mainly with the acute stage of the disease. Up to date, no attempt has been made to study a large group of patients in order to define the features of the chronic stage of farmer's lung so that they may be distinguished from the acute manifestations which follow recent exposure.

The purpose of this study is to clarify the relationship between the acute attack and the chronic disease, and to demonstrate the range of clinical, radiographic, lung function, and serological findings in both stages of farmer's lung.

MATERIAL

Two hundred and forty-five patients diagnosed as farmer's lung at Machynlleth Chest Clinic in Wales provided material for our study. They represented the total number of farmer's lung patients registered at this Chest Clinic, which serves a population of 90,000 in a rural area of 1,600 square miles (Fig. 1). Fourteen of these patients were diagnosed before 1954, during a period when the disease was generally not a well-recognized entity. Table I shows the annual incidence of new cases from 1941 to 1965; Fig. 2

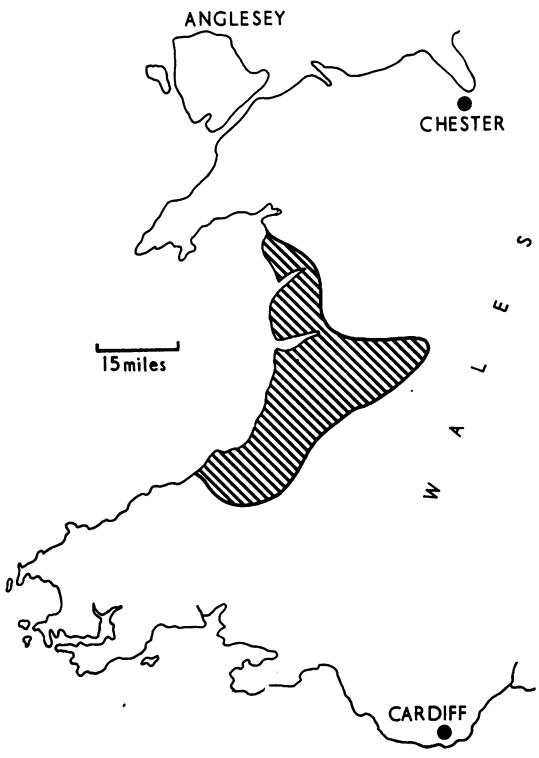


FIG. 1. *Map of Wales. Dark shading represents Machynlleth Chest Clinic area.*

illustrates the months in which these patients first reported to the Chest Clinic. Both the annual and seasonal incidences are similar to those reported by Staines and Forman (1961).

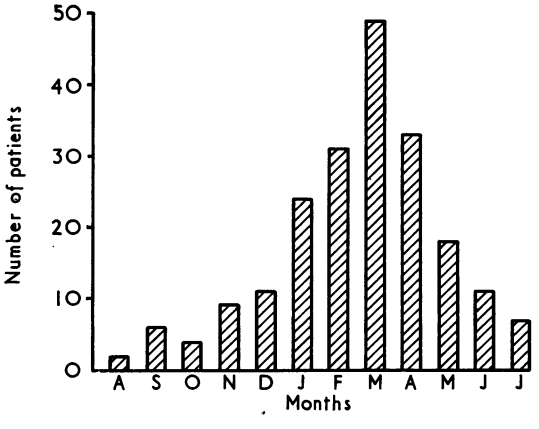


FIG. 2. *Monthly incidence of new cases of farmer's lung at Machynlleth Chest Clinic, 1955–65.*

TABLE I

ANNUAL INCIDENCE OF NEW CASES

Year	No. of Cases
1941–53	14
1954	33
1955	15
1956	6
1957	18
1958	9
1959	39
1960	11
1961	10
1962	16
1963	32
1964	24
1965	18

After reviewing the history and radiographs of the 245 farmer's lung patients, which we shall refer to as the 'pool', 34 patients were selected for detailed investigation. In the selection of these patients their clinical history and radiological findings were the major factors considered, as this group was intended to cover the range of sequelae known to have occurred from one or more acute farmer's lung episodes in our pool of farmer's lung patients. Other circumstances, however, also influenced the selection, such as the willingness and ability of the patient to leave his farm for the few days necessary for this investigation. Therefore, no attempt at proportional representation of the spectrum of clinical features could be made in this group. For example, 71 patients in the pool had suffered one attack only, with no remaining symptoms. Only three of these patients were chosen for intensive study.

All 34 patients selected had been diagnosed as farmer's lung in previous years and were not in an acute episode when, for the purpose of this study, they were admitted to Machynlleth Chest Hospital during February or March 1965. These patients will be referred to in this report as the 'chronic group', although some of them were asymptomatic.

During the two-month period required for study of the chronic group, 11 new patients presented at Machynlleth Chest Hospital and Clinic with symptoms of acute farmer's lung. These new patients were also studied intensively at the time of their first presentation and at intervals over an 11-month period. These patients are designated the 'acute group'.

Within a week of the first clinic visit of these acute patients, one of the investigators visited their farms, obtained a sample of the offending hay, and interviewed all persons over 10 years of age living or working on the farm and being exposed there to the same risks as the patient. Forty-five such per-

sons were interviewed; three of them gave a history strongly suggesting farmer's lung disease, and were excluded from the study. The remaining 42 persons who had no symptoms form the group referred to as 'co-workers'.

Lastly, 355 registered blood donors from urban areas of South Wales were used as 'controls' for serological investigations only. This group was chosen as it was unlikely to include farmer's lung patients or even subjects likely to have been in contact with mouldy hay.

Thus, the groups forming the material for our study are as follows:

1. Pool: 245 patients, the total number diagnosed as farmer's lung at Machynlleth Chest Clinic between 1941 and 1965;
2. Chronic group: 34 patients, selected from the pool for intensive study, not being in a current acute episode;
3. Acute group: 11 patients, presenting for the first time to the Chest Clinic suffering from acute farmer's lung;
4. Co-workers: 42 persons exposed to a farmer's lung environment but without evidence or history of farmer's lung illness;
5. Controls (for serological purposes only): 355 blood donors from urban areas of South Wales.

METHODS

HISTORY AND CLINICAL EXAMINATION All patients in the acute and chronic groups were interviewed and examined independently by two of the investigators. The history was taken according to a questionnaire, which was designed to investigate:

1. The duration of illness and number of acute farmer's lung episodes which had occurred in the past;
2. The mode of onset and the character of acute symptoms following exposure;
3. The state of health between farmer's lung episodes; if any symptoms, their nature;
4. The state of health before the onset of any farmer's lung symptoms, *e.g.*, history of asthma, pneumonia, chronic cough, etc.;
5. The smoking habits, which were then recorded according to gradings recommended by Doll and Hill (1950) and Higgins (1959); and
6. The degree of the patient's disability at the time of examination. This was based on statements of the patient regarding his ability to perform the daily work on the farm normally expected of him. The grading is not necessarily that of the dyspnoea on exertion, as this was not the only stated cause for disability. The grading was as follows:

Mild—if the patient was able to continue farm work but had to avoid heavy tasks, *e.g.*, heavy lifting;

Moderate—if the patient continued on the farm performing light duties only, and at a slow pace;

Total—if the patient was unable to perform any physical work.

Table II is a descriptive clinical classification for acute patients based on the results of our questionnaire. Table III is a similar classification for chronic patients. Clinical possibilities not encountered in our group of patients studied are not depicted in Table II or III; for example, a solitary episode can lead to permanent symptoms, was not encountered in our chronic group, and therefore

TABLE II

CLINICAL FEATURES OF ACUTE PATIENTS

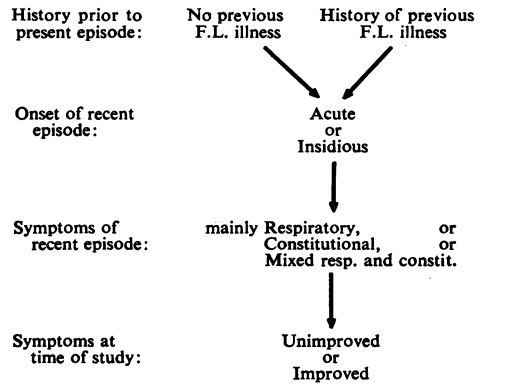
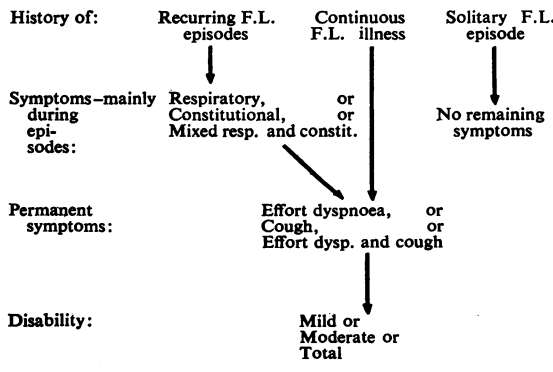


TABLE III

CLINICAL FEATURES OF CHRONIC PATIENTS



is not depicted in Table III. Each of our patients could thus be categorized clinically for the purpose of this investigation.

The chronic patients were examined on one occasion only. The acute patients were reassessed 10 days, 40 days, six months, and 11 months after the initial examination.

Each examination consisted of a history, physical examination, a postero-anterior chest radiograph, pulmonary function studies, and serological studies.

Ten of the 11 acute patients were treated with corticosteroids immediately after the initial study (prednisolone, 40 mg. for 10 days, 30 mg. for the second 10 days, and 10 mg. for a further 40 days, followed by a slow withdrawal over two weeks). One patient had recently suffered from peptic ulcer and was therefore not treated with corticosteroids.

In the evaluation of the co-workers a similar, though somewhat less detailed, questionnaire was used in obtaining the history, and a sample of blood was taken for serological investigation.

RADIOLOGY From observations made by the investigators on chest radiographs of the patients in the pool and farmer's lung patients previously seen from other areas of Wales, a radiographic classification was devised (Table IV).

TABLE IV

RADIOGRAPHIC CLASSIFICATION OF FARMER'S LUNG

O—Normal	
A 'miliary appearance' 1 minimal 2 definite 3 marked	C 'fibrotic changes' 1 fine diffuse 2 slightly deforming 3 grossly deforming

The following are details for reading films according to this classification:

A1. Abnormalities so slight that they would be passed as within normal limits by a clinician or radiologist not alerted by the clinical history to the possibility of farmer's lung.

A2. Definite change ; discrete, sharply defined, punctiform, or so fine as to be ground-glass in appearance (Figs 3a and b).

A3. Changes similar to A2 with additional poorly defined 'soft' opacities which become confluent in places, predominantly in the middle and lower zones. The normal sharp definition of the pulmonary vessels is reduced and soft Kerley B and C lines may be present (Fig. 4).

C1. Reticular and diffuse, fine, linear or peripheral, ill-defined, nodular opacities of varying size (Fig. 5).

C2. Coarse linear opacities, radiating from the hila. There may be slight contraction of one lobe.

C3. Coarse linear opacities, small cyst formation, and deformity due to contractions of lung often mainly in the upper lobes and apices of the lower lobes. Areas of increased translucency in the lower lobes. Sometimes enlarged right ventricle and main pulmonary arteries suggesting associated cor pulmonale (Fig. 6).

Type A changes ('miliary appearance') usually are associated with acute clinical disease, and type C ('fibrotic') changes with the chronic stage of farmer's lung. Where a miliary appearance persists for more than one year, experience has shown that resolution will not occur and such cases will ultimately progress to type C chronic changes. Such films may be classified B. The place of these changes in the radiology of farmer's lung will be discussed later.

One of the authors (J. C. M.) read the radiographs of all patients in the pool according to this classification. The findings in the 34 selected chronic patients were then separated and compared to the overall findings in the pool. This enabled us to assess the position of the chronic group in the pool with regard to the severity and chronicity of the radiological abnormalities. In addition to the reading by the above-mentioned author, the films of patients in the chronic and acute groups were also read by two other authors (E. J. H. and G. O. T.) and independently graded by them according to the above classification. There was good agreement between the three observers, except for occasional differences in opinion between grades A2 and A3, and less often between C1 and C2.

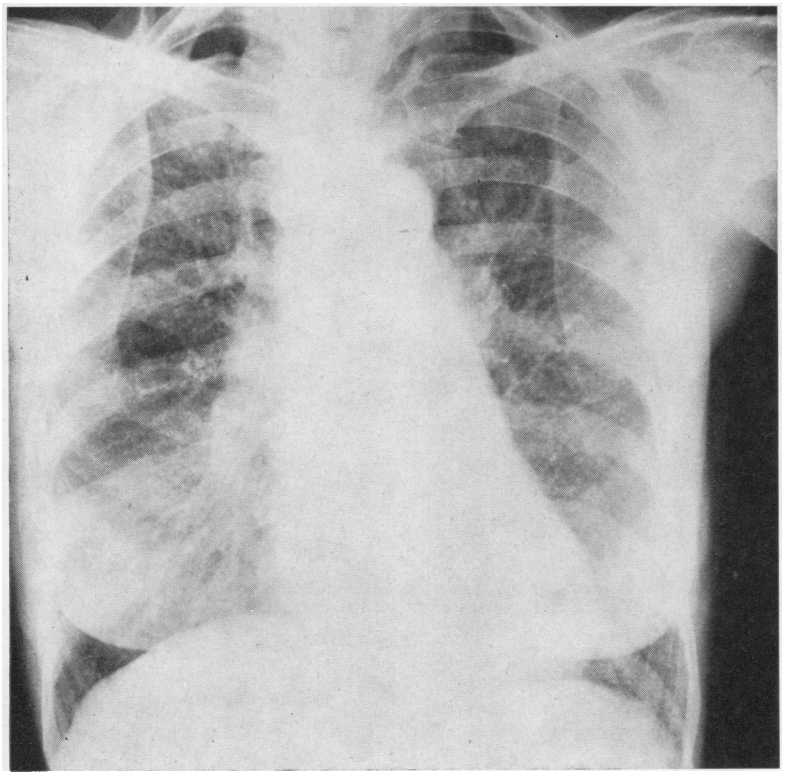
PULMONARY FUNCTION Pulmonary function studies performed on acute and chronic patients during February and March 1965 were carried out at Machynlleth Chest Hospital, using equipment transferred from Sully Hospital (Wales). For subsequent tests the same equipment was used at Sully Hospital.

The following pulmonary function studies were performed[1 2]:

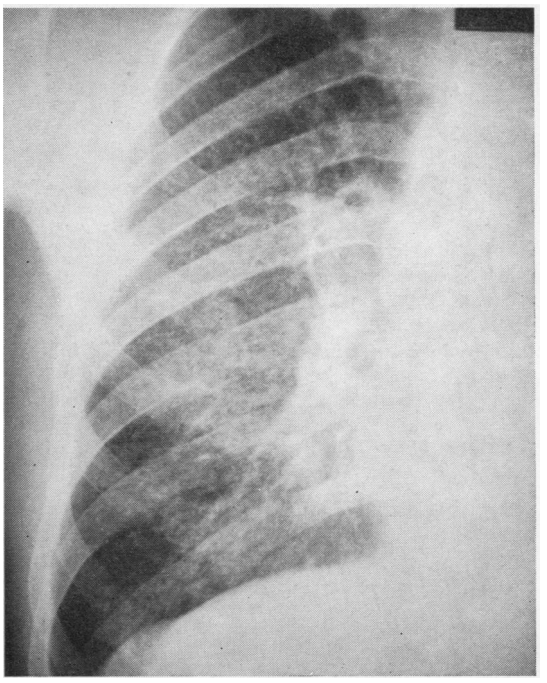
1. Lung volumes: the functional residual capacity (F.R.C.) was determined by the closed-circuit helium dilution method (Gilson and Hugh-Jones, 1949). The other compartments of the total lung capacity were measured from a spirogram (normal values for lung volumes used: Needham, Rogan, and McDonald (1954)).

[1] All pulmonary function tests were carried out with the patient in the sitting position.

[2] Together with the F.E.V.$_{1.0}$ the results of these tests were used to assess airways obstruction. As there was good correlation between all four tests, the results of F.E.V.$_{1.0}$ alone are reported in this paper as an indication of airways obstruction.



(a)



(b)

FIG. 3. (a) *Moderate acute changes. Grade A2.* (b) *Similar change demonstrated by macroradiography.*

2. Forced vital capacity (F.V.C.): determined with a low inertia spirometer. F.E.V.$_{1\cdot0}$ was measured and reported as a percentage of the total F.V.C. (normal range of F.E.V.$_{1\cdot0}$ = >70% of F.V.C.).

3. Maximum voluntary ventilation (M.V.V.): measured during a 15-second period at a rate chosen by the patient, usually in the range between 50 and 60 breaths per minute.[2]

4. Maximal expiratory flow (M.E.F.) and maximal inspiratory flow (M.I.F.): measured with a Fleisch pneumotachograph and a differential manometer.[2]

5. Pulmonary diffusing capacity for carbon monoxide (DLco): determined by a modification of the breath-holding technique of Ogilvie, Forster, Blakemore, and Morton (1957). Formula for normal values used:

$$DL = [(\text{surface area in m.}^2) \times (18{\cdot}84)] - 6{\cdot}8$$

Ogilvie *et al.* (1957).

6. Pulmonary compliance, dynamic (as ratio of change in volume to change in oesophageal pressure): A 15-cm. thin-walled latex balloon fixed around a polyethylene tube was placed in the lower third of the oesophagus (Fry, Stead, Ebert, Lubin, and Wells, 1952). The patient was breathing at a rate between 20 and 24 breaths per minute, using about the lower third of his inspiratory capacity. Pressure and volume changes were recorded as differences in the

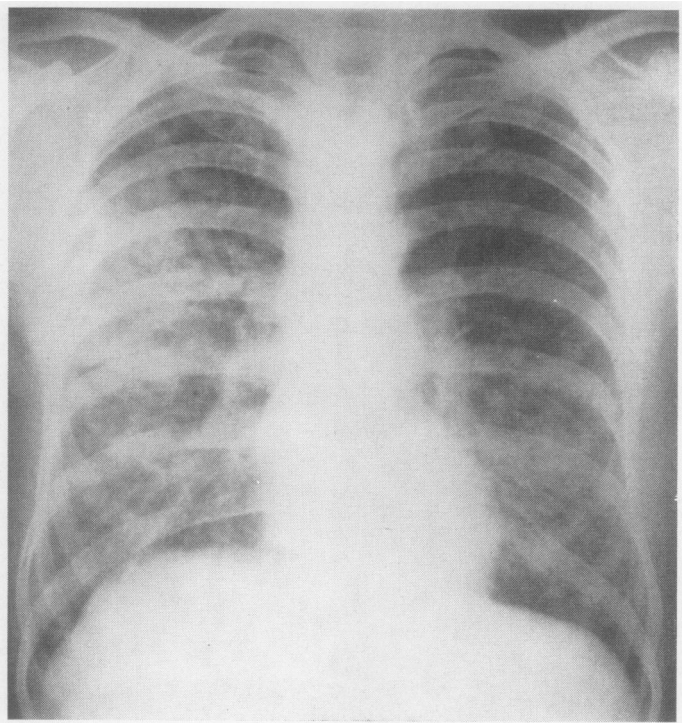


FIG. 4. *Severe acute change with additional signs indicating pulmonary oedema and alveolar exudate.*

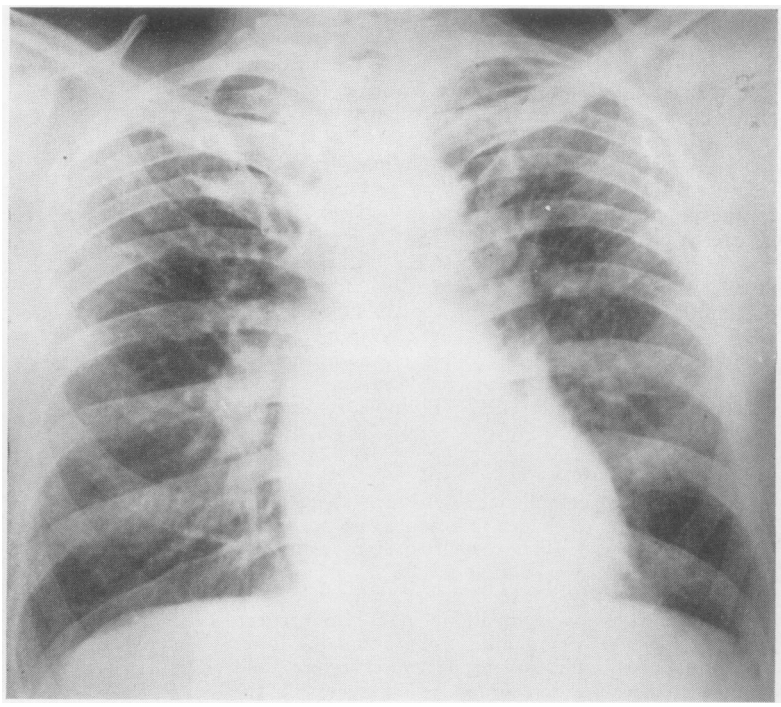


FIG. 5. *Reticular and diffuse nodular signs, the first evidence of chronic change.*

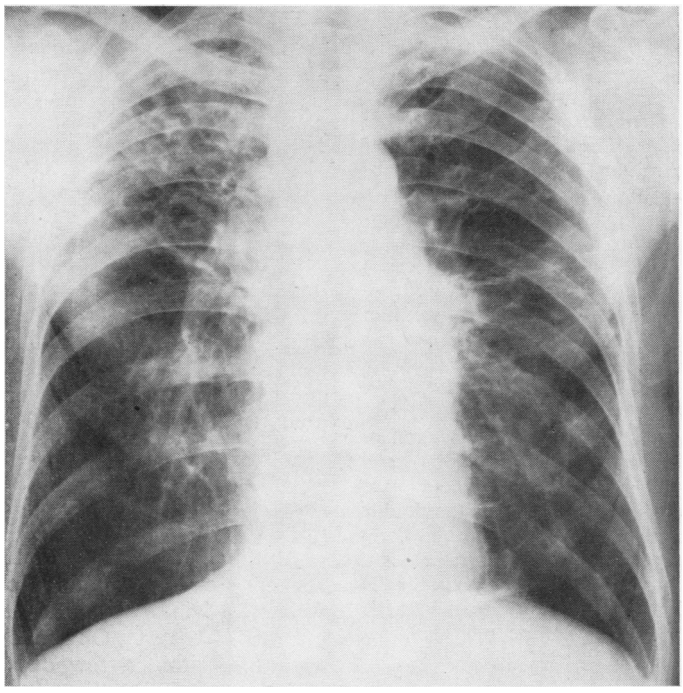


FIG. 6. *Coarse linear opacities and contracted upper lobes due to fibrosis of advanced chronic change.*

respiratory cycle between points of flow conversion. The mean of at least 12 measurements of respiratory cycles was used as the reported value for each patient. The pressure changes were recorded on an A.C. capacitance bridge transducer; simultaneous change in volume was measured using the above-mentioned spirometer.

Normal values used: compliance (l./cm. H_2O) = 0·5 × actual F.R.C. (l.) (Marshall, 1957).

7. Arterial blood gases (oxygen content and capacity, CO_2 content): determined by the method of Van Slyke and Neill (1924). *p*H and $Paco_2$ were measured by an E.I.L. 48B blood *p*H meter and a Pco_2 electrode system (Severinghaus).

On all patients in the acute group (at the six months' follow-up), and on a number of chronic patients, measurements of pulmonary diffusing capacity were made during exercise at various work-loads using a hyperbolic bicycle ergometer. During the performance of these tests electrocardiographic tracings were taken and samples of arterial blood were obtained for gas studies.

SEROLOGY The following procedures were carried out on the sera of acute and chronic patients:

1. Agar-gel double diffusion studies using (*a*) aqueous extracts of two mouldy hays; extracts of the culture fluid from (*b*) *Thermopolyspora polyspora*,[1] (*c*) *Actinomyces* sp. I.M.I. 45560, and (*d*) *Aspergillus fumigatus* I.M.I. 48340; and (*e*) aqueous extracts of 12 additional hays obtained from farms of acutely ill farmer's lung patients.

2. Immuno-electrophoretic studies using one hay extract and the *T. polyspora* antigenic extract.

3. Serial two-fold serum dilution tests using the hay and *T. polyspora* antigens.

The serum of chronic patients was tested once, at the time of the patient's clinical examination; in acute patients these tests were repeated at the above-mentioned intervals.

The serum of co-workers was subjected to the same agar-gel double diffusion and immuno-electrophoretic studies as that of the patients. Serial two-fold serum dilution tests, however, were performed using *T. polyspora* antigen alone, and only on sera reacting to *T. polyspora*.

The 355 sera of the controls were tested by the double diffusion technique according to procedure 1a, b, c, and d; sera reacting to hay and *T. polyspora* extracts were then subjected to immuno-electrophoretic studies according to procedure 2. In 100 of the control sera, double diffusion tests were performed using the 12 additional hay extracts (procedure 1e).

[1] This organism is now renamed *Micropolyspora faeni*.

Aqueous extracts were prepared by defatting mouldy hay in ether, followed by extraction in Coca's solution. The extract was then concentrated by dialysis in Carbowax, dialysed overnight in running water, Seitz-filtered, and freeze-dried or dehydrated over phosphorus pentoxide. The freeze-dried material was dissolved in sterile saline to give a final concentration of 100 mg./ml.

The fluids from cultures of *T. polyspora*, *Actinomyces* sp., and *A. fumigatus* were Seitz-filtered, concentrated, and freeze-dried. The freeze-dried material was dissolved in sterile saline so that the final concentration was 10 mg./ml. One millilitre of a 1% solution of sodium azide was added to 20 ml. of the extracts as a preservative. When not in use the extracts were stored at 4° C.

Agar-gel double diffusion and immuno-electrophoretic studies were carried out by a modification of the methods described by Ouchterlony (1953) and Grabar and Williams (1953).

The hay extracts were diluted 10-fold for the double diffusion studies but used in more concentrated form (100 mg./ml.) for the immunoelectrophoretic tests. Plates were read after incubation at 4° C. for 24 hours. Only the precipitin lines that remained after staining with aqueous Ponceau S were recorded.

RESULTS

ACUTE GROUP

Clinical features Table V presents the clinical features of the acute patients together with their pulmonary function findings on initial examination.

The onset of the acute episodes was classically sudden in five and insidious in six patients. We do not feel that for the purpose of our study a designation of the latter six as 'subacute' is desirable, since they did not differ either in severity or in type of symptoms from the other patients. None of the 11 patients complained solely of respiratory or solely of constitutional symptoms. Five patients experienced mainly respiratory symptoms ('tightness' or 'fullness' in the chest, dyspnoea on exertion, and occasional dry cough), and in six patients both respiratory and constitutional symptoms were equal in severity. Constitutional symptoms complained of were malaise, shivering, sweating, anorexia with nausea and vomiting, weakness and prostration, and anxiety.

Four of the acutely ill patients gave a history of previous farmer's lung episodes, and two of these (D. B. and D. D.) had residual permanent respiratory symptoms.

At the initial examination fine to medium inspiratory crackling sounds over both lung bases were heard in 10 patients, and in two there was cyanosis at rest. On follow-up, cyanosis disappeared within a few days, and these crackles had cleared in all patients at the 40-day follow-up examination.

Radiographic findings As seen in Table VI, 10 of the acute patients showed 'miliary' abnormality (type A changes) in their initial chest radiograph. The films of patient D. D., who was known to have had one previous farmer's lung attack,

TABLE V

CLINICAL FEATURES AND RESULTS OF INITIAL PULMONARY FUNCTION TESTS IN ACUTE PATIENTS

Patient	Age	Sex	Farming Prior to Illness (yrs)	Duration (weeks) of Illness Prior to Study	Clinical Classification of Recent Episode				Results of Pulmonary Function Tests					
					Past F.L. History	Type of Onset	Type of Symptoms	Status of Symptoms	V.C. (% of normal)	R.V. (% of normal)	$\frac{F.E.V._{1.0}}{F.E.V.} \times 100$	D_{LCO} (% of normal)	Compliance (l./cm. H_2O)	Sa_{O_2} (rest)
R.T.B.	48	M	10	8	N	b	r+c	u	99	132	81	113	0·19	96
G.E.D.	48	M	*	7	N	a	r	u	111	87	77	94	0·09	93
D.M.E.	45	M	*	4	N	b	r+c	u	94	101	79	110	0·16	92
J.E.M.	17	M	2*	3	N	a	r	u	68	102	86	50	0·09	96
D.H.O.	33	F	*	7	N	b	r	u	48	138	89	79	0·18	82
E.J.W.	49	M	*	8	N	a	r+c	u	76	120	66	74	0·22	91
W.M.J.	42	M	*	3	N	a	r	u	71	150	68	96	0·18	90
D.B. ..	50	M	*	5	R	b	r		63	97	81	67	0·07	85
D.D. ..	61	M	*	6	R	b	r+c		80	116	76	105	0·25	93
E.M.E.	58	F	*	11	R	a	r+c	i	96	134	83	43	0·06	87
M.M.H.	52	F	27	3	R	b	r+c	u	127	139	74	66	0·26	92

Explanation of symbols

* Years of farming = all of patient's working life.

2* = worked for two years, but grew up on farm.

Clinical classification: past F.L. history, N = no previous F.L. illness; R = previous F.L. illness. Type of onset, a = acute; b = insidious. Symptoms, r = mainly respiratory; c = mainly constitutional; r+c = mixed, respiratory and constitutional. Status of symptoms, u = unimproved; i = improved.

Predicted V.C. according to Baldwin, Cournand, and Richards.

Predicted D_{LCO} = (surface area × 18·85) - 6·8.

TABLE VI

RADIOGRAPHIC PROGRESS OVER 11-MONTH PERIOD OF OBSERVATION IN ACUTE PATIENTS

Patient	Initial	10 days	40 days	6 months	11 months
R.T.B.	A2	A1	—	—	A1
G.E.D.	A2	A2	A2	0	0
D.M.E.	A2	A1	—	0	0
J.E.M.	A2	A1	A1	0	0
D.H.O.	A2	A2	—	0	0
E.J.W.	A1	—	A1	A1	—
W.M J.	A2	—	A2	A1	0
D.B.	A2	A2	A2	A1	C1
D.D.	C1	C1	—	C1	C1
E.M.E.	A2	A2	A1	A1	A1
M.M.H.	A2	A1	A1	0	0

For explanation of symbols see Table IV.

showed fine, diffuse, 'fibrotic' changes. His mild, acute symptoms at the time of study had not produced any recognizable superimposed acute radiographic signs. At the end of the follow-up, films were normal in six patients, one of whom had a history of farmer's lung illness prior to the current episode; two patients continued to show minimal 'miliary' abnormalities. The remaining two patients showed fine diffuse 'fibrotic' changes. These were the two patients with residual permanent symptoms from previous farmer's lung episodes.

Pulmonary function Initial pulmonary function studies (Table V) revealed reduction in vital capacity in six patients[1]; spirometric studies revealed in two patients evidence of mild airway obstruction. Diffusing capacity was decreased in six patients,[2] but in four of them it was in fair proportion to the reduction in vital capacity. Only in patients E.M.E. and M.M.H. was the diffusion defect considerably greater. A decreased compliance[2] was observed initially in five patients; in four it was moderate, and in the other patient of mild degree.

Figure 7 demonstrates the course of vital capacity, diffusing capacity, and compliance over the 11 months of observation. During this period vital capacity returned to normal in all but two patients, with most of the improvement occurring between the first and second assessments, which encompassed the first 10 days of steroid therapy.

The improvement observed in diffusing capacity was similar, the greatest increase coinciding with improvement in volume. At the end of the 11-month period the diffusing capacity remained subnormal in only two patients, one of whom also had a subnormal vital capacity (patient D. B.).

[1] Values above 85% of the predicted value were considered within normal range.

[2] Values above 80% were considered within normal range.

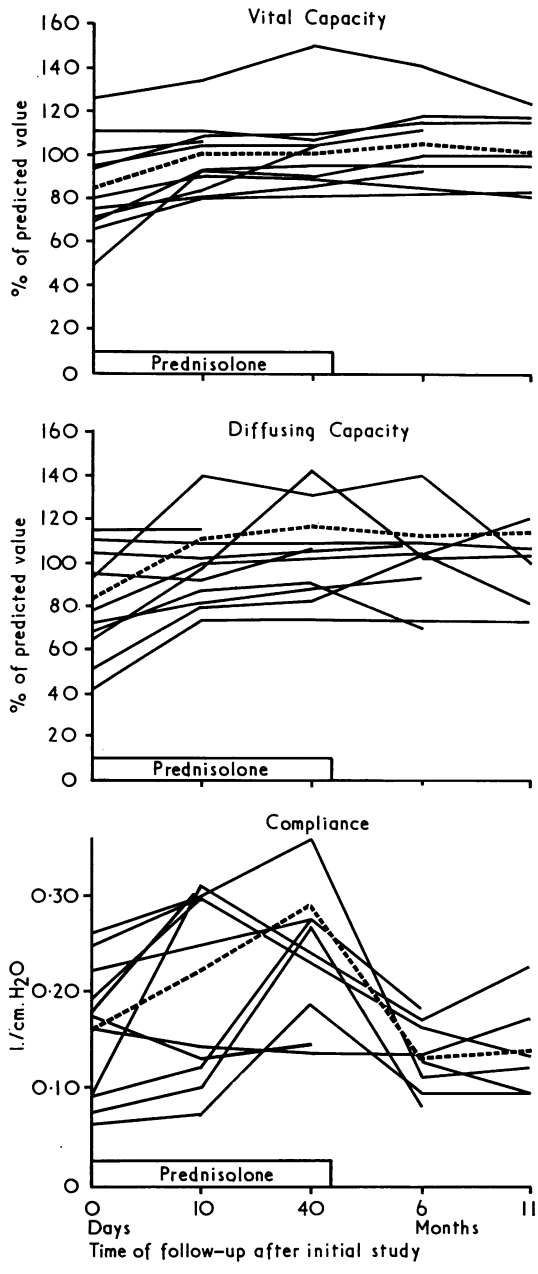


FIG. 7. *The course of vital capacity, diffusing capacity, and compliance over the 11 months of observation.*

As demonstrated in Fig. 7, there was improvement in compliance during the period of steroid treatment, but this was not maintained after cessation of treatment. At the end of the follow-up period pulmonary compliance was below 80% of

the predicted value in five patients, values being less than 60% of predicted in three of them.

At the initial examination oxygen saturation of arterial blood at rest was near cyanosis level in two patients (85% and 82%), and $Paco_2$ was low in all patients. Both the blood gases returned to normal values within 10 days. The subnormal $F.E.V._{\cdot 1 \cdot 0}$ in one patient returned to normal value at the 10-day follow-up; the value of the other patient remained unchanged.

Both patients in whom lung volume remained low, the one patient whose diffusing capacity alone remained subnormal, and three of the five patients whose compliance was still decreased at the end of the follow-up had suffered from farmer's lung illness prior to their recent acute episode.

SEROLOGY The results of agar-gel double diffusion studies on the sera of the acute patients are shown in Table VII.

TABLE VII

SEROLOGICAL PROGRESS OVER 11-MONTH PERIOD OF OBSERVATION IN ACUTE PATIENTS

Patient	Antigen	Initial	10 Days	40 Days	6 Months	11 Months
R.T.B ..	TP	1/8	1/8	—	—	1/16
	Hay	1/4	1/4			1/16
G.E.D. ..	TP	1/2	1/4	1/1	1/1	1/1
	Hay	1/2	1/2	1/1	1/2	1/1
D.M.E...	TP	1/4	1/1	—	—	1/2
	Hay	1/4	1/2	—	—	1/1
J.E.M. ..	TP	1/16	1/32	1/16	1/2	1/2
	Hay	1/2	1/4	1/2	1/2	1/2
D.H.O...	TP	1/16	1/8	—	1/4	1/2
	Hay	1/8	1/4	—	1/4	1/1
E.J.W. ..	TP	1/8	—	1/2	1/2	—
	Hay	1/8	—	1/2	1/2	—
W.M.J...	TP	1/32	1/8	1/16	—	—
	Hay	1/32	1/8	1/8	—	—
D.B. ..	TP	1/1	1/1	1/1	1/1	1/2
	Hay	1/2	1/1	1/1	1/1	1/2
D.D. ..	TP	1/2	1/2	—	1/2	1/2
	Hay	1/2	1/2	—	1/2	1/2
E.M.E...	TP	1/16	1/8	1/8	1/8	1/4
	Hay	1/2	1/1	1/2	1/2	1/2
M.M.H.	TP	1/2	1/2	1/1	0	0
	Hay	1/2	1/2	1/2	1/2	1/2

Serial two-fold serum dilution technique. TP = *T. polyspora*.

All patients reacted to *T. polyspora* at initial testing. The titres obtained by serial two-fold serum dilution were, in the main, higher for *T. polyspora* than those for hay. Over the period of follow-up a remarkable stepwise drop in the titres for *T. polyspora* was observed in four, and also for hay in two patients (Table VII). Three of these patients were suffering their first acute episode. The highest titres to *T. polyspora* and hay (1/16) at the end of the 11 months were found in patient R. T. B., who discontinued steroid therapy after the first five days. Our acutely ill patients had generally higher titres of *T. polyspora* and hay than those found in our chronic patients.

Kobayashi, Stahmann, Rankin, and Dickie (1963) also determined the antibody level in sera of patients with farmer's lung. In four of their patients titres were even higher than we observed in our patients, but they too noted considerable variation.

CHRONIC GROUP

Clinical features Table VIIIA shows the clinical, radiographic, and lung function classifications of the 34 patients at the time of study.

Twenty-two patients complained at the time of study of dyspnoea on exertion and five of these also complained of chronic cough. Eight other patients complained of chronic cough alone. With the exception of weakness, especially in the muscles of the thighs, noticeable on exertion only, there were no complaints of persistent constitutional symptoms in this group.

Continuous progression of dyspnoea on exertion and chronic cough since the start of their illness was claimed by 11 patients. Four of these have never suffered actual acute farmer's lung episodes and thus are among the five patients classified in Tables III and IX as having a 'continuous farmer's lung illness'.

Physical signs on examination of the chest did not contribute to the diagnosis. In none of these chronic patients, however, could basal crepitations, so characteristically present in the acute episode, be heard. Digital clubbing was noted in two patients.

The history of smoking in the chronic patients is summarized in Table IX: of the 16 patients (47%) who were smokers, 11 had given up smoking 2 to 13 years prior to our examination, in most cases on the advice of the chest physician. Five of the smokers admitted to chronic cough prior to their farmer's lung illness, productive and mild in two and dry in three cases.

The past history revealed that three of the chronic patients had suffered previous chest illnesses, pleurisy or pneumonia many years prior to their farmer's lung illness. Patient 16 gave a history of repeated heavy colds. In only three patients was there a personal or family history of allergy.

Radiographic findings The chest radiographs of the chronic patients at the time of study were classified (Table VIIIB).

Study of previous films available from this group revealed that of the 22 patients presently

TABLE VIIIA

CLINICAL FEATURES, RADIOGRAPHIC FINDINGS, AND LUNG FUNCTION IN CHRONIC PATIENTS

Patient No.[1]	Sex	Age	Illness prior to Study (yrs.)	Classification at Time of Study					Lung Function	
				Clinical				Radio-graphic		
				Past History	Symptoms		Disability			
1	M	61	5	II	—	P	2	C1	Int+Ob	s
2	M	62	10	I	r	D	3	C1	Int+Ob	m
3	M	47	10	I	r+c	D	2	A2	Nor	—
4	M	68	1	I	r+c	—	—	C1	Nsp	—
5	M	56	25	I	r+c	D	3	C3	Int−3	s
6	M	52	8	I	r+c	P	2	C2	Int−2	s
7	F	54	3	III	—	—	—	A1	Nor	—
8	F	59	7	I	r	D	2	C1	Int−3	m
9	M	58	11	I	r	P	2	C1	Int−1	s
10	F	53	5	I	r	D	1	C3	Int−3	s
11	M	37	9	I	r	D+P	1	C1	Ob	m
12	F	60	4	I	r	D	1	C1	Int−1	m
13	M	37	6	I	c	D	1	A1	Ob	m
14	M	45	18	I	r	D	2	C3	Int−1	s
15	M	60	10	II	—	P	2	0	Ob	s
16	M	43	5	I	r	D	3	C3	Int−3	s
17	M	54	17	I	r	D+P	2	C3	Int−Ob	s
18	M	58	6	I	r	D	1	C3	Ob	s
19	M	25	3	I	r	D	1	A1	Nsp	—
20	M	44	3	I	r	D	2	C3	Int+Ob	m
21	M	48	2	I	r	D+P	2	C1	Int+2	s
22	F	65	5	I	r	D	2	C1	Int−2	m
23	M	55	8	II	—	D+P	1	A2	Int−3	m
24	M	62	42	I	r	P	2	C1	Int+Ob	s
25	M	59	7	II	—	P	3	A1	Ob	m
26	M	64	15	I	c	D+P	2	A2	Nsp	—
27	M	58	3	I	r	D	1	C1	Nsp	—
28	M	59	5	I	r	P	1	A2	Int−1	m
29	M	47	2	III	—	—	—	0	Ob	s
30	M	57	3	III	—	—	—	C1	Nsp	—
31	M	56	34	I	c	D	3	E	Ob	s
32	M	47	14	I	r+c	D	2	E	Ob	s
33	M	49	12	II	—	D	3	C3	Int−1	s
34	F	68	5	I	r+c	P	2	C1	Ob	s

[1] Patients were serially numbered as they entered the study.

Explanation of Symbols. Clinical: I=recurring F.L. episodes; II=continuous F.L. illness; III=solitary F.L. episode in the past; r=mainly respiratory symptoms during episodes; c=mainly constitutional symptoms during episodes; r+c=mixed symptoms during episodes; D=permanent effort dyspnoea; P=permanent cough; D+P=effort dyspnoea+cough as permanent symptoms; 1=mild disability; 2=moderate disability and 3=total disability. Radiographic: see Table IV. E=emphysema, Lung function: Int='interstitial disease profile'; −1=compliance reduced; −2=diffusing capacity reduced; −3=compl.+diffusing capacity reduced; Ob='obstructive profile'; Int+Ob=combination of both types; Nsp=non-specific; Nor=normal; m=mild abnormality; s=abnormality of more than mild degree.

TABLE VIIIB

Radiographic Findings		No. of Patients
Fibrotic changes (C)		22
Fine diffuse (C1)	13	
Slightly deforming (C2)	1	
Grossly deforming (C3)	8	
'Miliary appearance' (A)		8
Minimal (A1)	4	
Definite (A2)	4	
Emphysema (E)		2
Normal (O)		2

showing 'fibrotic changes', 18 were already in this category when first radiographed 2 to 10 years before, and in six of these on films taken over the years 'miliary' changes were recognized as intermittently superimposed on those 'fibrotic changes'. The remaining four patients, now in category C, had, when first seen at the clinic, radiographic changes of category A, persisting from one to seven years before the 'fibrotic' appearance of category C developed. The chest film of eight patients showed category A changes at the time of our examination. Review of previous films available showed that these changes had been constantly present throughout the course of the patient's follow-up, varying from one to 10 years. This observation makes us suggest that such fine, micronodular opacities are not necessarily acute type changes and, if persisting for more than a year, as in our patients here, should be looked upon as representing chronic type changes. We feel that it is important to recognize the existence of this type of chronic radiographic change. We are also aware, however, that such changes can only be interpreted as chronic if serial films are observed to remain unchanged for at least one year or longer following a clinical episode of farmer's lung. Any one of these films read individually could be interpreted as showing the 'typical' acute type miliary change.

A comparison of the radiographic findings of all patients in the pool with the findings in our

TABLE IX

Patient	Total Years of Smoking	No. of Years stopped Smoking	Cigarettes/day	Pipe oz./week	Cough prior to F.L. Illness
1	40	3	70	—	d
2	37	10	15	—	—
3	24	12	10	—	—
4	0		—	—	—
5	40		—	2	—
6	0		—	—	—
7	0		—	—	p
8	0		—	—	—
9	34	4	10	—	—
10	0		—	—	—
11	0		—	—	—
12	0		—	—	—
13	10	8	15	—	—
14	20	2	25	1	d
15	35	10	30	—	p
16	20		6	—	—
17	18		—	2	—
18	35	6	20	2	—
19	0		—	—	—
20	0		—	—	—
21	0		—	—	—
22	0		—	—	—
23	0		—	—	—
24	0		—	—	—
25	35	7	—	2	—
26	27		30	—	—
27	0		—	—	—
28	0		—	—	—
29	32		—	3	—
30	0		—	—	—
31	13	13	—	3	—
32	7	7	10	—	d
33	0		—	—	—
34	0		—	—	—

d = Dry cough.
p = Productive cough.

selected 34 chronic patients indicated that our chronic group was radiologically biased toward the more severe and chronic form of the disease. In spite of this bias, several important radiological findings of the pool are reflected in the films of our chronic group, such as the above-mentioned persistence of 'miliary' changes over long periods, and the small number of patients changing from 'miliary' to 'fibrotic' abnormalities or showing recurrent miliary changes with normal intervening films over years of observation.

Pulmonary function The results of pulmonary function tests in the patients of the chronic group are shown in Table X, and Table VIIIA presents the classification of these patients according to their pulmonary function findings. The categories used in this classification are as follows:

1. 'Interstitial disease profile' (Int): Decreased diffusing capacity and/or compliance with or without reduction in lung volumes. No evidence of airways obstruction 13 patients (39%)

Reductions in diffusing capacity and compliance of between 60 and 80% of the predicted value were considered a mild abnormality; values under 60% of predicted were considered an abnormality of more than mild degree.

TABLE X

RESULTS OF PULMONARY FUNCTION TESTS AT TIME OF STUDY IN CHRONIC PATIENTS

Patient	V.C. (l.)	% of Predicted	R.V. (l.)	% of Predicted	R.V./T.L.C. ×100	$\frac{F.E.V._{1.0}}{F.V.C.} \times 100$	Compliance (l./cm. H_2O)	D_{LCO} (ml./min./mm. Hg)	% of Predicted	Sa_{O_2} (rest)
1	3·76	105	3·86	146	51	40	0·10	39	140	98
2	3·01	92	3·03	127	50	55	0·12	20	73	94
3	4·47	119	2·14	99	32	77	0·30	28	107	95
4	3·24	118	2·86	113	47	74	0·29	25	101	94
5	3·34	96	2·54	97	43	85	0·14	7	28	77
6	2·84	79	3·53	142	55	65	0·27	13	53	88
7	3·72	154	2·01	119	35	76	0·19	24	106	95
8	1·89	86	2·53	146	57	79	0·13	15	77	91
9	3·45	107	2·56	113	43	67	0·08	24	94	86
10	1·14	54	1·67	100	59	83	0·04	8	49	79
11	3·89	93	3·44	155	47	66	0·22	25	95	97
12	2·14	85	2·11	123	50	83	0·07	16	85	95
13	4·24	110	2·42	128	36	65	0·24	38	159	92
14	2·07	54	2·50	113	55	72	0·04	19	82	96
15	2·75	72	6·40	230	70	53	0·16	44	149	92
16	1·58	44	1·60	74	50	74	0·02	12	61	91
17	2·80	71	4·11	151	60	57	0·09	15	54	88
18	3·82	119	5·82	256	60	58	0·19	34	116	92
19	3·01	70	0·93	57	24	85	0·27	21	88	94
20	3·09	82	2·85	130	48	63	0·19	18	76	93
21	3·23	87	1·74	78	35	88	0·16	14	43	94
22	1·69	87	2·35	131	58	78	0·27	13	69	89
23	3·98	103	2·86	110	42	78	0·13	19	68	90
24	4·27	122	5·65	215	57	51	0·09	40	141	97
25	2·59	98	2·19	110	46	59	0·20	24	120	93
26	3·75	125	2·28	88	38	65	0·22	19	78	97
27	3·74	117	2·19	94	37	57	0·12	24	99	93
28	3·17	96	2·22	88	41	72	0·10	24	93	93
29	4·74	114	4·55	200	49	68	0·15	35	117	92
30	4·43	148	1·60	86	27	71	0·15	25	99	90
31	2·27	65	5·70	234	72	34	0·21	33	126	91
32	2·55	69	3·64	164	54	47	0·17	31	133	98
33	1·57	41	2·09	83	57	69	0·04	25	99	89
34	2·34	110	2·77	154	72	60	0·29	14	73	88

2. 'Obstructive profile' (O): Increased R.V./T.L.C. ratio and slowing on forced expiration 10 patients (39%)

The presence and degree of airway obstruction was assessed according to the results of spirometric tests, the volume of R.V., and the ratio R.V./T.L.C. $F.E.V._{\cdot 1\cdot 0}$ less than 70% F.V.C. was considered abnormal. Airway obstruction was considered of more than mild degree if $F.E.V._{\cdot 1\cdot 0}$ was less than 60% of F.V.C. and/or the R.V. above 200% of predicted.

3. Combination of airway obstruction and 'interstitial disease features' (Int+Ob): 5 patients

4. 'Non-specific' (Nsp): Abnormalities in pulmonary function tests are mild and not specific enough to justify placement in any of the above categories but are sufficiently abnormal not to be called normal 4 patients

5. 'Normal' (Nor): 2 patients

A reduction in diffusing capacity was found in 13 patients. In five of these the diffusing capacity was less than 60% of the predicted value. Restriction in lung volumes was found in five patients, four of whom also showed a markedly decreased compliance.

Some of our chronic patients who claimed to be moderately or totally disabled had normal or only mildly impaired pulmonary function at rest. For this reason, pulmonary function was tested in 20 patients during exercise. Figure 8 illustrates the findings of this study in one of the chronic and two of the acute patients (tested at the six-month follow-up); the diffusing capacity (DLco), arterial oxygen tension, and heart rate are shown at various exercise levels. Patient D. M. B., although having a less than expected increase in DLco during exercise, was able to maintain the arterial oxygen tension within normal limits. His pulse rate increased steadily in a normal fashion. The other two patients showed no increase in their diffusing capacity; oxygen tension fell during exercise, though their pulse rate increased as normally expected. No abnormalities were observed on the electrocardiograms. Patient D. B. suffered an episode of right heart failure four weeks after the exercise test was performed. This emphasizes his poor pulmonary condition, evident on exercise but unsuspected from pulmonary function studies performed at rest.

Serology Table XI shows the results of agar-gel double diffusion tests performed on the group of chronic patients, together with the results of the initial testing of acute patients and the findings in the co-workers. Fifty-three per cent of the chronic patients reacted to *T. polyspora* at the time of study, as compared to 100% of the acutely ill patients at their initial testing. In our co-workers there was only one reaction. None of the 355 control sera reacted to *T. polyspora*. Hay and *T. polyspora* used as antigens therefore appear to

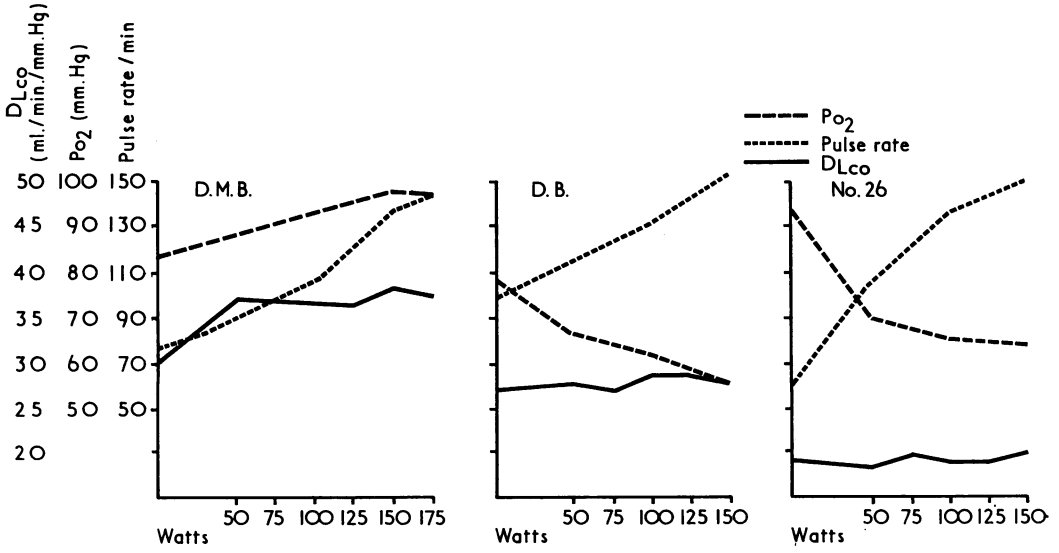


FIG. 8. *Changes in diffusing capacity, heart rate, and arterial oxygen tension during exercise in three farmer's lung patients.*

TABLE XI

SEROLOGICAL RESULTS
(agar-gel double diffusion technique)

Reaction	Acute Patients (11)	Chronic Patients (34)	Co-workers (42)
None	—	12	34
Hay	—	2	1
T.P.	—	—	—
Act.	—	—	3
Asp.	—	—	—
Hay; T.P.	—	—	—
Hay; Act.	—	1	3
Hay; Act.	—	1	—
T.P.; Act.	—	1	—
T.P.; Asp.	—	—	—
Act.; Asp.	—	—	—
Hay; T.P.; Act.	6	15	—
Hay; T.P.; Act.; Asp.	5	2	1

T.P. = *Thermopolyspora polyspora.*
Act. = *Actinomyces* sp. I.M.I. 45560.
Asp. = *Aspergillus fumigatus* I.M.I. 48540.

separate the majority of farmer's lung patients from symptomless farm workers similarly exposed, and from normal controls.

With one exception, all patients, acute and chronic, who reacted to *T. polyspora* also reacted to hay, but four of the chronic patients reacted to hay in the absence of a *T. polyspora* reaction. In our 42 co-workers there were five reactions to hay; this includes the solitary reactor to *T. polyspora* in this group. As can be seen in Table XI, all sera reacting to *T. polyspora* also reacted to *Actinomyces* sp. One chronic patient reacted to *Actinomyces* sp. without *T. polyspora* reaction, and so did six of the co-workers; in three of these this was the only reaction. Reaction to *A. fumigatus* occurred in three chronic patients and in only one of the co-workers. With one exception it accompanied reactions to all other antigens and therefore has little diagnostic value.

Immuno-electrophoretic studies yielded no additional diagnostic information to the results obtained by double gel diffusion. The distribution of the number of lines in reactors to *T. polyspora* was similar to the distribution reported by Pepys and Jenkins (1965).

While 71% of the 45 acute and chronic patients reacted to hay when the two original extracts were used as antigen, 92% reacted to at least one hay when tested against the additional 12 hay extracts. The number of co-workers reacting to hay, however, remained unchanged when similarly tested.

There was little variation in the potency of the 14 hay extracts used for testing; the least potent hay reacted with the serum of 50% of the hay-positive patients, and the most potent with no more than 66%. Although all the patients tested reacted to their own hay, they also reacted to one or more of the other hay extracts.

CORRELATION AND DISCUSSION

In the acute farmer's lung patients there was good correlation of clinical, radiographic, pulmonary function, and, to a certain extent, even serological findings. This was evident in the results of the initial examination as well as within the subsequent progress of findings over the 11 months of observation. Much improvement in the disease process within the first 10 days was manifested by clearing of crepitations, diminution of radiological abnormalities, and improvement in pulmonary function. The initially observed combination of fine crepitations and reduced vital capacity without significant reduction in compliance, as seen especially in patient D. H. O., would be compatible with the presence of alveolar fluid, and absorption of this fluid could account for the rapid improvement during the first 10 days. This speedy radiological change from category A3 to A2 (not demonstrated in our patients here but observed in films from the pool), which represents improvement in definition of pulmonary vessels, disappearance of confluence in infiltration, and disappearance of Kerley B and C lines, supports this concept.

Later improvement, both radiographic and in pulmonary function, is much more gradual, as granulomatous lesions, interstitial pneumonia, and vascular involvement seen histologically have yet to resolve. Radiographic abnormalities and lung function impairment persisting for six months and longer seem to indicate a failure of complete resolution and suggest the onset of the chronic state. This was evident not only from observations made on reviewing the past history of chronic patients but already seemed apparent within the 11-month follow-up of our acute patients. There also is evidence that the more severe the clinical attack, the grosser the radiographic changes; the more extensive the exudation and the bronchial and vascular involvement, the less likely is complete resolution and the more likely is transition into the irreversible chronic state. Patients 18 and 23 present good examples to support this concept. Their histological findings are described and illustrated as cases 2 and 3 in the second part of this series (Seal, Hapke, Thomas, Meek, and Hayes, 1968).

In contrast to the acute group there was poor correlation of clinical, radiographic, and pulmonary function observations made at the time of study in the chronic patients. In previous publications on farmer's lung (Ministry of Pensions and National Insurance, 1964; Bishop, Melnick, and Raine, 1963), it is stated that shortness of breath is the presenting symptom, consistently found in all stages of the disease. Markedly reduced diffus-

ing capacity is a prominent feature, and widespread fibrosis is a sequel to repeated farmer's lung attacks. In chronically ill farmer's lung patients, especially those with moderate or total disability, as were 21 of our 34 patients, a combination of these features may accordingly be expected to be present in the majority of cases.

Figures 9 and 10 illustrate the combinations of permanent symptoms, radiographic findings, and pulmonary function results as observed in our chronic patients. The centre columns of Fig. 9 show the total number of patients complaining of the three types of permanent symptoms; the columns to the left and right show the radiographic and pulmonary function findings observed in these three groups of patients. In the centre

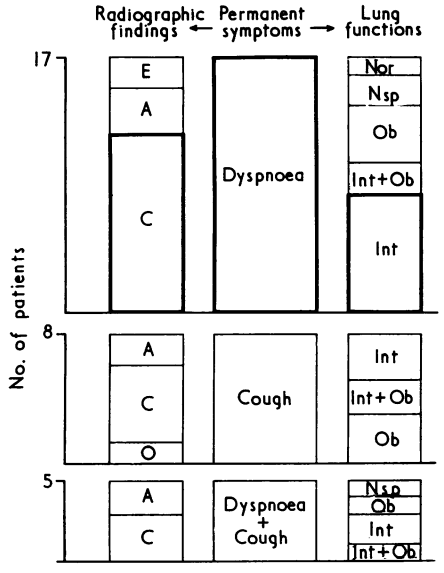


FIG. 9. *Correlation of symptomatology with radiographic and lung function findings in chronic patients.*

columns of Fig. 10 the patients are arranged according to the three major types of lung function, and the corresponding symptoms and radiographic findings are illustrated in the columns to the left and right. The variety of combinations is readily apparent, and, although the majority of patients had 'fibrotic changes' on their chest radiograph, 50% complained of effort dyspnoea and 38% showed an 'interstitial disease profile' on pulmonary function tests; only eight of the 34 patients had the combination of all three classical features. Five of these eight patients had severe effort dyspnoea, and a reduction in diffusing capacity was their prominent pulmonary function abnormality.

These findings confirmed our prior observations on farmer's lung patients, which suggested a greater variety in the features of chronic farmer's lung than previously described and a relatively small percentage of patients satisfying the classical concept of the disease.

It has been stated that airway obstruction is not a feature of farmer's lung disease or that no evidence of airway obstruction was found in patients studied (Ministry of Pensions and National Insurance, 1964; Bishop *et al.*, 1963). In other publications airway obstruction has been reported in patients with farmer's lung. Dickie and Rankin (1958) found on pulmonary function studies a significant increase in residual volume and a moderate reduction in vital capacity together with a reduction in maximum breathing capacity, timed vital capacity, and expiratory flow rates. A review of the pulmonary function data of farmer's lung (Rankin, Jaeschke, Callies, and Dickie, 1962) suggested an increase in residual volume and a reduction in the $F.E.V._{\cdot 1\cdot 0}/F.V.C.$ ratio in at least one patient. Williams (1963b) found in two of 16 patients studied $F.E.V._{\cdot 1\cdot 0}/F.V.C.$ ratios under 70%, and in two other patients residual volumes

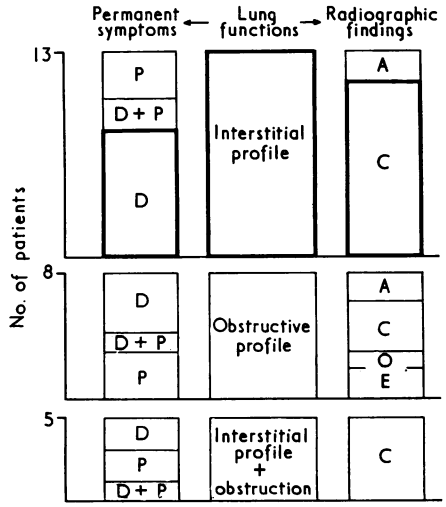


FIG. 10. *Correlation of symptomatology with radiographic and lung function findings in chronic patients. P=permanent cough; D=permanent dyspnoea; D+P=permanent cough and dyspnoea; Int=interstitial disease profile; Ob=obstructive profile; Int+Ob=combination of above; Nsp=non-specific; Nor=normal; A=acute miliary appearance; C=chronic fibrotic appearance; E='emphysematous' changes; O=normal.*

were abnormally high. Emanuel, Wenzel, Bowerman, and Lawton (1964) mentioned chronic cough as the most constant symptom of their group of 24 patients, and found organizing endobronchial exudate (bronchiolitis obliterans) in 25% of their lung biopsies. They concluded that progressive pulmonary fibrosis and emphysema can develop with repeated exposure.

It may also be of interest here to mention that Weill, Buechner, Gonzalez, Herbert, Aucoin, and Ziskind (1966), reporting on pulmonary function findings in bagassosis, a disease closely related to farmer's lung, found in two of their patients evidence of diffuse airway obstruction. They concluded that this obstruction was the result of permanent damage to the airway due to exposure to bagasse, and not superimposed chronic bronchitis.

Of our chronic patients, eight complained of cough as their most prominent permanent symptom. Figure 9 shows the pulmonary function findings in three of them as 'obstructive profile' and in three others as 'interstitial disease profile'; the remaining two patients had 'interstitial disease features' together with airway obstruction. As also seen in Fig. 9, four of the patients complaining of effort dyspnoea without cough showed airway obstruction in pulmonary function tests.

We investigated the possibility that these patients with cough and/or pulmonary function evidence of airway obstruction might actually be suffering from chronic bronchitis rather than farmer's lung, or from chronic bronchitis superimposed on farmer's lung. Table IX shows that nine of these 20 patients were non-smokers. Of the nine patients with obstructive features as the only pulmonary function abnormality, five of whom also complained of cough, all had been serologically positive at some time during the previous four years, and six had a history of recurring typical farmer's lung episodes. Only two of the nine patients had cough prior to their first acute episodes. Of the 13 patients with cough at the time of examination, only two produced purulent sputum (one was a non-smoking female). It appears, therefore, that the airway obstruction in at least some of these patients is the result of the farmer's lung illness. The organizing bronchiolitis reported by Emanuel *et al.* (1964) and also seen in lung biopsies taken from two of our chronic patients after an acute attack in 1959 (Nos 18 and 23) provides a morphological explanation for such clinical and pulmonary function features.

Since no attempt was made in the chronic group to achieve proportional representation of the clinical features found in the total number of patients in our pool, no conclusions can be drawn from our findings about the numerical incidence of chronic cough or pulmonary function evidence of airway obstruction in farmer's lung.

Bishop *et al.* (1963) reported an increase of pulmonary arterial pressure at rest in three of six farmer's lung patients in whom cardiac catheter studies were performed. Five of the six had pulmonary hypertension during exercise, and they suggested that in these patients the pulmonary vascular bed was partially obliterated. The results from our exercise studies suggest similar changes in some of our patients. As the increase in the diffusing capacity during exercise is considered to be mainly due to an expansion of the pulmonary capillary bed (Johnson, Spicer, Bishop, and Forster, 1960; Johnson, Taylor, and Lawson, 1965), patients D. B. and No. 26 (as well as other patients not shown in Fig. 8) were probably incapable of this expansion. Pulmonary hypertension during exercise in such patients would therefore be easily understood. The episode of right heart failure in patient D. B. supports this concept.

Twenty-one of our chronic patients claimed to be moderately or totally disabled due to their disease, dyspnoea on exertion being by far the most important cause of disability. In only 14 of these patients, however, did pulmonary function tests reveal sufficient impairment of any type to account for the disability. The disability of the other seven without objective evidence supporting their claim would probably be difficult to assess. Fortunately for us, our patients in the chronic group were all self-employed and therefore had nothing to gain by exaggerating their complaints. In some of these patients exercise tests detected the impairment of pulmonary function to account for their intolerance to effort; in others the disability remained unexplained. This discrepancy between the severity of patients' complaints and the results of pulmonary function tests at rest in farmer's lung must be taken into account in assessing claims for compensation. We feel that simple lung function tests are often not an adequate means of assessing the extent of disability.

Three of our chronic patients had a solitary farmer's lung episode in the past, leaving no apparent residual symptoms. One of these was found to have normal pulmonary function, one a mild abnormality, and one marked airway obstruction. This raises the possibility that a solitary episode of farmer's lung may be the unsuspected cause of chronic respiratory illness in a farming community.

The radiographs of two patients with an obstructive profile on pulmonary function tests but

complaining of permanent effort dyspnoea showed signs of emphysema only. Both patients had clear farmer's lung histories and positive serology, and neither had pre-existing chronic respiratory disease. No biopsy material has become available as yet from such patients, but it is possible that there is fine diffuse interstitial fibrosis with much related 'irregular emphysema' and therefore we suggest that in our present state of knowledge for the purpose of compensation such patients should be considered favourably by examining panels. If there is evidence of pre-existing chronic bronchitis, the contribution of any farmer's lung episode to the patient's radiological findings and disability will be difficult to assess.

As demonstrated in Table XI, all our acutely ill patients were positive to *T. polyspora* on initial testing, whereas only 53% of our chronic patients were positive at the time of study. Similar findings were reported by Kobayashi *et al.* (1963), using hay alone. It would appear, therefore, that it is important to distinguish the acute episode from the chronic state of illness, not only for proper evaluation of the serological findings in any tested patient in particular, but also for assessing the diagnostic values of these serological tests in farmer's lung disease in general. Of the 16 chronic patients negative to *T. polyspora* at the time of examination, 11 suffered the last acute episode more than three years previously. We were fortunate in that Professor J. Pepys at the Brompton Hospital had tested 10 of these patients between one to three years prior to our study and found eight positive. In six of these the blood had been taken within three years of their last acute episode. One of the two patients, whom Professor Pepys as well as we found to be negative, is known to have had no farmer's lung attacks for at least nine years.

In order to assess the persistence of a positive serological reaction to *T. polyspora* after an isolated farmer's lung episode, we selected from our pool 35 patients who had had a solitary typical episode from one to 10 years previously. The results of serological testing using *T. polyspora* in this special group revealed 82% positivity in patients whose acute episode had occurred less than three years previously, in contrast to 22% positivity in patients whose attack had occurred more than three years previously. It should, however, be emphasized that these 35 patients were not chronic patients in that they had no permanent symptoms.

The effectiveness and limitation of *T. polyspora* as a diagnostic antigen in farmer's lung is delineated by our serological results. Pepys and Jenkins (1965) reported in their group of 'normal farmers' a 19% reaction to *T. polyspora*, whereas in our 42 'co-workers', presumably a comparable group, there was only one reaction. The possibility that some of Pepys' 'normal farmers' had, in fact, suffered an undiagnosed farmer's lung illness in the past could be a reasonable explanation for this discrepancy, especially as we had taken great care to exclude such persons from our group. Another possibility worth considering is that our 'co-workers', half of whom were women and children, were not as heavily exposed to the antigen as Pepys's group of 'normal farmers'.

It is certainly possible that another antigen or antigens besides *T. polyspora* may be involved in the aetiology of farmer's lung. This is suggested by the considerable increase in the positivity to hay observed in our chronic patients when instead of one hay extract 12 additional hay extracts were used for testing, while no alteration was observed in the original hay positivity of the co-workers or normal controls. The results of our acute group and the fact that most of our hay-positive, *T. polyspora*-negative patients were previously *T. polyspora*-positive suggest that the antibodies evoked in the patient by this 'unidentified' antigen in hay persist for longer than those evoked by *T. polyspora*. Our observations do not suggest that *Actinomyces* sp. is this antigen, but the relatively high percentage of our co-workers who reacted to *Actinomyces* sp. has yet to be explained. That another antigen not yet identified is involved is suggested by Williams's observation (1963a) that extracts made from the 'coarse' and not the 'fine' moiety of hay dust evoked an attack on inhalation testing. *T. polyspora* spores (1 μ) would predominate in the 'fine' and not in the 'coarse' moiety, where the particles were much larger.

We wish to thank Dr. H. M. Foreman, M.B.E., and Professor Ross Kory for valued criticism and advice; Mrs. M. Ninan, Miss D. Harding, Mrs. D. M. Barron, and Miss J. M. Dabbs of the Respiratory Function Laboratory, Sully Hospital, for additional work and much inconvenience; Mr. J. Edwards for serological work; Professor J. Pepys of the Brompton Hospital for the use of previous serological findings; and many colleagues who helped in various ways.

We thank Mr. F. W. Midgeley for the illustrations and photography and Mrs. M. J. Evans and Miss E. M. Jackson for the typing.

This work was supported by a grant from the Welsh Hospital Board and by endowment funds of the Mid-Wales H.M.C.

REFERENCES

Bishop, J. M., Melnick, S. C., and Raine, J. (1963). Farmer's lung; studies of pulmonary function and aetiology. *Quart. J. Med.*, **32**, 257.

Campbell, J. M. (1932). Acute symptoms following work with hay. *Brit. med. J.*, **2**, 1143.

Dickie, H. A., and Rankin, J. (1958). Farmer's lung: an acute granulomatous interstitial pneumonitis occurring in agricultural workers. *J. Amer. med. Ass.*, **167**, 1069.

Doll, R., and Hill, A. Bradford (1950). Smoking and carcinoma of the lung; preliminary report. *Brit. med. J.*, **2**, 739.

Emanuel, D. A., Wenzel, F. J., Bowerman, C. I., and Lawton, B. R. (1964). Farmer's lung: clinical, pathologic and immunologic study of twenty-four patients. *Amer. J. Med.*, **37**, 392.

Fry, D. L., Stead, W. W., Ebert, R. V., Lubin, R. I., and Wells, H. S. (1952). The measurement of intraesophageal pressure and its relationship to intrathoracic pressure. *J. Lab. clin. Med.*, **40**, 664.

Fuller, C. J. (1953). Farmer's lung: a review of present knowledge. *Thorax*, **8**, 59.

Gilson, J. C., and Hugh-Jones, P. (1949). The measurement of the total lung volume and breathing capacity. *Clin. Sci.*, **7**, 185.

Grabar, P., and Williams, C. A. (1953). Méthode permettant l'étude conjuguée des propriétés électrophorétiques et immunochimiques d'un mélange de protéines: application au sérum sanguin. *Biochim. biophys. Acta (Amst.)*, **10**, 193.

Higgins, I. T. T. (1959). Tobacco smoking, respiratory symptoms, and ventilatory capacity. *Brit. med. J.*, **1**, 325.

Johnson, R. L., Spicer, W. S., Bishop, J. M., and Forster, R. E. (1960). Pulmonary capillary blood volume, flow and diffusing capacity during exercise. *J. appl. Physiol.*, **15**, 893.

—— Taylor, H. F., and Lawson, W. H. (1965). Maximal diffusing capacity of the lung for carbon monoxide, *J. clin. Invest.*, **44**, 349.

Kobayashi, M., Stahmann, M. A., Rankin, J., and Dickie, H. A. (1963). Antigens in mouldy hay as the cause of farmer's lung. *Proc. Soc. exp. Biol. N.Y.*, **113**, 472.

Marshall, R. (1957). The physical properties of the lungs in relation to the subdivisions of lung volume. *Clin. Sci.*, **16**, 507.

Ministry of Pensions and National Insurance (1964). Farmer's lung. A report by the Industrial Injuries Advisory Council. H.M.S.O., London. Cmnd. 2403.

Needham, C. D., Rogan, M. C., and McDonald, I. (1954). Normal standards for lung volumes, intrapulmonary gas-mixing, and maximum breathing capacity. *Thorax*, **9**, 313.

Ogilvie, C. M., Forster, R. E., Blakemore, W. S., and Morton, J. W. (1957). A standardized breath holding technique for the clinical measurement of the diffusing capacity of the lung for carbon monoxide. *J. clin. Invest.*, **36**, 1.

Ouchterlony, O. (1953). Antigen-antibody reactions in gels. *Acta path. microbiol. scand.*, **32**, 231.

Pepys, J., and Jenkins, P. A. (1965). Precipitin (F.L.H.) test in farmer's lung. *Thorax*, **20**, 21.

Rankin, J., Jaeschke, W. H., Callies, Q. C., and Dickie, H. A. (1962). Farmer's lung: physiopathologic features of the acute interstitial granulomatous pneumonitis of agricultural workers. *Ann. intern. Med.*, **57**, 606.

Seal, R. M. E., Hapke, E. J., Thomas, G. O., Meek, J. C., and Hayes, M. (1968). The pathology of the acute and chronic stages of farmer's lung. *Thorax*, **23**, 469.

Staines, F. H., and Forman, J. A. S. (1961). A survey of "farmer's lung". *J. Coll. gen. Practit.*, **4**, 351.

Van Slyke, D. D., and Neill, J. M. (1924). The determination of gases in blood and other solutions by vacuum extraction and manometric measurement. *J. biol. Chem.*, **61**, 523.

Weill, H., Buechner, H. A., Gonzalez, E., Herbert, S. J., Aucoin, E., and Ziskind, M. M. (1966). Bagassosis: a study of pulmonary function in twenty cases. *Ann. intern. Med.*, **64**, 737.

Williams, J. V. (1963a). Inhalation and skin tests with extracts of hay and fungi in patients with farmer's lung. *Thorax*, **18**, 182.

—— (1963b). Pulmonary function studies in patients with farmer's lung. *Ibid.*, **18**, 255.