"Until lately all chest affections were confounded under the term pneumonia, or inflammation of the lungs; and there is no reason for pushing our distinctions too far, except that it is satisfactory to know the precise nature of the disease which destroys our cattle, for that will probably lead us to the discovery of the actual cause of the malady."

(Youatt, 1858.)

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A BOVINE RESPIRATORY DISEASE SIMILAR TO FARMER'S LUNG IN MAN

TWO VOLUMES

VOLUME I

by

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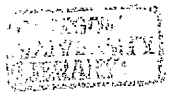
May, 1978.



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Alasdair Wiseman
May 11th, 1978.

DECLARATION

I declare that the work presented in this thesis has been carried out by me. The serology was done in conjunction with Dr. C.O. Dawson, Department of Veterinary Pathology, the pathology in conjunction with Dr. H.M. Pirie, Department of Veterinary Pathology and the radiology in conjunction with Dr. R. Lee, Department of Veterinary Surgery.

Some of the material in this thesis has already been published in the following papers:-

(1) Breeze, R.G., Pirie, H.M., Dawson, C.O., Selman, I.E. and Wiseman, A. (1975). The pathology of respiratory diseases of adult cattle in Britain. Folia vet. Latina, 5, 95.

(2) Dawson, C.O., Wiseman, A., Pirie, H.M. and Breeze, R.G. (1977). Studies on the incidence and titres of precipitating antibody to Micropolyspora faeni in sera from adult cattle. J. comp. Path. Ther., 87, 287.

(3) Pirie, H.M., Dawson, C.O., Breeze, R.G., Selman, I.E. and Wiseman, A. (1971). Fog fever and precipitins to micro-organisms of mouldy hay. Res. vet. Sci., 12, 586.

(4) Pirie, H.M., Dawson, C.O., Breeze, R.G., Selman, I.E. and Wiseman, A. (1972). Precipitins to Micropolyspora faeni in the adult cattle of selected herds in Scotland and North-West England. Clinical Allergy, 2, 181.

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(6) Selman, I.E. and Wiseman, A. (1973). Bovine farmer's lung (an extrinsic allergic alveolitis). I Clinical signs and pathology. IN: Proceedings of the Second Meeting of the Academic Society for Large Animal Veterinary Medicine, 1973, Utrecht.

(7) Wiseman, A., Dawson, C.O., Pirie, H.M., Breeze, R.G. and Selman, I.E. (1973). The incidence of precipitins to Micropolyspora faeni in cattle fed hay treated with an additive to suppress bacterial and mould growth. J. agric. Sci., Camb., 81, 61.

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SUMMARY

During a clinico-pathological investigation of fog fever, precipitating antibodies to Micropolyspora faeni were detected in sera from ten hay-fed housed cattle that had developed acute respiratory disease but they were not detected in 12 cattle that had developed classical pasture-associated fog fever. A case of "indoor" fog fever was subjected to detailed investigation and it was found to be very similar clinically, epidemiologically, pathologically and serologically to acute farmer's lung in man. The disease in cattle was subsequently called "bovine farmer's lung".

The clinical signs of bovine farmer's lung had developed suddenly in 18 cases (acute form) while in 27 animals they had developed insidiously (chronic form). With acute farmer's lung there were obvious constitutional signs (agalactia, anorexia) in addition to respiratory distress whereas with the chronic form the major presenting signs were almost wholly referable to the respiratory system (coughing, hyperpnoea). On admission to the Veterinary School, the clinical differences between the two forms of the disease were not very great because of the time that had elapsed since the animals had first been seen to be ill.

The 45 clinical cases of bovine farmer's lung were admitted from 29 farms and on six of these farms the farmers suffered from farmer's lung while on another seven they experienced an adverse clinical reaction during, or soon after, working with mouldy hay. The keeping of dairy cattle tied up in byres was closely associated with the development of farmer's lung in their attendants. The prevalence of bovine farmer's lung was higher in dairy than in beef cattle except in Westmorland where the opposite was found.

Every clinical case had been admitted from the mainly hilly areas of north-west Britain where there is often rain during the hay-making season. Only mouldy hay was associated with the development of clinical disease although on one farm, where only silage had been fed, precipitins to M. faeni developed in a single cow as a result of her having been fed mouldy rolled wet-stored barley.

During the first year of a serological investigation, great variation in the prevalence of precipitins to M. faeni was found bet-

ween selected herds. The prevalence of precipitins was significantly higher at the beginning of winter in herds selected because the farmer suffered from farmer's lung than it was in the other herds and, during the winter, significantly more cattle developed precipitins in these "farmer's lung" herds. In contrast during the second winter, a significant increase in the prevalence of precipitins did not occur in any of the herds because particularly mouldy hay had not been fed. Considering both years of the study, it was found that the prevalence of precipitins in a herd at the end of winter was determined by the mouldiness of the hay and that the mouldiness of the hay was closely associated with the number of raindays in July. During the summer between the two winter housing periods referred to above, the prevalence of precipitins decreased in every herd.

It was deduced that regular exposure to mouldy hay dust had a cumulative effect because the prevalence of precipitins was significantly greater in herds in which farmer's lung had been confirmed, either in the cattle or in the farmer, than in the other herds. There was a positive correlation between the age of the cattle sampled and the prevalence of precipitins as well as between age and the number of clinical cases of bovine farmer's lung. There was also a good correlation between the prevalence of precipitins at the end of winter and the frequency of coughing in the herd.

As a means of confirming the clinical diagnosis of bovine farmer's lung several procedures were studied because, as a result of the serological survey, it was found that the presence of precipitins to M. faeni confirmed only that an animal had been exposed to M. faeni (mouldy hay dust) not that it was suffering from clinical disease. Radiography proved to be of limited practical use even though there was a generalised reduction in the radiolucency and an increased reaction around the major bronchi and blood vessels in the diaphragmatic lobes. Following the intra-dermal injection of M. faeni antigens, the reactions which developed within four to eight hours appeared to be entirely dependent upon the presence of precipitins in the serum. Histopathological examination of skin biopsies taken six hours post-injection indicated that the reactions were typical of a type III (Arthus-type) hypersensitivity reaction.

The diagnosis of farmer's lung was not difficult at necropsy because of the presence of characteristic lesions which were similar

in acute and chronic cases although their severity and extent differed. On macroscopic examination, large numbers of small grey spots (1-2 mm) were seen in the centre of lobules which were pale around their edges. Microscopically, there was thickening of the alveolar septa and walls which had resulted mainly from a mononuclear cellular infiltration. Epithelioid granulomata were more prevalent in acute than in chronic cases. The degree of inter-alveolar fibrosis varied from foci in young animals with the chronic disease to diffuse pulmonary fibrosis in old long-standing cases. Bronchitis, bronchiolitis and bronchiolitis obliterans were invariably present.

In eight calves continually exposed to mouldy hay dust, precipitins to M. faeni became detectable after four to seven weeks although clinical signs of respiratory disease did not become apparent even after four calves had been exposed for 18 weeks. When the latter four animals were given two massive exposures of mouldy hay dust, a single animal developed a mild clinical response seven to ten hours after the first exposure only. Following both massive exposures, the mean number of circulating neutrophils in the group decreased during the first four hours and then returned to the pre-exposure levels within the next four hours. At necropsy, a variably degree of thickening of the alveolar septa due to infiltration with mononuclear cells was present in all eight calves although definite epithelioid granulomata were only seen in two animals. In the four calves killed after their second massive exposure to mouldy hay dust, there were more neutrophils in the lungs of the two killed after six hours than in the lungs of the two killed after 24 hours. It was deduced, therefore, that the presence of precipitins not only confirmed exposure to M. faeni but also indicated that sensitisation had occurred since every experimental calf with precipitins to M. faeni had pulmonary lesions characteristic of farmer's lung. The clinical and haematological findings together with the histopathological changes in the lungs and in the skin biopsies indicated that a type III hypersensitivity reaction was closely associated with the development of farmer's lung disease in cattle.

As a result of this investigation it has been shown that farmer's lung is a specific respiratory disease of adult cattle. It has also been established that farmer's lung is the most common respiratory disease of housed adult cattle in Britain.

APPENDIX I

In Appendix I the following abbreviations have been used regarding the individual farmer's clinical reaction after working with mouldy hay: NR = no reaction, PR = positive clinical reaction, FL = farmer's lung, OD = other respiratory disorder.

CLINICAL TERMS

(1) Presenting signs

The presenting signs include the clinical abnormalities detected on the farm at the first veterinary clinical examination and also the farmer's reasons for seeking veterinary advice.

(2) Respiratory rate

The resting respiratory rate of a healthy adult bovine animal in a cool environment is less than 30 respirations per minute. Tachypnoea was considered to be present when the resting respiratory rate was equal to or greater than 30 respirations per minute.

(3) Respiratory depth

During the respiratory cycle in a healthy adult bovine animal, the movement of the abdominal muscles on the right side is almost imperceptible. Hyperpnoea was considered to be present when it was obvious that the abdominal muscles were being used at rest to assist respiration. Animals were considered to be slightly hyperpnoeic when their abdominal respiratory effort was just noticeable, to be moderately hyperpnoeic when there was an obvious increase in their abdominal effort and to be grossly hyperpnoeic when a marked abdominal effort was involved and the individual was seen to rock antero-posteriorly while breathing.

(4) Dyspnoea

The presence of respiratory distress in cattle can only be assessed objectively. An animal with a marked abdominal respiratory effort and respirations that could be heard without the use of a stethoscope was considered to be dyspnoeic. When an individual was seen to be mouth-breathing with its tongue protruding and was heard to be grunting on expiration, it was

considered to be severely dyspnoeic.

(5) Auscultation

The boundaries of the area of pulmonary auscultation extend from the point of the elbow dorsally to the posterior tip of the scapula then posteriorly to the eleventh inter-costal space and finally antero-ventrally to the point of the elbow.

(6) Adventitious lung sounds

Two main types of adventitious sounds are recognised in cattle with pulmonary disease; crackles which term is self-explanatory and rhonchi which include both low and high pitched squeaks.

(7) Pyrexia

The normal rectal temperature range in adult cattle is from 100.5°F to 102.5°F and an animal was considered to be pyrexic when its rectal temperature was equal to or greater than 103°F.

NOMENCLATURE

Corbaz and others (1963) found that Thermopolyspora polyspora and Micromonospora vulgaris were the commonest species of thermophilic actinomycete in mouldy hay associated with farmer's lung disease. However, Thermopolyspora polyspora Henssen (1957) had been incorrectly identified and it has since been described as a new species, Micropolyspora faeni Cross, McIver and Lacey (1968). Micromonospora vulgaris Waksman, Umbreit and Cordon (1939) and Thermoactinomyces vulgaris Tsiklinsky (1899) were found to be the same organism (144) and the latter name is preferred (78). The names M. faeni and T. vulgaris have been used throughout the following discussions.

REFERENCES

In the reference section, the contractions for the various journals quoted are those given in the World List of Scientific Periodicals, published by Butterworths, London.

STATISTICAL METHODS

The statistical methods used were the chi-squared test,

"Student's" t test and the coefficient of correlation. The calculations were carried out on an "Olivetti programma 101" desk computer (British Olivetti Ltd., Berkley Square, London). Unless otherwise stated, when a difference is described as "significant" (S) this implies that the probability of its resulting from chance is less than 5 per cent ($p < 0.05$). When a difference is described as "highly significant" (HS) this implies that the probability of its resulting from chance is less than 1 per cent ($p < 0.01$). When a difference is described as "very highly significant" (VHS) this implies that the probability of its resulting from chance is less than 0.1 per cent ($p < 0.001$).

INTRODUCTION

The term "fog fever" was originally used to describe an acute respiratory syndrome which affected adult cattle usually while they were grazing fog or aftermath pastures in the autumn (18, 44, 141, 150, 162, 221). However, within the last 30 years, the term has been used indiscriminately to describe sudden onset respiratory distress in calves as well as in adult cattle and in housed as well as grazing animals (63, 132, 161, 167, 188). In one report (132) an undefined respiratory disorder named "indoor fog fever" which developed following exposure to mouldy hay dust was compared with the human disease, farmer's lung. In that report the suggestion was made that there could be a farmer's lung-like respiratory disorder of cattle since the prevalence of precipitating antibodies to M. faeni in hay-fed cattle was much higher in those with "indoor fog fever" than in others free from respiratory disease. That there was a bovine respiratory disease very similar to farmer's lung was proved during a clinico-pathological investigation of acute respiratory disease in adult cattle begun at the Glasgow Veterinary School in 1969 (207).

The aims of the investigations undertaken for this thesis were four-fold: to define the clinical and epidemiological aspects of farmer's lung in cattle, to investigate the prevalence and significance of precipitating antibodies to M. faeni in adult cattle populations in areas where farmer's lung had been confirmed, to study the criteria on which a diagnosis of farmer's lung could be made and to reproduce, under controlled conditions, farmer's lung in cattle.

As a result of this work, it has been established that farmer's lung is a respiratory disease of housed adult cattle being kept in the mainly upland areas of western Britain. Clinical signs are usually first noticed during the winter housing period and they are the result of the cattle regularly inhaling the dust of mouldy hay. Consequently, it has been proven that bovine farmer's lung is different epidemiologically (236), serologically (205) and pathologically (207, 291) from fog fever (204, 236), the acute pulmonary disorder with which it was originally confused.

CHAPTER 1

REVIEWS OF THE LITERATURE ON RESPIRATORY DISEASE IN ADULT CATTLE AND FARMER'S LUNG IN MAN

SECTION I

REVIEW OF THE LITERATURE ON RESPIRATORY DISEASE IN ADULT CATTLE

The earliest British references to bovine respiratory disease were in eleventh century manuscripts in which it was stated that lung disorders were common in cattle (243). The cattle plagues which appeared at regular intervals during the middle ages were not described in any detail although "longsought", as it was called by Fitzherbert (1523), was likely to have been contagious pleuropneumonia (243). These diseases had been introduced with cattle imported from the continent of Europe but they did not spread nationwide because of the small numbers and the very limited movement of livestock within Britain at that time.

As a result of the Industrial Revolution, which began in the early eighteenth century, many people left agriculture to work in the new industrial areas and this led to a rapid increase in the total population. It is doubtful whether the momentum of the Industrial Revolution could have been maintained had not an Agricultural Revolution taken place at the same time. In essence, agriculture changed from being a subsistence economy to the production of "cash" crops (179). The enclosure of common grazing lands enabled new methods of crop husbandry to be introduced and this, together with the use of new fodder crops such as clover and turnips which had been imported from the Netherlands (179), meant that large numbers of cattle could be housed and fed throughout the winter instead of having to be slaughtered in the autumn.

In the first book written in English that dealt only with diseases of cattle, Topham (1788) stated that, although inflammation of the lung was not well understood, several different types had been described. The common clinical signs were "coughing with short, difficult breathing and fever". He also reported that animals in good condition could develop signs of respiratory disease very quickly when grazing lush clover or foggage.

During the seventeenth and eighteenth centuries there was an increased movement of cattle throughout Europe, particularly as a result of the numerous wars, and this was responsible for the

dissemination of many local disease problems. Animals imported from Holland into the north-east of England not only gave the local Teeswater (later Dairy Shorthorn) breed an increased genetic potential to produce milk but it has been alleged that they also introduced bovine tuberculosis (85). This condition was subsequently spread throughout England because the Dairy Shorthorn breed became the most popular in the large number of town dairies which sprung up in the latter half of the eighteenth century (241). Skellet (1807) commented that "consumption (cough of long standing) is seldom seen in the country, but is confined more to cows that are kept to the stall in towns ...". He described another chronic respiratory disease (asthma) that was characterised by wheezing and dyspnoea and which was said to be "peculiar to cows feeding on grains". This condition did not appear to have an adverse effect on the general health of affected animals.

Knowlson (1834), who was a veterinary practitioner in Yorkshire, was the first to use the term fog fever to describe specifically the dyspnoea which affected adult cattle after they had been moved onto foggage in the autumn. Affected animals only coughed occasionally whereas there was frequent coughing and weight loss with the other two respiratory conditions he described. Inflammation by cold (a hoose) was the more severe disease and affected animals were dull with pyrexia, tachypnoea and often dyspnoea. Cows with "asthma" were said to be short of breath, particularly in the spring and autumn, but they usually remained bright with a normal temperature.

In a most informative text on British cattle and their diseases, Youatt (1858) stated that acute epidemic, or gangrenous, pneumonia was a common disease in which affected animals were very dull and usually died within 48 hours of their becoming ill. Youatt appreciated that disease was a dynamic and progressive process for he considered that catarrh (hoose), which arose less than two weeks after a change of management or environmental temperature, could develop into bronchitis (inflammation of the substance of the lung). This was a more severe condition after which there often developed a chronic lung disorder with wasting called phthisis or consumption. Although phthisis was regarded as an "end-stage lung" and not as a specific disease, lesions identical to those of pulmonary tuberculosis were frequently present. Youatt (1858) was probably the first to write about differential diagnosis based on the interpretation of clinical

findings when he suggested that individual respiratory diseases could be differentiated depending on the character and frequency of the coughing and on the presence or absence of thoracic pain.

The respiratory disease picture prior to the introduction of contagious pleuropneumonia around 1840 was that infectious pneumonias were prevalent and the variations in clinical severity may have been due to the effects of different aetiological agents. Fog fever had been recognised although parasitic bronchitis had only been reported in cattle less than one year old (180). Consumption was very common but was considered to be the final stage of many respiratory conditions.

Immediately after restrictions to the importation of cattle were removed in 1840, contagious pleuropneumonia was imported simultaneously from Holland and from Ireland so that by 1842, this disease was very common particularly in the London town dairies (170). The clinical and pathological features of "the present pleuropneumonia epizootic among cattle" were reported in detail for the first time in English by Barlow (1842; 1843). Gamjee (1861), who was the main veterinary protagonist of the germ theory of disease, noticed that contagious (epidemic) pleuropneumonia only appeared on farms where cattle had been bought-in. This was in contrast to sporadic pleuropneumonia which was a relatively common disease in self-contained herds and which looked similar to contagious pleuropneumonia at necropsy. However, the two conditions could be differentiated clinically. In the sporadic form, there was sudden onset anorexia, agalactia and pyrexia with tachypnoea and minimal coughing. On the other hand, epidemic pleuropneumonia developed more slowly and the clinical signs which included coughing, depressed appetite, tachypnoea and reduced milk yield, became progressively more severe. Cattle were usually said to recover from sporadic pleuropneumonia within ten days whereas the epidemic form was invariably fatal.

Lung abscesses, which were often found in chronic wasting animals with halitosis, were recognised as being one of the sequels of bronchitis and of pneumonia (92). Although he reported that lung worms could be associated with respiratory disease in adult cattle, Gamjee (1861) considered tuberculosis to be simply a complication of contagious pleuropneumonia that could be seen at necropsy.

Dobson (1872) described a condition, chronic bronchitis, which other veterinary practitioners called "phthisis pulmonalis or consumption ... because of its similarity to the human condition of the same name". This was a chronic, progressive, coughing, wasting and low milk yield syndrome in which tubercules and abscesses were often found at necropsy. On the other hand, Williams (1884) believed that phthisis was not only rare and hereditary in cattle, but also that it was entirely different from human pulmonary tuberculosis. The tubercules found in bovine lungs he considered to be the result of any respiratory infection. A frequent cause of coughing and wasting was considered to be chronic bronchitis, but Williams (1884) gave no indication of how this disease differed from phthisis. Paradoxically, he suggested that tuberculosis in cattle be made notifiable because of the danger to children who drank milk from "pining" cows.

The clinical signs of pneumonia with pleurisy, which was considered to be the most common chest disease, were pyrexia, tachypnoea, dullness and rigors with breathing which became more distressed, abdominal and painful as the pleurisy developed (288). Newly-calved cows suddenly exposed to cold, wet weather were said to be particularly susceptible to this condition. Like Dobson (1872), Williams (1884) was of the opinion that bronchitis rarely occurred by itself but was usually accompanied by a degree of pneumonia. The clinical signs were dullness, listlessness, a paroxysmal cough and a respiratory rate equal to or greater than the pulse rate. At necropsy, the large and small bronchi were found to be full of thick, yellow fluid and, when the cut surface of the lung was squeezed, small yellow pellets could be expressed.

When store cattle imported from North America in 1879 were slaughtered on arrival in Britain because they were said to be affected with contagious pleuropneumonia, only Williams (1892) of the recognised veterinary experts disagreed with the Board of Agriculture veterinary inspectors. He stated that the American cattle were affected with a different condition which he called "catarrhal bronchopneumonia". History repeated itself in 1891 but this time Williams' opinion was supported by Nocard (1892) who had himself been investigating a respiratory disease in American cattle landed in Paris. Nocard (1892) was of the opinion that the English and French conditions were virtually the same. However, the Board of Agriculture refused to admit that their representatives had erred (7) although they did

acknowledge that contagious pleuropneumonia and "the American lung disease", as it became known, were different disease entities.

Rinderpest was imported into Britain in 1865 (170) and one unexpected benefit of the subsequent eradication campaign was the marked decrease in the incidence of contagious pleuropneumonia. This was almost wholly due to the severe restrictions on cattle movement that were strictly enforced. Contagious pleuropneumonia became a notifiable disease in 1870 and, within a few years of the implementation of a national eradication policy, the condition was brought quickly under control. The last case was slaughtered in 1898 and during the final three years of the eradication campaign, the few confirmed cases occurred in the London town dairies where the disease had been so prevalent for so long (170).

The veterinary inspectors who examined the carcases of cattle slaughtered under the Animal Disease (Pleuropneumonia) Act, 1890, reported that the prevalence of pulmonary tuberculosis ranged from 12 to 20 per cent (85). In virtually all the herds that he had slaughtered out, McCall (1891) had found more animals affected with tuberculosis than with contagious pleuropneumonia. In one milking herd, 83 per cent of the cows had macroscopic evidence of tuberculosis at necropsy (3). Indeed, McCall (1889) had already suggested that, as pleuropneumonia did not affect man, public health would benefit more from the slaughter and condemnation of animals affected with tuberculosis. The prevalence and hence the importance of bovine tuberculosis had been completely under-estimated because all animals with chronic lung disease were considered to be suffering from "pleuro" (288) and the tubercules seen so frequently at necropsy, were thought to result from any respiratory infection and were therefore not associated with one specific infectious agent.

The suggestion that human and bovine tuberculosis were the same disease (249) had been accepted generally by the end of the nineteenth century. From his observations of tuberculosis in soldiers and in Parisian dairy cows, Villemin (1868) concluded that inhalation and not ingestion was probably the most important route of infection in adults. This conclusion was supported by Fleming (1874) and by MacFadyean (1898) who also reported that the tuberculous lesions were confined to the thoracic cavity in 64 per cent of bovine cases. The importance of the aerosol route of infection was confirmed

experimentally by Chaussé (1913) who also demonstrated that pulmonary tuberculosis in cattle was virtually always "open".

Although the mortality rate from tuberculosis in man has decreased steadily since the beginning of the nineteenth century (52), these figures failed to show that, around the beginning of the twentieth century, tuberculosis was responsible for about 40 per cent of the deaths in young children subjected to detailed post-mortem examination (227, 228). These children had become infected as a result of drinking milk from cows with tuberculosis of the udder. Consequently, a case for the state control of tuberculosis in cattle was promoted almost wholly from the public health aspect as this disease was considered to be the greatest single cause of mortality in man (126), many of whom had become infected through drinking milk from diseased cattle. As a result of the fourth government enquiry into bovine tuberculosis which established beyond all doubt that Mycobacterium tuberculosis var. bovis did affect man and cattle, an Order making tuberculosis of cattle a scheduled disease came into effect in 1913 (170). However, pulmonary tuberculosis was excluded from the legislation because this form of the disease was considered to be very difficult to diagnose (122). Hence a 20 year period in which the bovine veterinary literature was dominated, and sometimes almost overwhelmed, with discussions, opinions and reports of tuberculosis finished with the passing of government legislation.

The topical nature of bovine tuberculosis probably contributed in no small way to the awakening of interest in cattle diseases and the advances that had been made during the previous 20 years were brought together in Hoare's comprehensive text on veterinary medicine (120). There, it was stated that the most common acute pulmonary disease was aspiration broncho-pneumonia and the clinical signs, which were usually severe, included anorexia, pyrexia and dyspnoea (121). Although various bacteria had been isolated from the lung lesions, it was not known whether any could be regarded as specific aetiological agents. Two other relatively uncommon acute conditions were also mentioned; croupous pneumonia in which the pathological lesions were similar to those of contagious pleuropneumonia and pulmonary emphysema which, it was alleged, could develop following tuberculosis, broncho-pneumonia, violent exertions and puncture wounds in the thorax. A specific reference was also made to a veterinary practioner from York who, in common with a few

others, had reported several cases of pulmonary emphysema the aetiology of which was obscure.

Cattle affected with pulmonary tuberculosis, which was a common chronic or insidious onset condition, coughed with increasing frequency, were tachypnoeic then became dyspnoeic and began to lose weight. Acute broncho-pneumonia often flared up shortly after calving in such cows. There were two other syndromes which depended on a negative tuberculin reaction for their differentiation from tuberculosis; chronic bronchitis which affected older cows and was unusual in the variety of adventitious lung sounds that could be heard on auscultation and chronic pneumonia which was diagnosed usually because there had been an incomplete recovery from an acute pneumonic episode.

There are many references in Hoare's book to continental workers who had been much more active in the field of bovine medicine than their British counterparts. The diseases of the lower respiratory tract were very well described both clinically and pathologically by Friedberger and Fröhner (1910). They stated that not only was tuberculosis by far the most important and most widespread bovine disease, but that it was also the most commonly diagnosed respiratory disorder. In stressing the difficulty associated with the diagnosis of the pulmonary form, Muller (1910) is quoted as saying "that the diagnosis can only be made in about 50 per cent of the animals with clinical disease". Other causes of chronic coughing and wasting had been recognised but they were not considered to be important. Of the acute infectious pneumonias, broncho-pneumonia was stated to be the least severe with the majority of cases recovering after a two to three week illness although a chronic suppurative pneumonia could develop subsequently in a few animals. There was marked pyrexia and severe constitutional signs with croupous pneumonia which was rapidly fatal. Gangrene and halitosis developed in cases of inhalation pneumonia and also with embolic pneumonia which usually followed suppurative thrombo-phlebitis. Little was known about pulmonary emphysema although references were made to a disease "pneumatosis" which affected cattle grazing swampy districts in the Netherlands and Belgium.

The pulmonary disorders that had been recognised by the beginning of this century in Britain and on the continent (88, 121)

can be separated into two major clinical groups. Firstly, there were the acute pneumonias in which severe constitutional as well as respiratory signs were often present; these pneumonias were frequently fatal. The second group was made up of the chronic respiratory diseases in which coughing, tachypnoea and weight loss were the predominent clinical signs. This is still the method of choice in classifying respiratory disease because it makes clinical differential diagnosis must simpler. However, neither group can be considered to be mutually exclusive since, for example, parasitic bronchitis can be an acute disease and also a chronic disease within the same herd. Henceforth, in this review, the specific respiratory disorders of adult cattle shall be discussed from a clinical differential diagnosis aspect.

Tuberculosis had been shown to be the most important disease of cattle as well as the commonest pulmonary disorder and, when the Tuberculosis Order was reintroduced in 1925 provision was made for the slaughter, with compensation, of dairy cows "having a chronic cough with definite clinical signs of tuberculosis" (170). Nevertheless, a more positive approach to the problem of bovine tuberculosis was still advocated, particularly in Scotland, and largely as a result of their persistence, the Attested Herds Scheme was introduced in 1935 (170). Progress in the setting-up of tuberculosis-free herds remained slow, however, even although the Scheme was extended in 1937 to include beef and rearing herds. As with contagious pleuropneumonia, significant progress was made only after a national plan with full government financial assistance had been adopted. The final campaign, which began in 1950, was based on the single comparative intra-dermal tuberculin test, the slaughter of all reactors with the payment of full compensation and a cash bonus payment for milk produced by "tuberculin tested" herds. The campaign was carried out area by area until in 1960, after only ten years, the Minister of Agriculture was able to report that the whole of Britain was an attested area and that British cattle could be considered free from bovine tuberculosis (170). The cost of the eradication campaign was approximately 130 million pounds (177), but the saving in children's lives alone made this eminently worthwhile.

Just as the slaughter of cattle suspected of having contagious pleuropneumonia finally established the importance of pulmonary tuberculosis, so during the eradication of tuberculosis other

causes of chronic coughing and wasting were recognised. One type of chronic pneumonia, which was said to be relatively common, resembled advanced pulmonary tuberculosis although affected cows were bright and usually had a normal temperature and appetite (244). In some cases, clinical signs developed suddenly around calving whilst in others coughing had been noticed for several days or weeks before more severe signs of respiratory disease were observed. Hyperpnoea was obvious at rest and there was marked exercise intolerance with frequent productive coughing. On auscultation, loud rales and wheezing noises were heard all over the chest but no thoracic pain was elicited on percussion. Although affected cows lost weight and their milk yields decreased during the course of the disease, the condition did not appear to be fatal. The pathological lesions were said "to greatly resemble those occurring in contagious pleuropneumonia", but there was no pleurisy and emphysema was usually present. From the above description, it would appear that this respiratory disorder had a non-infectious aetiology.

Lung phthisis was an "umbrella-term" used to describe cases of chronic respiratory disease with progressive weight loss and weakness (88). Although tuberculosis was the most frequent cause of this syndrome, other conditions including mycotic infections, lung tumours, lung abscesses and chronic suppurative pneumonia were also responsible for a proportion of cases.

Mycotic infection was not mentioned by Hoare (1913b) as a specific pulmonary disorder despite the inclusion of aspergillosis in the list of conditions with which contagious pleuropneumonia might be confused (51). In this latter context, there was said to be an "absence of marked respiratory symptoms" in cases of pulmonary aspergillosis. The importance of mycotic infections of farm animals in Britain was still unknown in 1951 and, during a two year survey of fungal associated diseases, Ainsworth and Austwick (1955) failed to find a single case of mycotic pneumonia in cattle. Confirmation that Aspergillus fumigatus did penetrate deep into the lungs of cattle was provided by Austwick (1962) who found "asteroid" bodies in 66 per cent of adult bovine lungs during an abattoir survey in south-east England. Over a ten year period, only 12 cases of mycotic pneumonia in calves (11) and two in adults (12) have been confirmed at Weybridge.

Almost all the information regarding pulmonary neoplasia is based on the pathological examination of material from either

individual cases (191) or from abattoir surveys (5, 137). During the period from 1932 to 1940, three out of every one thousand cattle which had been slaughtered because of a tuberculous-like respiratory disease was found to have pulmonary neoplasia (137). Lung tumours represented 30 per cent of the total number of tumours found. When Anderson and Sandison (1968) examined tumours submitted from abattoirs all over Britain, they found that the frequency of lung tumours in cattle was 19 per one million cattle slaughtered. At least half the animals examined in this latter survey would have been less than three years old because virtually all cattle reared for beef production are slaughtered from one to two years of age. Secondary tumours in the lung were more than twice as prevalent as primary lung tumours. Overall, lung tumours made up 26 per cent of the number of tumours examined by Anderson and Sandison (1968) and this figure is similar to the 30 per cent reported by Kenny (1944).

In his discussion on suppuration in cattle, Ward (1917) commented on the lack of information regarding the bacterium Bacillus pyogenes (synonym Corynebacterium pycgenes) in the English language compared with the Dutch and German literature. B. pyogenes had been recognised in Europe as being the cause of a chronic broncho-pneumonia which particularly affected the anterior lobes of the lungs (217). Even at necropsy, it was considered to be difficult to differentiate between chronic suppurative broncho-pneumonia produced by B. pyogenes and pulmonary tuberculosis (26, 123, 217).

During the course of their meat inspection duties, Tweed and Edington (1930) discovered that pneumonia in adult cattle was much commoner than had been appreciated hitherto. Based on the pathological examination of pulmonary lesions, they considered that there were two types of non-tuberculous pneumonia and at least some were due to specific bacterial infections. In the first type, from which no specific organism would appear to have been isolated, "the lungs showed patches of broncho-pneumonia, with areas of collapse and marked emphysema of the inter-lobular septa. The bronchi of the infected areas were usually plugged with a thick, tenacious muco-purulent secretion". In the second type, from which Pasteurella boviseptica Group 1 was readily recovered, "the lungs were markedly consolidated and the inter-lobular septa thickened".

The attempt by Tweed and Edington (1930) to classify the pneumonias of mature cattle on a gross pathological basis occurred

during a period of controversy in the British veterinary profession. The argument concerned the possible existence in Britain of haemorrhagic septicaemia, an acute, severe, primary pasteurellosis which at that time was relatively common in Africa and in the Far East. The condition as reported in this country mainly affected cattle less than two years old, it was quickly fatal and at post-mortem examination, many focal areas of haemorrhage were seen (165). This haemorrhagic septicaemia-like disease was claimed to be associated with the ingestion of bracken fern (Pteridium aquilinum) (152, 159) and also with Bacillus bovisepticus infection (163).

In several incidents of an "infectious pneumonia of adult bovines" (226), several animals had died after a clinical illness characterised by tachypnoea, pyrexia (up to 107°F), anorexia, a dry painful cough, painful grunting when lying and distinct rales in the chest. The lung lesions seen at necropsy were similar to those of croupous pneumonia (121) and B. bovisepticus was isolated in pure culture from the lungs. As a result of their bacteriological, clinical and pathological findings, Edington, Sampson and Tweed (226, 265) considered that some of these cases had died from the pectoral form of haemorrhagic septicaemia. Gaiger (1931) did not accept this and pointed out in considerable detail the differences between "true" haemorrhagic septicaemia and the pneumonia of British cattle from which pasteurellae had been isolated. However, Edington (1931) and other workers (106, 210) remained unconvinced. The considerable discussion that followed in the Veterinary Record was aptly summarised by Shirlaw (1938) who wrote that "much of the confusion surrounding this disease has arisen through loose definitions, inaccuracy of observations and unwarranted assumptions based on these observations". He pointed out that confusion would not have arisen had the term "bovine pasteurellosis" been used originally since there was no doubt that both pneumonic and septicaemic forms of pasteurellosis were present in Britain.

The clinical and pathological features of bovine pasteurellosis (239) were identical to those of transit fever, a condition which had originally been described in 1925 (117) and from which B. bovisepticus had been isolated from the lungs in almost pure culture. Transit fever was a sudden onset, severe and rapidly fatal disease of Orkney and Irish cattle imported into Aberdeenshire. The importance of adverse environmental factors in predisposing cattle to

this syndrome was highlighted by Hepburn (1925) who pointed out that transit fever wasn't seen in cattle imported from Canada due to their being transported under far better conditions.

Pasteurellosis was diagnosed in two large outbreaks of pneumonia in tuberculosis-free Jersey cows that had recently been imported from the island of Jersey (172). Individual animals developed sudden onset anorexia, pyrexia (up to 107°F) and rales were heard on auscultation. When the first animals were initially seen to be ill in the autumn, all the Jersey cows in both herds were noticed to be coughing. C. pyogenes was isolated from the extensive exudative anterior lobe pneumonic lesions of several of the fatal cases and so it was considered to be the cause of the respiratory problem. An identical respiratory illness developed again the following July in the milking cows of one of the herds and also in some stirks at an out-farm. Parasitic bronchitis was diagnosed after one stirk had died and its lungs had been examined at Weybridge. The cows were housed immediately and no further cases developed although several apparently fully recovered animals did have a relapse of acute pneumonia a few days after calving. Retrospectively, it was recognised that these had been outbreaks of parasitic bronchitis complicated by C. pyogenes infection. It is interesting to note that with one exception, the treatments used by Mitchell (1939) had been equally ineffective in reducing the very high mortality rate. The exception was M. and B. 693 (sulphapyridine) which "achieved results in three of the cases such as I have not previously experienced"; in other words these cases did not die.

It was not entirely unexpected that Mitchell (1939) failed to associate parasitic bronchitis with sudden onset, severe respiratory disease in individual cows, in spite of widespread coughing in the rest of the herd because many people still considered that infestation with the cattle lungworm, Dictyocaulus viviparus, either did not affect adult animals (157), or produced only mild clinical signs (263). Nevertheless, there had already been several reports of fatal respiratory disease associated with patent parasitic bronchitis in cows (157, 222, 253, 282). The main clinical signs were widespread coughing, tachypnoea, dyspnoea, reduced appetite, weight loss and reduced milk yield. Penhale (1925) had stated that in adults, parasitic bronchitis was often complicated by pneumonia. In these and in other reports which followed shortly

afterwards (21, 245), parasitic bronchitis had been diagnosed because adult worms were present in the bronchi at necropsy.

The concept that there could be "two distinct kinds" of parasitic bronchitis was put forward by Taylor (1951). In the well-documented, typical form of the disease which affected both immature and adult cattle, adult worms were present in the bronchi and the finding of larvae in the faeces confirmed the diagnosis. In the atypical form which was said to occur mainly in adult cattle, immature worms were present in the bronchi and larvae could only rarely be detected in the faeces. It was considered that fully susceptible cattle developed typical parasitic bronchitis whereas in resistent animals, the larvae failed to reach sexual maturity (125). The suggestion that larvae could be inhibited in their development in resistent animals has since been confirmed (131, 208). In the light of more recent knowledge regarding the life history of D. viviparus, the above classification is of limited usefulness because pre-patent and post-patent parasitic bronchitis (128) must also be considered as forms of atypical parasitic bronchitis, which they are not.

The realisation that D. viviparus infection could produce sudden onset dyspnoea in adult cattle (125, 253) prompted Barker (1937) and later Bruford (1951) to draw attention to the difficulty in differentiating between parasitic bronchitis and fog fever. The similarity between fog fever, which had only been reported from north Wales (221) and from Yorkshire (141), and acute interstitial pulmonary emphysema (23) was commented upon by McLean (1948) and by Leslie (1949). In his review, Leslie (1949) confirmed that fog fever was a sudden onset respiratory distress condition which affected only adult cattle while they were grazing foggage. In the ensuing discussion, it was suggested that both parasitic bronchitis and fog fever might be the result of D. viviparus infestation (260).

Fog fever and atypical parasitic bronchitis were considered by Soliman (1952) to be similar diseases because both presented with sudden onset dyspnoea and adult lung worms could not be seen in the bronchi at necropsy. Consequently, it was implied that fog fever was an allergic reaction following a massive challenge with D. viviparus larvae. This was not an unreasonable hypothesis because fog fever appeared to be identical to the published clinical and pathological descriptions of hypersensitivity reactions in cattle which had been

produced by anthrax anti-serum (266), the death of warble fly (Hypoderma bovis) larvae (99, 105) and following vaccination with a commercial, bacterial vaccine (151). Referring to the work done by Kerr and Robertson (1943) who had produced experimental anaphylactic shock by instilling extracts of Trichomonas foetus into the uteri of cows, Davies (1946) had already suggested that the acute pulmonary emphysema which developed in cattle turned onto leguminous pastures "seemed to be some form of hypersensitivity to some agent in the pasture".

The start of the bovine tuberculosis eradication campaign in 1950 initiated the second major change in the importance of respiratory disease in adult cattle in Britain. During the second half of the nineteenth century, contagious pleuropneumonia was not only the most widely recognised bovine respiratory disease but it was also the most important disease of cattle. After the eradication of contagious pleuropneumonia in 1898, tuberculosis was accepted as the most common bovine respiratory disease and also as the most important cattle disease. During the first half of the twentieth century as interest in cattle diseases increased, respiratory conditions other than tuberculosis began to be reported (121, 157, 172, 221, 226, 244, 282) and some attempts were made at differential diagnosis. However, progress in this area would appear to have all but stopped following the introduction of new, very efficient anti-bacterial drugs (antibiotics and sulphonamides) into veterinary practice. It has been estimated that the mortality from all cases of pneumonia at the Cornell Ambulatory Clinic fell from 33 per cent during the period from 1927 to 1937, to only 5 per cent from 1945 to 1947 (224). The lack of emphasis on differential diagnosis led to a considerable amount of confusion when respiratory disorders from a known tuberculosis-free adult cattle population were discussed.

The problems associated with respiratory disease terminology in North America prompted Blood (1962) to propose that the "non-standard" forms of pneumonia in cattle be grouped together and he suggested that the term "atypical interstitial pneumonia" (AIP) be adopted. He considered there to be two clinical forms of AIP; an acute form in which affected animals developed sudden onset respiratory distress usually in the autumn while they were at pasture. It was stated that coughing was not a feature of this form of the condition. A form of chronic AIP,

which had only been reported from Canada and from Switzerland, was associated with the inhalation of hay dust and therefore was most common in winter when cattle were housed. The clinical signs developed gradually and included frequent coughing, tachypnoea, hyperpnoea and weight loss. No serious attempt was made to define a specific aetiology for AIP, although it was recognised that in many of the reports, the onset of respiratory disease was associated with a specific feeding regime.

The strict time relationship between onset of severe respiratory signs and the feeding of mouldy fodder seemed to indicate that inhaled or ingested allergens could be involved in the pathogenesis of certain types of AIP (31). An association between the onset of respiratory disease and the feeding of mouldy hay and of mouldy silage had also been noticed by Van Kruiningen (1962) who proposed that the syndrome be called bronchiolitis obliterans. Gibbons (1962) compared bronchiolitis obliterans in cattle with the human condition, silo-filler's disease, in which the respiratory signs result from the inhalation of nitrogen dioxide (153), whereas Jenkins and Pepys (1965) stated that bronchiolitis obliterans in cattle resembled the human respiratory disease, farmer's lung. As a result of their finding precipitating antibodies to M. faeni in the sera of a large percentage of cattle with respiratory disease, Jenkins and Pepys (1965) suggested that cattle which had been fed mouldy hay could develop a farmer's lung-like respiratory disorder. It had just been confirmed that farmer's lung was a hypersensitivity disease which could develop following the repeated inhalation of the dust of mouldy hay in which there were antigens derived from thermophilic actinomycetes, in particular M. faeni (199).

At this stage, it is apposite to summarise the respiratory disease picture in adult cattle in Britain when a clinico-pathological study of acute respiratory disease was begun at the Glasgow Veterinary School in 1969. The acute bacterial pneumonias were still said to be relatively common but it is probable that their importance had decreased in a manner similar to that reported by the Cornell workers (224). Typical clinical signs were sudden onset anorexia, dullness, pyrexia, tachypnoea and a degree of thoracic pain. A small proportion of acute bacterial pneumonia cases failed to make a complete recovery in spite of the use of new drugs and frequently it was found that they had developed a chronic suppurative pneumonia characterised by coughing

and weight loss (160). Although two forms of parasitic bronchitis had been recognised, their differentiation appeared to rely almost totally on the presence or absence of larvae in the faeces and therefore, on the presence or absence of adult worms in the bronchi. Frequent coughing, tachypnoea and a degree of respiratory distress were common clinical signs. A diagnosis of fog fever was usually made when the major presenting sign was sudden onset severe respiratory distress. Mycotic pneumonia, pulmonary abscesses and tumours were almost invariably diagnosed at necropsy.

SECTION II

REVIEW OF THE LITERATURE ON FARMER'S LUNG IN MAN

The respiratory syndrome known as farmer's lung was probably first described over 200 years ago when Ramazzini (1700) reported symptoms of respiratory disease in workers who handled dusty grain which had over-heated during storage. These grain workers developed a dry persistent cough and "almost all .... are short breath'd and cachectick and seldom live to be old; nay they are very apt to be seized with an orthopenoea and at last with a dropsy". Interest in organic dust-induced pulmonary disorders was awakened in Britain following the description of an acute, severe respiratory disease which affected farm workers who had been handling mouldy hay (40). Fawcitt (1936) concluded that this was a true bronchomycosis (broncho-mycosis feniseciorum) and furthermore, that it was an occupational disease because only "the farming classes were affected".

The name "farmer's lung" was proposed by Pickles (1944) who had noticed that the symptoms which appeared during the winter and were associated with the feeding of mouldy hay to housed cattle, tended to disappear during the summer when the cattle were grazing. This led him to speculate that individuals who developed farmer's lung had become sensitised to the dust of mouldy hay. As a result of a survey of fungous diseases in Britain, Duncan (1945) rejected the current view that farmer's lung was a true pulmonary mycosis and proposed that moulds, by their action on the hay fibre, produced a fine dust and that this was the cause of farmer's lung. In spite of these reports, farmer's lung remained a rather vague respiratory disorder until Fuller (1953) and Studdert (1953) presented details from a series of farmer's lung cases from the south-west and the north-west of England respectively.

Fuller (1953) who "consolidated, organised and defined" the available knowledge on farmer's lung (250), not only described the typical sudden onset (acute) form of the disease in detail, but he also reported that there was a chronic irreversible form which affected some individuals who had been exposed to mouldy hay dust for a number of years. In these cases, the symptoms resulted from the development of diffuse pulmonary fibrosis. Studdert (1953) drew attention to the fact that farmer's lung was rarely seen in hospital

practice despite being well recognised in rural practices in certain areas of England. This he attributed mainly to the reluctance of the agricultural community to seek medical attention unless and until they were severely incapacitated and, with specific regard to farmer's lung, to the fact that their symptoms disappeared during the summer without medical treatment. Farmer's lung was compared with other organic dust diseases such as maple bark disease and byssinosis and it was suggested that all three were the result of "a non-specific interstitial lung reaction to some material in the fungous-laden dust" (251). With regard to aetiology, Fuller (1953) was of the opinion that over a period of months, and possibly years, an individual gradually became sensitised to mould spores or grass particles and, that on further inhalation of these particles, a widespread pulmonary inflammatory response was produced.

When the College of General Practitioners began their survey of farmer's lung in 1957, less than 100 cases had been reported throughout the world even although the disease had also been recognised in France (214), Ireland (134, 252), Sweden (258), Switzerland (270) and in the United States of America (247). While the survey data was being collected, details of a large number of acute cases were reported from the United States (60, 86, 259).

The findings of the British survey mentioned above (250) emphasised the importance of climate and agricultural husbandry practices in the pathogenesis of farmer's lung which was found to be much commoner in the western, wetter upland areas of Britain than in the flat, dry, eastern parts. It was claimed that farmer's lung was more prevalent in the west of the country because the rainfall during the hay-making months was much higher than it was in the east and the prevalence of farmer's lung was said to be greater following a wet summer than after a dry one. Hay was associated with the development of clinical symptoms in more than two-thirds of the cases and most of these had been exposed while they had been feeding cattle. Most of the cases were first diagnosed during January, February and March. The sudden onset, typical form of the disease was the most prevalent although the symtoms had developed insidiously in slightly more than one-third of the cases.

That a diagnosis of farmer's lung should still be considered even in the absence of a history of acute respiratory symptoms was

emphasised by Bishop, Melnick and Raine (1963). Indeed, in a subsequent detailed clinical investigation, Pepys and Jenkins (1965) found that respiratory symptoms had developed insidiously in most of their cases.

Farmer's lung was suspected as being a hypersensitivity disease because of the close association between the inhalation of mouldy hay dust and the onset and severity of the clinical symptoms (60, 64, 86, 89, 202). This suspicion appeared to be confirmed when precipitating antibodies against extracts of mouldy hay were shown to be present in the sera of a large proportion of farmer's lung patients (201). It was postulated that these "farmer's lung hay" antigens had resulted from hay having heated and moulded (201) because in bagassosis, a respiratory disorder similar to farmer's lung, clinical symptoms were induced experimentally only in patients who had been exposed to over-heated bagasse (38). The reactivity in the sera of farmer's lung patients was confined to the gammaglobulin fraction and so was assumed to be antibody (142, 200).

When farmer's lung patients with precipitins against these "farmer's lung hay" antigens were exposed to mouldy hay dust and to water-soluble extracts of mouldy hay, they developed a clinical response identical to the field disease (287). However, individuals who did not have precipitins in their sera were unaffected by the same experimental procedures and so it was concluded that precipitating antibodies were necessary for the pathogenesis of farmer's lung and that the patients were hypersensitive either to the hay itself or to allergens associated with it.

When farmer's lung patients inhaled extracts prepared from fractions of mouldy hay dust separated according to particle size in a wind tunnel, an acute clinical response was produced only by the extracts of the "extra-coarse" and "coarse" fractions (287). Mould spores which were to be found in the "medium" and "fine" fractions, were consequently thought not to be involved in the aetiology of farmer's lung. Because there were more plant fragments in the two coarse fractions, it was suspected that grass fibre could have been altered chemically in some way due to the heating process. However, no clinical reaction was produced when extracts of autoclaved "good" hay were inhaled by farmer's lung patients and so Williams (1963) agreed with the view previously expressed by Pepys and his colleagues

(1962) that it was a combination of heating and moulding which changed "good" hay into "farmer's lung producing" hay.

Gregory and Lacey (1963) compared the microbiological flora of "good" hays with those of "farmer's lung associated" hays to study the role that the microbiological components of mouldy hay dust might play in the pathogenesis of farmer's lung. Although no difference was found in the amount of herbage fragments in the dust of the two types of hay, a specific feature of the farmer's lung-associated group was the very large number of thermophilic actinomycete spores, in particular those of M. faeni and T. vulgaris (50). Lacey and Lacey (1964) reported that there could be up to 1600 million thermophilic actinomycete spores per cubic metre of air when mouldy hay was shaken out and they estimated that a man doing light work in such an atmosphere could retain up to three quarters of a million spores per minute in his lungs. The spores of M. faeni and T. vulgaris have a diameter of one to two microns (10) and so can penetrate right down into the peripheral gas-exchanging parts of the lungs where the typical pathological lesions of farmer's lung are to be found (71, 234).

The connection between thermophilic actinomycetes and farmer's lung was finally estabished when it was found that "farmer's lung hay" antigens only developed in sterile hays that had been inoculated with thermophilic actinomycetes prior to their incubation (199). When inocula of individual actinomycete species were used, almost all the "farmer's lung hay" antigen activity was associated with M. faeni and T. vulgaris. Clinical symptoms similar to those of the naturally occurring disease developed in farmer's lung patients after they had been aerosolised with a carbol-saline extract made from a pure culture of M. faeni. When challenged in a similar manner, a single precipitin-negative individual experienced no adverse clinical reaction. These findings appeared to confirm that farmer's lung was a hypersensitivity disease and that sensitisation followed the inhalation of the spores of the thermophilic actinomycetes, in particular those of M. faeni. Since precipitating antibodies appeared to be necessary for the development of the acute disease, it was concluded that farmer's lung resulted from a type III, or Arthus-type, hypersensitivity reaction (196).

The similarity between the histopathological lesions found in an early, acute, fatal case of farmer's lung and those of

experimentally produced Arthus-type reactions in the lungs of rabbits (232) prompted Barrowcliff and Arblaster (1968) to endorse the view that acute farmer's lung was the result of a type III hypersensitivity reaction. However, a striking feature of lung biopsies taken routinely from suspected cases of farmer's lung was the large numbers of mononuclear cells that had infiltrated the alveolar septa and walls (71, 234, 259). This together with the presence of "tuberculoid" granulomata led several workers to suggest that a type IV, or delayed type, hypersensitivity reaction could also be involved in the pathogenesis of farmer's lung (30, 71, 234).

Mainly as a result of the survey reported by Staines and Forman (1961), farmer's lung became a prescribed disease in 1965 under the National Insurance (Industrial Injuries) Act and, for the purposes of this Act, has been defined as a "pulmonary disease due to the inhalation of dust of mouldy hay or of other mouldy vegetable produce, and characterised by symptoms and signs attributable to a reaction in the peripheral parts of the broncho-pulmonary system, and giving rise to a defect in gas exchange" (171).

Since the discovery of farmer's lung, a large number of respiratory diseases with similar clinical symptoms and microscopic lung lesions have been described (48, 111, 181, 196). It has been proposed that these conditions be grouped together and called "extrinsic allergic alveolitis" since the only obvious difference between them is the exciting organic dust (196). Purely from the pathological point of view, extrinsic allergic pneumonia (234) or extrinsic allergic bronchiolo-alveolitis (230) is a more precise term because significant lesions can be present in the respiratory bronchioles as well as in the peripheral gas-exchanging tissues. Farmer's lung is frequently used as the type example of extrinsic allergic alveolitis.

Since a type III hypersensitivity reaction is dependent upon the presence of precipitating antibodies (49), it should be possible to transfer this form of reactivity from a sensitised individual to a non-sensitised recipient with serum alone. When Hensley and others (1974) transferred serum from monkeys sensitised with pigeon serum to recipient animals and subsequently challenged both groups with an aerosol of pigeon serum, they found identical lesions in both donor and recipient monkeys. Furthermore, these

changes were similar to those of extrinsic allergic alveolitis (farmer's lung disease). The presence of vasculitis, which is a characteristic feature of a type III hypersensitivity reaction, together with the presence of immunoglobulins and complement (C3) within and surrounding medium sized blood vessels was reported following immunohistological studies of lung biopsies from two patients taken immediately after an acute episode of farmer's lung (94). Therefore, it would appear that a precipitin-mediated tissue damaging hypersensitivity reaction (type III) is involved in the pathogenesis of classical acute farmer's lung.

Jones (1970) concluded that farmer's lung was the result of a complex hypersensitivity reaction since microscopic changes associated with both type III and type IV hypersensitivity reactions were present in the lungs of rabbits sensitised to M. faeni after experimental challenge. It is now recognised that "tuberculoid" granulomata are not specifically associated with a type IV reaction because they can also result from the precipitation of insoluble antigen-antibody complexes in a type III reaction under conditions of antibody excess (46, 248). Despite demonstrating that respiratory tract lymphocytes from rabbits sensitised to M. faeni were capable of producing migration inhibition factor, Kawai and his colleagues (1973) cited other workers who indicated that the production of this factor was not a specific indicator of delayed hypersensitivity and "can only be regarded as the product of an immunologic reaction of undetermined type". Although type IV hypersensitivity does probably play a role in the pathogenesis of farmer's lung, conclusive proof of its importance is still lacking.

It has also been suggested that a type II reaction is involved in the pathogenesis of farmer's lung because of the absence of necrotising inflammatory lesions in the venules and the small numbers of neutrophils in some lung biopsies (278). This was considered probable since a major component of "farmer's lung antigen" is polysaccharide and some bacterial polysaccharides are particularly adept at fixing onto cells (49). However, it is difficult to interpret, with an absolute degree of certainty, histopathological changes found in lung biopsy material when the time of the patient's last exposure to the allergens is unknown.

Although clinical symptoms and signs suggestive of

bronchial asthma are not part of the typical acute farmer's lung picture (60, 71, 109), Pepys and Jenkins (1965) did find several patients who developed an immediate-type respiratory response. Initially, the respiratory signs had developed insidiously and, after further exposure, the patients developed typical acute episodes before passing into an immediate-type response phase. As these were almost certainly non-atopic individuals, these immediate-type reactions are likely to have been mediated by IgG short-term antibody (197) and not by serum IgE, the levels of which are known to be within the normal range in farmer's lung patients (223).

The M. faeni antigens responsible for farmer's lung were generally considered to be derived from spores since the onset of clinical symptoms developed within a few hours of a sensitised individual's being exposed to mouldy hay dust. However, Walbaum, Biguet and Tran Van Ky (1969) reported that, with sera from clinical cases of farmer's lung, precipitation reactions developed with antigenic fractions of M. faeni prepared from medium (metabolic extract) but not from those prepared from mycelium and spores (somal extract). It could be concluded, therefore, that the spores themselves were not particularly antigenic and, since many of the metabolic antigens had enzymatic activity, that the patient had become sensitised to metabolic products. This could have occurred as a result of the germination of previously inhaled spores. M. faeni has been grown from a lung biopsy taken immediately after an acute episode of farmer's lung (280) and T. vulgaris has been isolated from a lung biopsy after an illness of six months duration (279). Viable spores of M. faeni have been recovered from lung tissue and from macrophages for up to 59 days after guinea pigs had been exposed by the aerosol route, whereas the spores of A. fumigatus and Candida albicans were completely destroyed by alveolar macrophages within a few days of their being administered (269). Consequently, it can be said that M. faeni and T. vulgaris do have the ability to survive in the lung without their capacity to germinate being adversely affected to any significant degree. That the spores of M. faeni were able to germinate actually in the lungs was confirmed by Voisin and his colleagues (1971) who reported that they had seen mycelial proliferation of M. faeni in pulmonary smears from guinea pigs previously treated with anti-macrophage serum. This confirmed that M. faeni had the ability to grow in the lungs of guinea pigs although, in this context, it must be stated that the lung defence mechanisms of the animals used were not

fully functional.

As well as failing to obtain serologically active material from spore prepartions, Fletcher and Rondle (1973) also reported that these preparations did not remove antibody activity from farmer's lung sera. Edwards (1970; 1972) identified antibodies against two antigens that were so heat labile that the became denatured after only a short period at the temperature needed for M. faeni to develop ($50^{o}C$). These antigens could be demonstrated in preparations made from laboratory cultures of M. faeni but not in extracts of mouldy hay. Therefore, it appeared that hypersensitivity developed following exposure to mycelial antigens either carried into the lungs adsorbed onto fungal and actinomycete spores or plant materiai, or more likely they were produced in the lungs by germinating spores.

Many of the M. faeni antigens have since been shown to have enzymatic activity (29) and it would appear that those with chymotrypsin-like activity are the most antigenic (272). It has been known for some time that allergic respiratory disease can follow the inhalation of bacterial proteinases in modern washing powders (24, 87) and in the cotton spinning industry (240) as can the inhalation of bovine trypsin and chymotrypsin (298). Whether or not these enzymes do produce direct damage is not known at present but, regarding pigeon breeder's disease only, Berrens and Guikers (1972a) isolated and purified a specific enzyme product from the gastro-intestinal tract of pigeons and considered that human lungs would be relatively defenceless against the action of this enzyme since it was not inhibited by human serum. However, de Haller (1975) concluded that the enzymes produced by M. faeni behaved purely as antigens and that they did not damage the lungs directly because the lesions produced following their experimental introduction intra-tracheally were not similar to those of farmer's lung.

Consideration must also be given to the fact that the inhalation of chymotrypsin could have a detectable pharmacological effect in the lungs of farmer's lung patients because it has been claimed that broncho-constriction was produced in the lungs of dogs and cats experimentally exposed to this enzyme (96). It is obvious that "further investigations are needed to clarify the enzymatic and the pharmacological effects of the exogenous proteinases" of M. faeni on the respiratory tract (183) together with their interaction with

the proteinase inhibitors of the host and their importance in the pathogenesis of farmer's lung.

Discussions regarding the importance of the individual hypersensitivity reactions in the aetiology of farmer's lung have been somewhat over-shadowed by the finding that mouldy hay dust itself can induce the development of symptoms and signs of farmer's lung (68). Despite the absence of precipitins in the sera of a farmer's lung patient against mouldy cereal dust and extracts of organisms present in it, further exposure to the cereal dust led to a recurrence of his symptoms. It was also demonstrated that mouldy hay dust was capable of activating the alternative pathway of complement utilisation (98) so bypassing the need for immune complexes to mediate the classical immunological pathway of complement activation. These findings together with the fact that histopathological lesions similar to those of farmer's lung had been found in the lungs of guinea pigs and rabbits following a single exposure to mouldy hay dust and M. faeni (295) convinced Edwards and his colleagues (1974) that mouldy hay dust was pathogenic in its own right.

If the dust and complement were to interact on the surface of cells, these cells could die and the resultant microscopic changes would be identical to a type II hypersensitivity reaction (68). If the cells adjacent to the dust/complement interaction were not affected and neutrophils were attracted by the final sequence of complement fixation, then microscopic changes similar to a type III hypersensitivity reaction would result (68). It is also possible that lung damage could result from the direct toxic effect of mouldy hay dust on cells and also its effect on macrophages, perhaps by stimulating them to release hydrolases (68).

From the evidence presented above, it is obvious that immunological and non-immunological components are involved in the pathogenesis of farmer's lung and that both are likely to be genetically predetermined. Experimental studies have confirmed that, under identical conditions of sensitisation, individual rabbits vary greatly in their ability to produce precipitating antibodies (36) and it has been proposed that the same is also true in man (277). It has also been suggested that patients with pigeon breeder's disease and, perhaps all patients with extrinsic allergic alveolitis, have an intrinsically highly labile by-pass mechanism for complement

activation (28). The relative importance of these two pathways of complement activation in the development of farmer's lung in a particular individual is likely to be dependent upon the immunological reactivity of the subject together with the periodicity and weight of his/her exposure to the allergen containing dust.

CHAPTER 2

THE CLINICAL AND EPIDEMIOLOGICAL FEATURES OF FARMER'S LUNG IN CATTLE

In his review of farmer's lung, Fuller (1953) considered there to be three clinical phases. Firstly, there was a single, acute episode in which the severe constitutional symptoms appeared to be more distressing to the patient than the respiratory abnormalities. Many patients were said to recover from such episodes without a precise diagnosis having been made. In the second phase, the most common symptoms, which were breathlessness and non-productive coughing, became progressively worse as exposure to the dust continued. Patients usually recovered from phases one and two provided that further exposure to the dust was avoided. Exertional dyspnoea was the most common symptom of the third or chronic phase which was irreversible due to the development of diffuse pulmonary fibrosis. However, even during the chronic stage, acute episodes could still develop if there was further exposure to mouldy hay dust. Farmer's lung was considered to be a sudden onset respiratory disease until Staines and Forman (1961) reported that the clinical symptoms had developed insidiously in a significant proportion (39%) of the cases about which they had detailed information. Pepys and Jenkins (1965), who classified their large series of cases according to the mode of onset of the disease, found that symptoms had developed insidiously in most of them (68%). However, a proportion (27%) of these subsequently developed an acute episode on further exposure to mouldy hay. When clinical evidence of airways obstruction was confirmed in a number of chronic cases (109, 250), it contradicted the widely held view that the tissue-damaging reactions were wholly confined to the peripheral parts of the lungs concerned with gas exchange (30).

Since the original reports of farmer's lung from Britain, the disease has been described in almost every temperate country where cattle are housed during the winter and so the clinical symptoms and signs of the disease have been well documented (Table 1).

Farmer's lung is usually diagnosed in winter and spring and, in many instances, the patient has been feeding mouldy hay to cattle (250). When Pickles (1944) and Studdert (1953) drew attention to the similarity between the clinical features of farmer's lung in man

TABLE 1

The main clinical symptoms and signs of acute and chronic farmer's lung in man.

Clinical Symptoms and Signs	Acute Form	Chronic Form
Respiratory	Dyspnoea	Progressive Breathlessness
	Coughing	Frequent coughing
	Tightness across chest	
	Crepitations	
Constitutional	Fever (100-101°F)	Weight loss
	Night sweating	
	Headache	
	Anorexia	
	Weakness	
	Weight loss	

After Campbell (1932)
Dickie and Rankin (1958)
Fuller (1953)
Hapke and others (1968)
Pepys and Jenkins (1965)
Staines and Forman (1961)
Studdert (1953)

and broken wind in the horse, both commented that farm animals being fed mouldy hay were likely to be exposed to greater amounts of dust than their attendants. Mann and Miall (1952) recorded that the hay which had induced acute farmer's lung in a cattleman might also have been responsible for the widespread coughing that had developed at the same time in the cows.

Jenkins and Pepys (1965) considered initially that the bovine diseases bronchiolitis obliterans (139, 267) and AIP (fog fever) were equivalent to the human respiratory disorders acute farmer's lung and asthma respectively. However, following an investigation of the prevalence of precipitins to M. faeni in sera from housed cattle, they concluded that one form of fog fever was similar to acute farmer's lung (132). The clinical and pathological criteria on which fog fever had been diagnosed were not given and consequently, the only evidence that a farmer's lung-like disease might affect cattle was the presence of precipitins to M. faeni in the sera of some animals which had developed respiratory disease while being fed mouldy hay. Although farmer's lung had been recognised in 1932 in farm workers who looked after cattle, almost 40 years passed before a similar condition was confirmed clinically and pathologically in the animals themselves (207).

The clinical and epidemiological features of farmer's lung in cattle will be presented in three parts:

Section I: the history and clinical findings from four incidents in which farmer's lung presented as a group or herd problem.

Section II: the clinical abnormalities of 45 individual cases of farmer's lung.

Section III: the epidemiological details of these 45 individual cases of farmer's lung.

SECTION I

FARMER'S LUNG IN CATTLE AS A GROUP DISEASE

MATERIALS AND METHODS

(1) Selection of cattle

During the winter housing period, several cows in four dairy herds developed clinical signs of respiratory disease simultaneously. In herds 1 and 2, an undiagnosed respiratory condition was confirmed as being farmer's lung disease, but with herds 3 and 4, the general practitioners concerned suspected farmer's lung and asked for confirmation of their diagnoses.

(2) Clinical findings

Individual animals with signs of respiratory disease were examined on the farm and, when any were purchased for further study, they were examined again on admission to the Veterinary School. It is the findings from this second examination that are recorded in the individual case histories presented in Appendix 1.

(3) Feeding routine - roughage

Mouldy hay was being fed morning and evening to the cows in herds 1, 3 and 4 but only in the morning to herd 2 which was fed silage in the evening. Mouldy straw was given at mid-day to herd 4.

(4) Examination of blood samples

Blood was collected from the caudal vein of the housed adult cattle using 7 ml draw vacutainers with no additive (Becton, Dickinson and Co., Clarkson, Ontario). The blood samples were kept at 4°C overnight and, after they had been spun at 1300 g for 30 minutes, the serum was taken off and stored at -20°C until required. Herd 1 was sampled on three occasions (November, 1969, May, 1970, November, 1970), but the other three herds were only sampled at the time of the first visit (herd 2 in March, 1971, herd 3 in April, 1974, herd 4 in December, 1974).

(5) Preparation of Micropolyspora faeni antigens

Antigens 8 and 11 were used to examine the sera from herd 1

taken in November, 1969 and May, 1970 for precipitating antibodies to M. faeni.

Antigen 8 M. faeni strain 1156 was grown on horse serum dextrose agar for 19 days at 55°C. After the culture plates had been frozen and thawed three times, the fluid was decanted off and filtered then dialysed against running tap water for 36 hours, Seitz filtered and finally millipore filtered (pore size = 0.45 μ).

Antigen 11 M. faeni strain 1156 was grown on cellophane supported on horse serum dextrose agar for 19 days at 55°C. The cellophane and culture were removed and immersed in Coca's solution for 7 days at 4°C. This liquid was then dialysed against running tap water for 36 hours, Seitz filtered and then millipore filtered (pore size = 0.45 μ).

The two antigen preparations of M. faeni used to examine the sera from herd 1 in November, 1970, herd 2 in March, 1971, herd 3 in April, 1974 and herd 4 in December, 1974 were prepared by the same method as those for the survey of precipitating antibodies to M. faeni (Chapter 3, Section II).

(6) Double diffusion test procedure

The test procedure was identical to that used during the survey of precipitating antibodies to M. faeni (Chapter 3, Section II).

RESULTS

Herd 1

History Several cows had been treated for an acute pneumonia from February to April, 1969 and, while in the byre, the veterinary practitioner had noticed that a large number of the other cows were coughing and that some were also tachypnoeic and hyperpnoeic. On the byre wall in front of the more severely affected animals, there was thick, greenish-yellow mucus which, in one or two instances, appeared to be blood-streaked. Repeated treatment with broad-spectrum antibiotics was completely ineffective in reducing the severity of the respiratory signs. No animals had died as a result of this respiratory syndrome.

Retrospectively, the farmer was of the opinion that during the previous three winter housing periods there had been an increase in the frequency of coughing in the milking herd. He also considered that the cows were much thinner at the end of the winter and that the older cows were more severely affected than the heifers. The bodily condition of affected cows improved considerably during the summer grazing season and, at the same time, the respiratory signs became less obvious. The farmer was not too concerned about the respiratory disorder although he did think that the daily milk production was much less than it should have been.

The farmer gradually became aware that he too was suffering from a respiratory disorder which seemed to be worse during the spring. After this had been diagnosed as farmer's lung, precipitating antibodies to M. faeni were detected in the sera of three pneumonic cows. It was therefore decided to take blood samples from all the adults when they were housed at the beginning of the next winter in order to find the prevalence of precipitins to M. faeni.

Herd examination The farm was visited in November, 1969 about two weeks after the cows had been housed. The herd was made up of a mixture of pure Ayrshire and Friesian cross Ayrshire cows, most of which (80/92) were housed in a large, double byre while the others were kept in a small adjacent single byre. During the two hours while the blood samples were being taken, about half the cows were seen to cough and many were noticed to be slightly tachypnoeic. Four animals were moderate hyperpnoeic and, in front of each of them, there was a variable amount of tenacious, greenish mucus which appeared to have been brought up by their persistent coughing. No blood-streaking was observed in the mucus. Adventitious lung sounds were not detected in any of these four cows.

Feeding routine - hay The hay was made entirely from home-grown, permanent grass. The farmer considered that virtually all his 1969 crop was of poor quality and very mouldy because, after it had been baled, it has lain outside for several weeks before it had been stored in a Dutch barn adjacent to the double byre. There was an appreciable increase in the frequency of coughing when the hay was being shaken out and fed.

Cattle accommodation The double byre had an unlined asbestos roof, a small open ridge for outlet ventilation but no special provision had

made for inlet ventilation. At the time of the farm visit, there was considerable condensation on the under-side of the roof and the whole atmosphere in the byre was stuffy. The single byre, which was a traditional building with a lined roof, was well ventilated.

Serology Blood samples were obtained from all the adult cows in November, 1969, two weeks after they were housed and again in May, 1970 two weeks after they had been put out to grass. Precipitins to M. faeni were detected in 25 per cent (19/75) of the samples in November and in 29 per cent (23/80) in May. This increase was not statistically significant.

Investigation of individual animals Two cows which were said to be typical of this respiratory condition were purchased for further study; case C1 was admitted in December, 1969 and case A3 was admitted in October, 1970. At necropsy, lesions similar to those which had been described in farmer's lung in man were present in the lungs of both cases (234).

Herd 2

History During the winter and spring of 1970-71 many cows in this herd developed a peculiar respiratory disease. They calved down in good condition and, over the next few weeks, they became dull, excessively thin and they failed to achieve their anticipated peak milk yield as their frequency of coughing increased. In severely affected individuals, depression of appetite occurred and occasionally, green mucus was seen on the byre wall. No acute respiratory episodes had been seen and no animal had died as a result of this respiratory disorder.

For the last three or four years during the winter housing period, the farmer had noticed an increase in the amount of coughing in his milking cows especially in the late spring.

Herd examination The cattle involved were 53 Friesian cows and a Hereford bull. At the first visit in March, 1971, the herd as a whole was dull and most of the milking cows were in poor condition. During the 45 minute period while blood samples were being taken, 19 of the 42 milking cows were seen to cough and five were noticed to do so persistently. Seven animals, including two of those which coughed persistently, were tachypnoeic (Resp. Rate = 40-50 per minute) and were moderately hyperpnoeic. Coughing was easily induced in these

cows. No nasal discharge was seen but some thick green mucus was observed in front of two of those most severely affected. No adventitious lung sounds were heard in any of the severely affected cows.

In a small, single byre there was a Hereford bull which had been purchased only six months previously, five "dry" cows and six milking cows which were being used to suckle calves. There was only occasional coughing in this group and, although their respiratory rates were not elevated, a few individuals were hyperpnoeic.

At least five animals had been treated during late December and January and, because there had been no detectable clinical response to the antibiotics used, all further cases had been moved out of the milking byre into the single byre and given two calves each to rear.

Feeding routine - hay Since 1966 hay had been made in June or July whereas previously, the intended hay fields had been grazed in the spring and early summer prior to their being cut in late July or August. After baling, most of the hay was stored in a loft above the milking cows and was thrown down every day as required. The hay bales were grey and dusty on the outside and, when opened up, clouds of fine, grey dust were released (Figure 1). Close inspection of many different bales revealed whitish colonies on the hay similar to those produced by actinomycetes and fungi (Figure 2). Silage had also been made in 1970 and the results of analyses of representative samples of both hay and silage are given in Table 2.

Cattle accommodation The milking byre was J-shaped with the hay loft being directly over the 18 standings on the long side. A section of double-byre which held 24 cows had recently been added and so there was a total of 30 cows on one side and 12 on the other. The floor of the hay-loft section was only about eight feet above ground level and there was a high pitch on the new roof which was unlined asbestos. The farmer admitted that ventilation was a problem and that hay dust could be seen suspended in the air for a long time after he had fed the cows.

At the time of the farm visit, the atmosphere in the milking cow byre was stuffy while in the single byre it was cold and airy.

Serology Precipitating antibodies to M. faeni were detected in 83 per cent (45/54) of the samples taken.

FIGURE 1 A plume of grey-white dust rising from mouldy hay that has been agitated.

FIGURE 2 A close-up view of mouldy hay on which greyish-white colonies of actinomycetes and fungi can be seen.

TABLE 2

The results of analyses* carried out on representative samples of hay and silage fed to Herd 2.

	Hay	Silage
Dry Matter (per cent)	88.1	27.7
Crude Protein (per cent)	9.3	4.2
Protein Equivalent (lb)	4.6	2.78
	36	12
Fibre (per cent)	27	-
pH	-	4.7

* Analyses done by B.O.C.M. - Silcocks, Basingstoke, Hants.

Investigation of individual animals Three cows which were considered by the farmer to be representative of this problem were purchased for further study; cases C3 and C4 were admitted in April, 1971 and case C5 in June, 1971. At necropsy, lesions similar to those which had been described in farmer's lung in man were present in the lungs of all three cases (234).

Herd 3

History The cattle were housed at the beginning of November, 1973 and, after several weeks, the farmer noticed that many of his "dry" cows were coughing frequently and that one or two appeared to be breathing fast. There was hardly any coughing at all in the milking cows which were in another byre. In January and February, 1974, all the cows began to cough frequently and two of them, one milking and one "dry", developed an acute respiratory disease from which they recovered after treatment.

The farmer thought that several of his cows were thinner during the winter of 1973-74 than they had been in previous winters but he was unaware of a decrease in the milk yield of any particular individual or from the herd as a whole. However, no milk records were kept. This was the first time that the farmer had been aware of respiratory disease when the cows were housed.

Herd examination There were 24 Jersey cows in this herd in April, 1974. Although they had been going outside for about a week, 11 cows were seen to be coughing and four did so frequently, often in short paroxysms. Seven animals were slightly tachypnoeic (Resp. Rate = 30 per minute) and moderate hyperpnoea was detected in five cows with nine others being less severely affected.

Feeding routine - hay Most of the hay made in 1973 was poor quality and very dusty but initially the worst had been fed to the "dry" cows only. The better quality hay, which had been given to the milking cows, was finished by mid-January and so both milking and "dry" cows were then exposed to the very dusty hay until it had all been eaten by the end of February. Both cows which developed acute pneumonia did so while they were being fed the very mouldy hay. From the beginning of March, good quality bought-in hay was offered and a decrease in the amount of coughing was noticed afterwards.

Cattle accommodation The milking cows were kept in a good traditional double byre with a lined roof, numerous open ridge ventilators and one inlet ventilator per cow situated just below the eaves. The "dry" cows were housed in a small, traditional, single byre which had a low roof and no individual, inlet ventilators.

Serology Precipitating antibodies to M. faeni were detected in 67 per cent (16/24) of the samples taken.

Investigation of individual animals One cow was purchased for further study a year after it had been treated for acute respiratory disease. At necropsy, lesions typical of farmer's lung in cattle were observed.

Herd 4

History A chronic respiratory disease which had affected a Jersey herd for five to six years in succession, had been diagnosed as parasitic bronchitis. After precipitins to M. faeni had been detected in serum samples from four cows, it was thought that the problem could be farmer's lung.

There had been frequent coughing in the herd during the winter housing period for several years although it seemed to be worst in November and December, about six to eight weeks after the cows had been brought inside. In 1974, because of the high rainfall, the cows were taken inside at the beginning of October. Individual animals appeared to be most severely affected just after calving and, although cows calved down throughout the whole year most did so from January to April. There was a high proportion of old cows in the herd because this is a small farm (80 acres) and no replacement heifers had been reared for several years. The farmer was of the opinion that the respiratory disease had had no adverse effect on milk yield but no milk records were kept. It is significant that no deaths had been attributed to this respiratory syndrome even though many of the cows were over ten years old.

Herd examination There were 65 cows in the milking herd in December, 1974 and all were pure Jerseys apart from six which were Charolais cross heifers. The cows were kept in two cubicle houses each holding 31 animals and coughing was much more frequent in one house than in the other. The clinical findings detected on examination of severely affected individual animals are given in Table 3. It was the older animals in the herd which developed severe respiratory signs and

TABLE 3 The clinical findings of the severely affected cows in Herd 4.

Cow No.	Cough	Hyperpnoea	Respiratory Rate/minute	Adventitious Sounds
4	+	+	30	-
14	++	++	30	rhonchi - A/V - L.
16	+	+	40	rhonchi - A/V - L.
32	++	+	30	rhonchi - A/V - R.
48	+	+	40	-
50	+++	+++	40	rhonchi - widespread - R. L., crepitations - widespread - R. L.
51	++	++	40	rhonchi - A/V - R. L., crepitations - A/V - R. L.
56	+	++	30	-
60	++	+	45	-

+ - occasional coughing.
++ - moderate coughing.
+++ - frequent coughing.

+ - slight hyperpnoea.
++ - moderate hyperpnoea.
+++ - gross hyperpnoea.

R - right.
L - left.
A/V - antero-ventral.

required veterinary attention; the youngest cow which had been treated was said to be six or seven years old.

Feeding routine - hay The hay was all home-grown and cold air was usually blown through about one-third of it to control heating. In most years, the hay was dusty and 1974 was no exception. The worst hay was fed to the "dry" cows. Bought-in straw was also fed and in November and December, 1974, it was particularly mouldy.

Cattle accommodation The cubicle houses were lean-to buildings which had been built onto the old steading. Coughing was more frequent in the first house which was close and stuffy.

Serology Precipitins to *M. faeni* were present in 69 per cent (45/65) of the samples examined. Even although there was a difference in the frequency of coughing between the two houses, there was no significant difference in the prevalence of precipitins, there being 68 per cent and 71 per cent in houses one and two respectively.

Investigation of individual animals Five cows were bought from this herd all of which had been treated for respiratory disease during the previous three winters. Cases C23 and C24 were admitted in December, 1974, case C25 was admitted in March, 1975 and cases C22 and C27 were admitted in May, 1975. At necropsy, lesions of farmer's lung disease of cattle were present in all five animals.

DISCUSSION

The clinical signs of respiratory disease were first noticed in these four dairy herds during the winter housing period and while mouldy hay was being fed. Three of the farmers considered that there had been a gradual increase in the frequency of coughing in their herds for several winters prior to their becoming aware that the cows were suffering from clinical respiratory disease. The respiratory signs were considered to be most severe in the springtime although in herd 4, an increase in coughing was said to be particularly noticeable soon after the cows were housed at the beginning of winter. This slight variation in the clinical picture almost certainly arose because virtually all the milking cows in herd 4 were over six years old and, as a result of repeated, annual exposures to mouldy hay, many were likely to have had high titres of precipitating antibody which would

have persisted throughout the summer grazing season (57). Consequently, when they were housed and challenged again with mouldy hay dust, the signs of respiratory disease had quickly become obvious.

It is significant that none of these farmers was really worried about the respiratory syndrome in their cattle even after they had sought veterinary advice. Perhaps this was because not one of the affected cows had died. The owners of herds 1 and 2 were understandably more concerned about the depressed milk yields and poor appearance of their cows which they had attributed to the variable appetite of affected animals and to the poor quality of the roughage. Several workers (60, 71) have commented that even farmers who themselves had developed farmer's lung had failed to associate the onset of respiratory symptoms with working in a dusty environment. This being so, it is unlikely that farmer's would associate respiratory disease in their cattle with exposure to mouldy hay. Although some of the weight loss and poor milk production could possibly have been explained by the low feeding value of the mouldy hay, representative samples of both hay and silage from farm 2 had been analysed and the feeding values of both were considered to be within acceptable limits (220).

The clinical findings of the individual cows purchased from three of the four farms will be discussed in Section II but, in general, affected animals were hyperpnoeic, tachypnoeic and coughed frequently. Several cows in herds 1 and 4 had developed episodes of acute respiratory disease. It is interesting that there had been neither abortions nor early calvings within the last three or four years on these farms which were all brucella-accredited. It can be deduced, therefore, that sensitisation and subsequent exposure to M. faeni is not associated with abortion in cattle.

There was a wide range in the percentage of cows with precipitins to M. faeni when these farms were first visited, from 25 per cent in herd 1 in November to 83 per cent in herd 2 in March. The comparatively low percentage of precipitins in herd 1 was almost certainly the result of their having been tested at the beginning of our study of farmer's lung disease with the result that the preparations of M. faeni used in the double diffusion test were less antigenic than those used later. Consequently, the serological results obtained at the first herd examinations are not directly

comparable. When the "newer" antigenic preparations of M. faeni were used at the beginning of the following winter in herd 1, precipitins were detected in 51 per cent of the animals, an increase of 25 per cent from the previous spring. This rise had occurred during the summer grazing period when there was likely to have been very little, if any, antigenic exposure. From the results of the serological survey (Chapter 3, Section II), it can be said that a high percentage of precipitins to M. faeni in a herd does not automatically mean that the cattle are suffering from clinical farmer's lung disease. However, a high percentage of animals with precipitins does indicate massive recent exposure to M. faeni and it is probable that continued exposure at a high level could lead to the development of clinical disease in the cattle and, of much more importance, in the farmer too.

The respiratory syndromes on these four farms were considered to have been farmer's lung because of the mouldy nature of the hay, the clinical signs which were worst during the winter housing period and which tended to disappear while the animals were at grass and because of the pathological lesions present in the lungs of affected cows.

SECTION II

FARMER'S LUNG IN CATTLE AS AN INDIVIDUAL ANIMAL DISEASE

MATERIALS AND METHODS

(1) Selection of animals

The animals were admitted to the Glasgow Veterinary School either because

a) the farmer had noticed that they were suffering from respiratory disease and had requested veterinary advice; 18 acute and 21 chronic cases were in this category.

b) or signs of respiratory disease (coughing, hyperpnoea, tachypnoea) had been observed by the author while the cows were being blood sampled during the serological survey (Chapter 3, Section II). Six cows were in this category and they were admitted to the hospital when they were culled.

(2) Clinical findings

The cases which developed sudden onset, severe respiratory disease have been considered as examples of the acute form of farmer's lung whereas the other cases, in which the respiratory signs did not present in this manner, have been considered to be chronic or insidious onset cases.

The clinical signs of respiratory disease which were detected when the animals were first seen to be ill, the time of year, the treatment and other relevant background information has been summarised and is presented in Appendix 1. On admission, every animal was given a full clinical examination by the author when blood, faeces and urine samples such as were considered necessary were taken. The significant clinical findings detected on admission are also presented in Appendix 1.

(3) Examination of blood samples

a) Haematology After blood had been collected in bottles containing ethylene diamine tetra-acetic acid, the packed cell volume (PCV) was measured by the micro-haematocrit technique (81), the amount of haemoglobin was found by

using the cyanmethyl haemoglobin method, the total numbers of red and white cells were estimated using a model D Coulter counter (Coulter Electronics Ltd., Dunstable, Beds.). The differential white cell counts were made on Leishman-stained blood films and 200 cells were counted.

b) Blood biochemistry After blood had been collected in heparinised tubes the urea, bilirubin, inorganic phosphate, alkaline phosphatase, S.G.O.T., S.G.P.T. and the total protein values were measured using a Technicon autoanalyser (Technicon Instrument Corporation, Tarry Town, New York, U.S.A.). The potassium and sodium values were estimated using an EEL flame photometer, chloride was measured using an EEL chloride meter, the calcium and magnesium values were found using a Unicam S.P.90 (Pye-Unicam, Cambridge, England). The amounts of albumin and globulin were measured using zone electrophoresis scanned with a Kipp and Zonen microdensitometer. In diarrhoeic animals only, the plasma pepsinogen values were estimated by the method of Edwards, Jepson and Wood (1960) and expressed as milli-international units of tyrosine (milli-mols tyrosine per litre plasma per minute x 1,000).

c) Precipitins to Micropolyspora faeni Serum from each case was examined on admission for precipitins to M. faeni using the same antigenic preparations and the same double diffusion technique as was used for the serological survey (Chapter 3, Section II).

(4) Examination of faeces samples

In diarrhoeic animals only fresh faeces was examined for the presence of Strongyle eggs and D. viviparus larvae by a modification of the McMaster method of Gordon and Whitlock (1939) and also by the smear technique of Cunningham and Gilmour (1959) for the presence of clumps of acid-bast bacteria which morphologically resembled Mycobacterium johnei.

(5) Examination of urine samples

The amount of urine protein was estimated by the sulphosalicylic acid precipitation test as described by Kingsbury,

Clarke, Williams and Post (1926).

RESULTS

(1) Background information and history

a) Quality of hay The farmer's assessment of the quality of the hay which had been fed prior to the animals developing respiratory disease, is given in Table 4. Overall, 35 cases (78%) had been given hay classified as very mouldy or mouldy. The two forms of the disease were slightly different in that 11 acute cases (60%) had been fed mouldy hay compared with 24 chronic cases (89%).

b) History of respiratory disease in the herd during the winter Twenty cases (47%) came from herds in which respiratory disease in housed, adult cattle had not previously been recognised (Table 5) and ten animals (23%) from herds in which cases had only developed occasionally. The remaining 13 animals (30%) came from three herds in which pneumonia was regularly diagnosed during the winter and in each herd, farmer's lung had been confirmed as the major cause of the respiratory trouble (Section 1, Herds 1, 2 and 4). Either occasional or frequent coughing had been heard in the herds from which 38 cases (84%) came (Table 5).

Acute farmer's lung cases tended to develop on farms where respiratory disease in housed cattle was not a problem and only occasional coughing was herd. In contrast, chronic cases arose in herds in which there was a high incidence of respiratory disease and frequent coughing during the winter.

c) History of respiratory disease in individual animals Information regarding the respiratory disease history of the individual cases is given in Table 6. Four acute cases had experienced several pneumonic episodes prior to their being hospitalised; A3 had been treated for three successive years in the spring, A13 had been treated once in the spring and twice during the following winter, A14 and A17 had experienced their first attacks four days and three weeks respectively prior to that about which we were

TABLE 4

The relationship between the numbers of acute and chronic cases of farmer's lung and the farmer's assessment of the quality of the hay fed.

Farmer's Assessment	No. Acute Cases	No. Chronic Cases	Total
Very mouldy	8	15	23
Mouldy	3	9	12
Mixed quality	6	2	8
Not mouldy	1	1	2

TABLE 5

The incidence of pneumonia and frequency of coughing during the winter in the herds from which the individual cases were admitted.

Incidence of Pneumonia	No. Acute Cases	No. Chronic Cases*	Total
None	11	9	20
Occasional	6	4	10
Frequent	1	12	13
Frequency of Coughing			
None	3	2	5
Occasional	11	4	15
Frequent	4	19	23

* 2 farms - no information available.

TABLE 6

History of previous respiratory disease, or signs of respiratory disease, in individual cases before their final episode of farmer's lung.

	Acute Cases	Chronic Cases
Previous Respiratory Disease		
Acute Bacterial Pneumonia	-	C15: C26
Unidentified acute pneumonic episodes	A3: A13: A14· A17	-
Unidentified insidious-onset respiratory disorder	-	C17
Previous Signs of Respiratory Disease		
Coughing	A8: A12: A15: A16	C6: C26
Hyperpnoea	A15	C6: C26
Exercise intolerance	-	C26
Poor milk yield	A1	-
Weight loss	A16	C21
Vaguely "unwell"	-	C16
TOTAL	9 (50%)	7 (33%)*

* Total of 21 cases excludes 6 first seen to be ill by author.

notified. Four other animals were seen to be coughing prior to their developing acute farmer's lung.

Two chronic cases had been treated for acute bacterial pneumonia six years (C15) and three years (C26) before farmer's lung was diagnosed. After treatment, the former made a complete recovery but the latter was said to have been "left with a cough". In addition to this cough, C26 was also noticed to be hyperpnoeic and to have shown exercise intolerance which was becoming progressively worse before veterinary advice was requested. C17 was said to have had several minor episodes of an insidious onset and gradually worsening, unnamed respiratory disorder.

(2) Presenting signs of farmer's lung disease

Acute farmer's lung The presenting signs of the 18 cases of acute farmer's lung are set out in Table 7. Ten cases (56%) were lactating dairy cows and with every one, the farmer's main complaint was a substantial reduction in milk yield. This was the only presenting sign that affected every animal at risk. Anorexia and coughing were each noticed in 12 animals (67%) and with A3 and A8 the coughing was productive. The depth of respiration was increased in every animal apart from A11; 11 cases (61%) were said to have been dyspnoeic, five of which (A2, A5, A12, A14, A16) were mouth-breathing, while the other six (33%) were hyperpnoeic.

Tachypnoea was observed in eight cases (44%) and pyrexia was detected in six of the 15 cases (40%) in which the temperature was known; in A8 and A12 the temperature was 105°F. Five cases (28%) were said to have been dull and in two others (11%) a loss in weight had been noticed before (A16) and after (A3) the acute respiratory episode. Nasal discharge and collapse with trembling were each present in a single animal. Adventitious lung sounds were recognised in only four animals (22%) but the number actually auscultated was not known.

The acute respiratory disease episode had developed within four weeks of calving in cases A4, A6, A7 and A9. The respiratory signs would appear to have been brought on by exercise in A8 after she had walked in from the field to be

TABLE 7 The presenting signs of acute farmer's lung in cattle.

Clinical Sign	Case Number 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	Total No.	%
Reduced Milk Yield	1	1	1	1	S	1	1	1	1	S	S	1	S	1	S	S	H	H	10/10	100
Anorexia		1	1	1	1		1		1			1		1	1	1	1	1	12	67
Coughing			1	1		1	1	1		1		1	1		1	1	1	1	12	67
Sudden Onset Dyspnoea	1	1*	1		1*		1	1		1		1*		1*		1*	1		11	61
Tachypnoea	1		1	1		1			1		1		1	1					8	44
Pyrexia		103		103		104	NR	105			NR	105	NR				104		6/15	40
Hyperpnoea				1		1			1				1		1			1	6	33
Dullness	1	1			1	1			1										5	28
Weight Loss			1													1			2	11
Nasal Discharge										1									1	6
Collapse											1								1	6
Adventitious Lung Sounds		1			1					1	1								4	22

S = Suckler cow H = Non-lactating Heifer 1* = Mouth Breathing

103 = Actual Temperature NR = No Record.

milked and in A10 after she had been collected in a court to be blood sampled for brucellosis.

Chronic farmer's lung Coughing and hyperpnoea were by far the most common presenting signs of chronic farmer's lung and in 22 cases (81%) both were present (Table 8). Coughing was heard in 25 cases (93%) but only C26 was noticed to have a productive cough. An increased depth of respiration was observed in 23 animals (85%) but none was considered to be dyspnoeic.

Tachypnoea was seen in 11 animals (41%), weight loss was said to have occurred in ten (37%) and poor milk yield had been noted in seven of the lactating dairy cows (35%). Seven cases (26%) were considered to have been dull while some reduction in appetite and exercise intolerance were each noticed in five cases (19%). Adventitious lung sounds were recognised in only two cases (C20, C23), but again the actual number auscultated was not known.

(3) Clinical findings on admission to Veterinary School

Acute farmer's lung Of the 12 cases (66%) admitted within four weeks of their having developed an acute respiratory episode, 11 came in within two weeks. The other six animals came in from four to ten months afterwards (Table 9). Eleven cases (61%) were in poor or very poor bodily condition and only three (A2, A4, A6) were in good condition (Table 10). Sixteen animals (89%) were alert while the other two (A8, A16) were slightly dull. The coughing which was seen or heard in 17 cases (95%) was occasional in 15 (83%) and frequent in two (11%). Case A8 had frequent paroxysms of coughing which often terminated with the production of thick mucus. The only animal not seen to cough was A11.

Every case was hyperpnoeic; eight (44%) were slightly affected, eight (44%) were moderately affected and the remaining two animals (A8, A16) were grossly hyperpnoeic even at rest. Tachypnoea was also present in every case at rest. In nine animals (50%) the respiratory rate was 30 per minute, in five (28%) it was 40 per minute and in the other four (A8, A9, A13, A18) it was more than 40 per minute.

Adventitious lung sounds (Table 11) were heard in ten

TABLE 8 The presenting signs of chronic farmer's lung in cattle.

Clinical Signs	Case Number 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	Total No.	%
Coughing	1	1	1	1	1	1		1	1	1	1	1	1	1	1	1	1	1	1	1		1	1	1	1	1	1	25	93
Hyperpnoea	1	1	1	1		1	1	1	1	1	1		1	1	1	1	1	1	1	1		1	1	1		1	1	23	85
Tachypnoea	1	1			1			1	1		1	1			1	1			1							1		11	41
Weight Loss	1		1	1	1						1		1	1							1	1					1	10	37
Poor Milk Yield	1	S	1	1	1	1		S				S	1	1		S	S		S		S							7/20	35
Dullness	1		1	1	1								1	1					1									7	26
Poor Appetite			1	1	1								1	1														5	19
Exercise intolerance		1							1			1*									1*					1		5	19
Pyrexia			103	103	103																							3	11
Adventitious Lung Sounds																				1			1					2	7

S = Suckler cow. 1* - dyspnoeic after exercise.

TABLE 9

The time interval between a farmer's lung-like respiratory disease being suspected and the individual animals being admitted to the Veterinary School.

Time	Acute Cases	Chronic Cases
Less than 4 weeks	12	5
1 - 6 months	2	14
7 - 12 months	4	3
More than 1 year	-	5

TABLE 10

The clinical findings on admission of 45 cases of farmer's lung in cattle.

Clinical Findings		Acute Form		Chronic Form	
		No.	%	No.	%
Bodily Condition	Good	3	17	3	11
	Fair	4	22	4	15
	Poor	10	56	15	56
	Very Poor	1	6	5	19
Demeanour	Bright	16	89	24	89
	Slightly dull	2	11	2	7
	Dull	-	-	1	4
Coughing	Not heard	1	6	2	7
	Occasional	15	83	9	33
	Frequent	1	6	11	41
	Paroxysmal	1	6	5	19
Hyperpnoea	Not present	-	-	1	4
	Slight	8	44	6	22
	Moderate	8	44	11	41
	Gross	2	11	9	33
Tachypnoea (Respiratory Rate/ Min.)	< 30	-	-	4	15
	30	9	50	4	15
	40	5	28	8	30
	50	3	17	9	33
	60	-	-	1	4
	> 60	1	6	1	4

TABLE 11

The detailed findings in the 10 acute farmer's lung cases in which adventitious lung sounds were detected on auscultation.

		Case Number										Total No.
		2	7	8	10	11	12	13	16	17	18	
Crackles	Left	-	1	1	1	1	1	-	1	1	1	8
	Right	-	1	1	-	1	1	1	1	-	1	7
Rhonchi	Left - A/V	1	-	-	-	1	-	-	1	1	-	4
	Left - widespread	-	1	1	-	-	-	1	-	-	-	3
	Right - A/V	-	-	1	-	1	-	-	1	1	1	5
	Right - widespread	-	1	-	-	-	1	1	-	-	-	3

A/V - antero-ventral.

cases (56%). The crackles which were heard in nine animals were bilateal in six. When present, they were detected over the antero-ventral areas of the lung fields except for A16 when they were found to be widespread on the left side. The rhonchi, which were usually sibilant, were also heard in nine cases and they too were bilateral in six and unilateral in three cases. In five animals, they were only heard antero-ventrally while in the other four widespread rhonchi were heard on one or both sides of the chest. Crackles and rhonchi were present together in eight cases (44%) and both were heard bilaterally in four (22%). Only crackles were detected in A10 and only rhonchi in A2.

Cases A16 and A8 which were the most severely affected on admission, were slightly dull, both coughed frequently (A8 in paroxysms) and both were grossly hyperpnoeic at rest. Case A16 was in cor pulmonale with all the obvious signs of congestive cardiac failure in cattle (markedly enlarged, slightly pulsating jugular and mammary veins, brisket oedema, a palpably enlarged liver, tachycardia and a poor pulse volume). Case A8 was probably in the early stages of cor puimonale because there were enlarged, non-pulsating jugular veins, tachycardia and poor pulse volume.

Chronic farmer's lung Compared with the acute form of the disease, there was a much longer delay from the time that the chronic cases were first seen to be ill and their being admitted to the Veterinary School (Table 9). Only five animals (19%) came in within four weeks and, although 14 (52%) were admitted after one to six months, another five cases (19%) were not admitted until more than 12 months had elapsed.

When they were admitted (Table 10), 20 cases (75%) were in poor or in very poor bodily condition and, with the exception of C2, C16 and C21, all were alert. Of the 25 animals (93%) which were coughing, nine (33%) did so occasionally and 16 (59%) did so frequently; five of the latter group (C6, C12, C18, C19, C23) had frequent paroxysms. Productive coughing was observed with five animals, four of which coughed frequently (C3, C4, C20, C26) and one (C5) occasionally. Cases C21 and C24 were neither heard nor seen to cough.

Apart from C11, every case was hyperpnoeic with 20 (74%) being moderately or grossly affected. Twenty-three animals (85%) were tachypnoeic and in 11 (41%) the respiratory rates were in excess of 40 per minute. C16 had the fastest respiratory rate at 70 per minute.

Adventitious lung sounds (Table 12) were detected in 18 cases (66%). The crackles which were detected in 16 animals (59%) were bilateral in 13. When present, they were localised antero-ventrally except in C18 and C21 in which they were widespread over both lung fields and in C25, in which they were widespread on the left and antero-ventral on the right. The rhonchi which were present in 14 cases (52%) were bilateral in 11. In four of these 11 animals, they were localised antero-ventrally and in three they were widespread. In three of the remaining cases, the rhonchi were localised on one side and widespread on the other while in C23 they were localised antero-ventrally on the left but were only heard over the diaphragmatic area on the right. Crackles and rhonchi were present together in 12 cases (44%) and both were heard bilaterally in eight (30%). Crackles alone were detected in C1, C5, C6 and C18 and only rhonchi were heard in C8 and C14.

Cases C2 and C21 showed obvious signs of congestive cardiac failure and were therefore considered to be in cor pulmonale.

(4) Laboratory findings

Haematology In 14 acute cases (78%) at least one measurement was outwith the recognised normal range and in 11 (61%) they were markedly different (Table 13). The most common abnormality was a reversal of the neutrophil/lymphocyte ratio and this occurred in eight cases (50%) in which a differential white cell count had been done. A neutrophilia in excess of 60 per cent was present in four cases and in A5, there was a neutrophilia of 68.5 per cent and also a leucocytosis of 22,000 cells per cubic mm. There was a marked eosinophilia in two cases, 33 per cent in A10 and 31 per cent in A14, and a reduction in the amount of haemoglobin and in the number of red blood cells in four cases (24%).

TABLE 12

The detailed findings in the 18 chronic farmer's lung cases in which adventitious lung sounds were detected on auscultation.

		Case Number																	
		1	2	5	6	8	9	12	13	14	16	17	18	19	20	21	22	23	25	Total
Crackles	Left	-	1	1	1	-	1	1	1	-	1	1	1	1	1	1	1	1	1	15
	Right	1	-	1	-	-	1	1	1	-	1	1	1	1	1	1	1	1	1	14
Rhonchi																				
Left - A/V		-	-	-	-	-	-	1	1	1	1	-	1	-	-	1	-	1		7
Left - widespread		1	-	-	1	1	1	-	-	-	-	-	-	-	-	1	-	-	-	5
Right - A/V		1	-	-	-	-	1	1	-	1	1	-	-	-	-	1	-	-		6
Right -widespread		-	-	-	1	1	-	-	1	-	-	-	-	1	1	-	-	1		6
- dorsal		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	-	1

A/V - antero-ventral.

TABLE 13 The significant changes in haematology in cases of acute farmer's lung.

Parameter	Case Number											
	A4	A5	A6	A9	A10	A11	A13	A14	A15	A16	A17	A18
P.C.V.%	-	-	-	-	-	-	-	-	23	-	-	-
Hb.g./100 ml.	8.35	-	-	-	-	8.2	-	-	7.9	-	-	-
R.B.C.$10^6/mm^3$	4.06	-	4.80	-	-	4.74	-	-	4.14	-	-	-
W.B.C. mm^3	-	22,000	-	15,400	-	-	-	13,200	-	-	-	6,300
N.%	62	68.5	65.5	58	-	-	48	-	52	63	47	-
L.%	37	31.5	32.5	38	-	-	44.5	-	40	37	46	-
E.%	-	-	-	-	33	-	-	31	-	-	-	-

N = neutrophils, L = lymphocytes, E = eosinophils.

At least one measurement was outwith the normal range in every chronic case apart from C6, but in only 21 cases (78%) were they considered to be markedly different (Table 14). The most common abnormality was again found to be a reversal of the neutrophil/lymphocyte ratio and this occurred in 15 cases (63%) in which a differential white cell count had been done. There was a neutrophilia in excess of 60 per cent in three cases and in C13, the neutrophilia was 74 per cent. Leucocytosis was present in five animals and leucopaenia in three; in C27 the total white cell count was only 3,000 cells per cubic mm. An eosinophilia of 9 per cent or more was present in five cases (19%). There was a reduction in the amount of haemoglobin and in the number of red blood cells in five cases (19%).

Blood biochemistry In every animal with acute farmer's lung except A2, at least one parameter was outwith the normal range, but those considered to be significant are presented in Table 15. By far the commonest abnormality was an increase in the amount of globulin which occurred in 12 cases (67%). In A12 and A16, there was also a marked decrease in the amount of albumin. Parameters other than serum proteins were found to be abnormally high in seven animals (SGOT in four cases, bilirubin in three cases, alkaline phosphatase in two cases and urea in one case).

In every animal with chronic farmer's lung except C11, at least one parameter was outwith the normal range, but those considered to be significant are presented in Table 16. An increase in the amount of globulin was again the commonest abnormality and this occurred in 19 cases (70%). There was a marked decrease in the albumin level in five animals (19%) with the lowest values being in C6 and C16 in which there were 13 and 14 grams per litre respectively. Parameters other than serum proteins were found to be abnormally high in eight animals (bilirubin in seven cases, SGOT in three cases, alkaline phosphatase and urea each in two cases).

Precipitating antibodies to M. faeni were present in every case of farmer's lung discussed in this study.

In cases A16, C2 and C21, which were diarrhoeic, the plasma pepsinogen values were within the normal range.

TABLE 14 The significant changes in haematology in cases of chronic farmer's lung.

Parameter	Case Number																						
	C1	C2	C3	C4	C7	C8	C10	C11	C12	C13	C14	C16	C17	C19	C20	C21	C22	C23	C24	C25	C26	C27
P.C.V.%	-	-	24	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hb.g./100 ml.	-	-	8.0	8.4	-	8.2	-	-	-	-	8.5	-	7.6	-	-	-	-	-	-	-	-	-
R.B.C.$10^6/mm^3$	-	-	-	4.87	-	-	-	-	-	-	4.84	-	4.54	-	-	-	-	-	-	-	-	-
W.B.C. mm^3	-	11600	-	-	-	-	-	-	11400	13300	12500	-	-	5600	13600	-	5700	-	-	-	-	3000
N.%	-	-	59	-	-	57	60	58	51.5	74	57	57.5	-	52	-	55	57	56	53	62	-	46
L.%	-	-	33.5	-	-	40	39.5	41.5	42	22	36.5	36.5	-	34	-	44	43	43	46	32	-	52
E.%	15	-	-	11	9	-	-	-	-	-	-	-	-	14	-	-	-	-	-	-	18	-

N = neutrophils, L = lymphocytes, E = eosinophils.

TABLE 15 The significant changes in blood biochemistry in cases of acute farmer's lung.

Parameter		Case Number														
		A1	A3	A4	A5	A6	A7	A10	A11	A12	A13	A14	A15	A16	A17	A18
Total Protein	g/l.	-	-	102	-	-	100	-	-	-	-	-	-	-	-	-
Albumin	g/l.	-	-	-	-	-	-	-	-	17	-	-	-	17	-	-
Globulin	g/l.	64	68	-	-	60	71	65	-	78	72	60	62	65	67	62
S.G.O.T.	I.U.	-	-	-	198	-	-	-	211	-	-	-	-	188	-	251
Bilirubin	µ.mol/l.	-	-	17	-	-	-	-	-	-	-	16	-	-	-	13
Alk. phosphatase	I.U.	-	-	-	-	-	-	-	-	-	-	-	160	149	-	-
Urea	m.mol/l.	-	-	-	-	-	-	-	9.3	-	-	-	-	-	-	-

S.G.O.T. - serum glutamate oxaloacetate transaminase.

Alk. phosphatase - alkaline phosphatase.

TABLE 16 The significant changes in blood biochemistry in cases of chronic farmer's lung.

Parameter		C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C12	C13	C14	C16	C17	C18	C19	C20	C21	C22	C24	C25	C26	C27
Total Protein	g/l.	-	-	102	-	-	-	100	-	-	-	-	-	101	-	-	-	-	105	-	-	-	-	110	-
Albumin	g/l.	-	-	-	-	-	13	-	-	-	-	-	-	-	14	19	-	-	-	18	-	-	-	-	19
Globulin	g/l.	-	-	72	60	-	84	-	69	74	60	76	72	75	73	-	76	70	83	71	62	64	73	86	77
S.G.O.T.	I.U.	-	-	-	147	-	502	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	554	-	-
Bilirubin	µ.mol/l.	12	12	-	12	-	18	-	-	-	-	-	-	-	12	-	-	-	-	-	10	-	-	-	13
Alk. Phosphatase	I.U.	490	-	-	-	-	253	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Urea	m.mol/l.	14	9	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Calcium	m.mol/l.	-	8.6	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

S.G.O.T. - serum glutamate oxaloacetate transaminase.

Alk. phosphatase - alkaline phosphatase.

Faeces examination In cases A16, C2 and C21, which were diarrhoeic, no Strongyle eggs were seen and no clumps of acid-fast bacilli were observed. D. viviparus larvae were not identified in any of the samples from these 45 cases of respiratory disease.

Urine examination Proteinuria greater than twice the normal range was present in four cases (A13, C2, C12, C23). In C2 there were 7.0 grams per litre of protein in the urine.

(5) Treatment of farmer's lung cases

Details of the treatment given on the farm to 16 acute (89%) and four chronic cases (15%) are given in Table 17 and the individual farmers were asked for their assessment of the success of the treatments. A "good" clinical response was produced in eight of the 11 acute cases that were given betamethasone (Betsolan: Glaxo Laboratories Ltd., Middlesex) for three successive days. A poor clinical response resulted from the use of antibiotic therapy alone in eight cases and also when tripelennamine (Vetibenzamine: Ciba-Geigy, (U.K.) Ltd.) was given along with an antibiotic to A1. The antibiotics used were proprietary brands of penicillin, penicillin and streptomycin or oxytetracycline and the preparations were usually given intra-muscularly for three successive days.

DISCUSSION

It was found that farmer's lung in cattle could be either a sudden onset (acute) or an insidious onset (chronic) disorder. Respiratory distress, anorexia, coughing and a marked decrease in milk yield were the main presenting signs in the acute form while coughing and hyperpnoea were by far the commonest presenting signs of the chronic condition. In man, the patient's reasons for consulting his doctor together with the latter's abnormal clinical findings at the initial physical examination constitute "presenting signs". The clinical symptoms of farmer's lung have been said to be more striking that the physical signs (109, 198, 250). If what the patient himself feels is wrong and, therefore what he complains about to his doctor, are accepted as clinical symptoms and physical or clinical signs are the abnormalities which can be detected by the clinician during a physical examination (229), then it follows that the diagnosis

TABLE 17

The treatments given to 20 cases of farmer's lung and the resultant clinical response.

Case No.	Treatment			Clinical Response	
	Antibiotics	Betamethazone*	Tripelennamine+	Good	Poor
A1			+		+
A2	+	+		+	
A3	+				+
A4	+				+
A5	+				+
A6	+				+
A7	+	+		+	
A8	+	+			+
A9	+	+			+
A12	+	+		+	
A13	+	+		+	
A14	+	+		+	
A15	+	+		+	
A16	+	+			+
A17	+	+		+	
A18	+	+		+	
C3	+				+
C4	+				+
C5	+				+
C16	+				+

* - Betsolan, Glaxo.

\+ - Vetibenzamine, Ciba-Geigy.

of farmer's lung in cattle is likely to be much more difficult than in man.

Both consitutional and respiratory symptoms are present in the acute stage of farmer's lung in man (Table 1) and either may be the reason for medical advice being sought (89). Although the presence of consitutional symptoms cannot be confirmed in cattle, evidence of general malaise can be inferred from observed changes in the animal's performance and/or behaviour; these changes may be the reasons given by the farmer for seeking veterinary advice. Since the modern dairy cow is a highly "tuned" animal, anything that adversely affects her health will reduce her productive efficiency and this will manifest itself in a decreased production of milk. A detectable reduction in milk yield occurred in every lactating dairy cow which developed acute farmer's lung and, in the most severely affected animals, there was agalactia. This was the only clinical sign that affected 100 per cent of the population at risk. A common, non-specific sign of illness is a decreased appetite and most of the acute cases were anorexic. Although several animals were noticed to have been dull during the acute respiratory episode, not all dyspnoeic animals experienced a change in demeanour as might have been expected.

That pyrexia was detected in less than half the acute cases was also rather unexpected. However, it has been shown than an increased temperature is only present from about four to 12 hours after exposure in man (287) and from about seven to 11 hours post-exposure in cattle (207). Consequently, if the temperature had been taken outwith these relatively narrow time limits, then it would have been within the recognised normal range. Sweating was never observed in any of these cases, even when a temperature of 105°F was recorded; this is not because cattle do not have the ability to sweat but almost certainly because bovine sweat glands are much less active than are human sweat glands (6).

Constitutional symptoms are not usually associated with the onset of chronic farmer's lung in man (Table 1). In this series of 27 cases of chronic "bovine" farmer's lung, clinical signs suggestive of generalised malaise were detected in eight animals, five of which came from the same farm. These five were said to have been slightly dull, to have had a poor appetite, to have had a reduced milk yield and three of them were the only chronic cases in which pyrexia was

detected. One of the others came from a farm where farmer's lung disease was a confirmed problem in the herd and another had had several mild hyperpnoeic episodes. Despite their never having been observed to have had acute pneumonic episodes, seven of these eight cases were probably more typical of a sub-acute rather than a chronic phase (89).

In the human form of the disease, dyspnoea, or the feeling of breathlessness, has been stated to be at its worst during an acute attack particularly during the febrile period (71) and, in several of the initial reports, it was emphasised that the "dyspnoea was out of all proportion to the other clinical signs" (75, 164, 251, 286). An increase in the depth of respiration was observed in every acute case except A11, which was examined on the farm while in lateral recumbency. When they were first seen to be ill, half the dyspnoeic cases were mouth-breathing and, with other respiratory diseases, this is a grave prognostic sign. Yet, not one of these five animals died, or even looked like dying, on the farm with the possible exception of A16 which was in cor pulmonale. Indeed, two farmers commented on the speed with which their cows recovered; A14 was said to have given four gallons of milk only 24 hours after she had been severely dyspnoeic. Hyperpnoea was a presenting sign in 23 chronic cases and in another two animals, dyspnoea was observed after a minimal amount of walking. Although exertional dyspnoea was a presenting sign in seven animals in this series (two acute and five chronic), lesser degress of exercise intolerance in other animals had probably gone unnoticed.

In their survey of farmer's lung, Staines and Forman (1961) found that dyspnoea and coughing were the most troublesome symptoms and, in 75 per cent of their cases, a combination of these two symptoms was the first evidence of respiratory disease. In this survey, these two clinical signs were observed together in the same proportion of cases (76%), although coughing was noted less frequently in the acute compared with the chronic form of the disease. The coughing was only noticed to have been productive when large amounts of tenacious, grey-greenish mucus were observed on the byre wall in front of the individual animals. Several dairy farmers said that, retrospectively, that they had observed mucus in front of a few cows which had subsequently been culled because of their unsatisfactory performance.

With both forms of the disease, tachypnoea was reported as being present in slightly less than half the cases. It would appear that "lifting" or "tifting", as hyperpnoea is called colloquially, is more easily appreciated in cattle at rest or is considered to be a better indication of respiratory disease than simply an increase in the respiratory rate. Perhaps this is because widespread tachypnoea is commonly observed when cows are housed in a warm environment, and, in the absence of other clinical signs of respiratory disease, an elevated respiratory rate is not considered to be important.

There was a history of weight loss with 12 animals, ten of which were chronic cases. Since 11 had been fed hay said by the farmer to have been mouldy or very mouldy, the most obvious explanation for their loss in condition is that the heating and moulding had markedly reduced the nutritive value of the crop. The hay from a farm from which five of the 11 cases were admitted (Chapter 2, Section 1, Herd 2) was analysed and no gross deficiencies were found (220). However, it is difficult to obtain a sample of hay for analysis that is representative of one bale let alone of the total crop. Nevertheless, a decrease in feeding value must still be borne in mind particularly with regard to beef cattle for which hay may form the major part of the diet in winter, compared with dairy cattle which have access to other food stuffs. In older cows, a gradual loss of weight is usually considered to be more a sign of old age rather than an indication of disease. A significant loss in weight can occur in the human within a relatively short period following an acute attack of farmer's lung (60, 71, 251, 286) as well as during the chronic stage of the disease (89). In neither of the acute bovine cases could the weight loss be attributed directly to the acute episode of farmer's lung; A16 had been seen to be losing weight for several weeks prior to the sudden onset pneumonic attack and A3 had lost weight during the three previous winters only to put it back on again during the following summer grazing period. This finding of weight loss during the winter and weight gain during the summer was noticed by several farmers and provided fairly strong circumstantial evidence that it was exposure to mouldy hay that was responsible for these animals losing condition.

In addition to their gaining weight during the summer while at grass, the respiratory signs became less severe and this is

one reason why severe respiratory disease was apparent in so few animals on admission. When it was obvious that these cases were not going to die, they were kept and sold at the end of the next summer when they were worth more money. Even allowing for the delay between the time that the animals were first seen to be ill and their being admitted to the Veterinary School, clinical evidence of respiratory disease was still detected in every case.

All 12 cows in which dullness had been a presenting sign were alert on admission although five others, four of which had cor pulmonale, were considered to be dull. Not one of the 45 cases was dyspnoeic at rest in the Veterinary School, although all bar one were hyperpnoeic. The exception (C11) had been coughing, hyperpnoeic and tachypnoeic during the serological survey but, following a six month grazing period, occasional coughing was the only evidence of respiratory disease that persisted. Nine of the 11 cases that were grossly hyperpnoeic were examples of the chronic form of the disease.

Although coughing was not noticed to be a presenting sign in six acute and two chronic cases, on admission only three of these animals were not heard to cough and one of them (C21) was in the terminal stages of cor pulmonale. When they were first seen to be ill, some of these cows may very well have been coughing but this had gone unnoticed since many farmer's and even some veterinary surgeons still do not regard coughing in cattle as abnormal (110, 294). Coughing was "normal" in many herds not because the cows were healthy as were generally supposed, but because many were affected with mild farmer's lung disease. This has been confirmed by the purchase of "healthy" cull cows from a few of these herds and, despite the absence of other signs of respiratory disease, lesions of farmer's lung were found at necropsy (292). Tachypnoea was noticed to be a presenting sign in less than half the cases and yet 85 per cent were tachypnoeic when admitted. Three of the four cows which had normal respiratory rates were admitted at the end of the summer and the lack of exposure to M. faeni had led to a marked improvement in their pulmonary function.

Adventitious lung sounds were detected in only six cases (four acute and two chronic) when respiratory disease was first diagnosed whereas, on admission, they were heard in ten acute (56%) and 18 chronic (66%) cases. In both forms of the disease, the

adventitious sounds were usually heard in the antero-ventral or dependent parts of the lungs. In the more severely affected cases, they could be heard all over one or both lung fields. It was assumed that the higher prevalence of bilateral adventitious sounds in the chronic compared with the acute cases was indicative of a more severe pulmonary involvement, a finding that was confirmed at necropsy (Chapter 4, Section V). In both forms of the disease, crackles were most frequently heard towards the end of inspiration and sometimes they were only present for four or five respirations after the animal had coughed. Widespread fine crackles (crepitations) are heard in acute as opposed to chronic farmer's lung in man (30, 40, 71, 75, 89, 109, 198, 202, 251). Rhonchi have not been mentioned in the recent clinical reports of farmer's lung (30, 71, 109, 198) although in the earlier descriptions it was stated that they were present in a few cases (40, 75, 250). It is now accepted that the physiological abnormalities in farmer's lung cannot be explained on the basis of a simple diffusion defect and an obstructive profile similar to that of chronic bronchitis has been found in almost 30 per cent of cases (107, 109, 233). As rhonchi can be produced by air passing through narrowed airways (52), then it is not surprising that they can be heard on auscultation. Bronchitis and bronchiolitis were present in all these cattle cases at necropsy (Chapter 4, Section V).

Emphysema was not detected in any of the 45 bovine cases although it is often present in the terminal stages of the chronic disease in man (71, 89, 234). In cattle, pulmonary emphysema is almost always to be found in the relatively loose, inter-lobular connective tissue having resulted from rupture of the alveoli. On auscultation, loud crackling can often be heard, usually over the diaphragmatic lobes, and this is a characteristic feature of specific pulmonary disorders such as fog fever and parasitic bronchitis.

It is universally agreed that apart from the presence of precipitating antibodies to M. faeni in acute cases, there is no confirmatory laboratory test for farmer's lung in man (52, 86). Precipitins to M. faeni were present in all these bovine cases and, although farmer's lung-like lesions have been observed in a few M. faeni precipitin-negative cattle (292), such cases have not been included in this study. In spite of at least one of the haemato-logical and blood biochemical estimations being outwith the accepted

normal range in almost every case, no regular pattern was found that would be useful in the diagnosis of farmer's lung in cattle. Perhaps this was to be expected since most of these cases were admitted and sampled at least four weeks after the respiratory signs were first noticed. Therefore, the search for specific abnormalities was limited to the ten acute cases admitted within three weeks following an acute respiratory episode.

The normal neutrophil/lymphocyte ratio in cattle is around 0.5 and, in six of the ten selected cases, this ratio was reversed and in four, a neutrophilic leucocytosis was present. Some of this effect may indeed have resulted from an acute episode of farmer's lung but neutrophilia is a non-specific response often associated with "non-infectious conditions which stimulate the stress reaction" (231).

Although eosinophilia in cattle is usually associated with parasitic infestations of the gastro-intestinal or respiratory tracts of grazing immature animals, this is unlikely to be the reason why in two cases, more than 20 per cent of the white cells were eosinophils. As both these cows were being fed very mouldy hay, it may be that their eosinophilia was associated with a non-parasitic reaction such as allergic aspergillosis (119). This disease has not yet been confirmed in cattle despite precipitating antibodies to A. fumigatus being common in the adult cattle in this country (292). Precipitins to A. fumigatus were present in both cases but they were also detected in several others in which there was no eosinophilia. In addition, the finding of large numbers of "asteroid bodies" in the lungs of A15, indicated that massive numbers of aspergillus spores had been inhaled and yet she still had an eosinophilia of only 8 per cent.

Occasionally in the human form of the disease, eosinophilia (60, 71, 89) and a neutrophilic leucocytosis have been reported (71, 216, 250); in one series, a neutrophilic leucocytosis was found in 26 per cent of the acute farmer's lung patients (60). Elevated serum gamma-globulin levels have been reported in extrinsic allergic alveolitis cases in general (216) and also specifically in clinical cases of farmer's lung (30). Raised total globulin levels were also found in rabbits that were repeated exposed to dust (297). Raised globulin levels were present in 75 per cent of the ten selected acute bovine cases but it can only be stated that farmer's lung may have been

a contributory factor in some or all of them. The several other values that were outwith the recognised limits of normality were probably referable to mild specific organ malfunction.

While in hospital, the three cases with obvious cor pulmonale were observed to have profuse diarrhoea. This must have been due to congestive cardiac failure since laboratory and pathological investigations ruled out ostertagiasis and Johne's disease and no other reason for the diarrhoea was found at necropsy.

Perhaps the most interesting laboratory finding was the presence of an excessive amount of protein in the urine of seven cases (one acute and six chronic). In four of them, the proteinuria was greater than twice the upper limit of normality and was particularly massive in A13 (3.75 g/l) and in C2 (7.0 g/l). An enlarged left kidney was detected per rectum in C2 and renal amyloidosis was confirmed at necropsy. The presence of farmer's lung and proteinurea may well have been coincidental but, on the other hand, the pathogenesis of both conditions may have been related either because of the deposition of immune complexes in both organs (36) or because of common basement membrane antigens (39).

The use of betamethasone appeared to be beneficial in acute cases and was said to have produced a speedy and obvious clinical improvement in eight of the 11 animals treated. As two of the three cases which did not improve were in cor pulmonale, it could be argued that a marked clinical improvement had been produced in eight of the nine cases (89%). This improvement had occurred despite the animals not being removed from the source of the allergens.

The clinical differences between the acute and chronic forms of farmer's lung in cattle did not appear to be as obvious as they are in man. Almost certainly this is because the clinical symptoms, which are so significant in the acute stage of the human disease, cannot be defined with the same accuracy in cattle because of the lack of verbal communication between the physician and patient. Nevertheless, with acute farmer's lung, respiratory distress, anorexia and a significant reduction in milk yield developed suddenly compared with the chronic form in which coughing, hyperpnoea and also weight loss were the characteristic presenting signs.

SECTION III

THE EPIDEMIOLOGICAL FEATURES OF FARMER'S LUNG IN CATTLE

MATERIALS AND METHODS

(1) Selection of cattle

The epidemiological findings presented here are those of the 45 individual cases of farmer's lung, the clinical details of which were discussed in the previous Section.

(2) Epidemiological parameters

The epidemiological details of farmer's lung in cattle were studied with specific reference to the age of animal affected, the month that respiratory signs were first noticed, the system of husbandry, the area in which the cases arose and finally, the farmer's reaction on exposure to mouldy hay dust.

For discussion purposes only, those cases aged from two to six years have been put in a "less than six years old" group while those seven years of age and older have been called "greater than six years old". Similarly, cows said to have been ten years old or more have been grouped together because the exact age of many of the older animals was not known.

The winter housing period has been divided into three parts, from September to December, from January to March and from April to June.

The term "farmer" has been used for the person who fed the cows but who was not necessarily the landowner. The farmers were classified according to whether or not they developed an adverse clinical reaction during, or after, they had worked with mouldy hay. Those who were unaffected were put in the "no reaction" group while those who experienced a reaction were put in the "positive reaction" group. This latter group was sub-divided; if the clinical reaction had been confirmed as farmer's lung, they were put in the "farmer's lung" group, otherwise they were put in the "other disorder" group.

RESULTS

The major epidemiological features of the 45 cases of farmer's lung are presented in Appendix 1 - Table 24.

(1) The relationships between age of animal affected and other factors

The mean age of the 45 cases was 7.4 $\pm$ 0.3 years and the difference between the mean age of the 18 acute cases (6.5 $\pm$ 0.6 years) and the 27 chronic cases (8.0 $\pm$ 0.4 years) was statistically significant. There was a significant positive correlation between age and the total number of cases ($r = 0.7200$, $p < 0.02$) and also between age and the number of chronic cases ($r = 0.7468$, $p < 0.01$). There was no significant correlation between age and the total number of acute cases although there was a significant correlation up to six years of age ($r = 0.9030$, $p < 0.01$). Although both forms of the disease were confirmed over a wide age range (Table 18), 11 of the acute cases (61%) were six years of age or less compared with only seven chronic cases (26%).

There appeared to be an association between age and the time of year that the signs of respiratory disease were first noticed. From September to December, only two cases (11%) less than six years old became ill while nine (50%) did so from January to March and seven (39%) from April to June. This compared with 11 cases (41%) over six years old which were first seen to be ill from September to December, nine (33%) from January to March and seven (26%) from April to May. However, there was no significant difference in the mean age of the animals which became ill from September to December (8.2 $\pm$ 0.5 years) compared with those that did so from January to March (7.2 $\pm$ 0.6 years) or from April to June (6.9 $\pm$ 0.6 years).

There was no significant difference in the mean ages of the cases admitted from different parts of the country; the mean age of those from England was 7.3 $\pm$ 0.4 years, from Westmorland alone was 6.9 $\pm$ 0.4 years and from Scotland was 7.8 $\pm$ 0.6 years. The number of cases less than six years old admitted from England, Westmorland alone and from Scotland was 14 (40%), 13 (46%) and four (40%) respectively. Of the 18 cases less than six years old, 13 (72%) came from Westmorland.

TABLE 18

The relationships between the age of animal affected and other epidemiological factors.

	Age (years)										
Epidemiological factors	1	2	3	4	5	6	7	8	9	10 or more	Total
No. of Cases	-	1	1	2	4	10	5	7	2	13	45
Form of Disease											
Acute	-	1	1	1	3	5	-	3	1	3	18
Chronic	-	-	-	1	1	5	5	4	1	10	27
Month Disease first noticed											
Sept. - Dec.	-	-	-	1	-	1	3	2	1	5	13
Jan. - March	-	1	-	1	1	6	1	2	1	5	18
April - June	-	-	1	-	3	3	1	3	-	3	14
Geographical Origin											
England	-	1	1	2	3	7	4	6	2	9	35
Westmorland	-	1	1	2	2	7	3	6	2	4	28
Scotland	-	-	-	-	1	3	1	1	-	4	10
System of Husbandry											
Beef	-	-	-	1	3	-	-	4	1	4	13
Dairy	-	1	1	1	1	10	5	3	1	9	32
Farmer's Reaction to Dust											
No reaction	-	1	-	-	2	4	-	5	-	8	20
Positive reaction	-	-	1	2	2	6	5	2	2	5	25
Farmer's lung	-	-	-	-	-	4	4	2	2	4	16
Other disorder	-	-	1	2	2	2	1	-	-	1	9

The form of livestock husbandry did not appear to have exerted a great effect on the age at which an animal developed obvious respiratory signs. The mean age of the beef cows was 7.7 $\pm$ 0.6 years compared with 7.3 $\pm$ 0.4 years for the dairy cattle and four of the beef cows (31%) were less than six years old compared with 14 (44%) of the dairy animals. The mean ages of the tied beef cows (7.6 $\pm$ 0.8 years) was the same as that for the loose-housed animals (7.7 $\pm$ 1.0 years) but the dairy cattle developed farmer's lung at a significantly earlier age when they were tied (6.7 $\pm$ 0.4 years) than when they were loose housed (10.0 $\pm$ 0.0 years).

There was no significant difference in the mean ages of the cases admitted from either the "no reaction" farms (7.8 $\pm$ 0.5 years) or from the "positive reaction" farms (7.0 $\pm$ 0.4 years). However, the cases admitted from the "farmer's lung" farms (mean age = 7.9 $\pm$ 0.4 years) were significantly older ($p < 0.01$) than those from the "other disorder" farms (mean age = 5.6 $\pm$ 0.7 years). Only four (25%) of the cases from the "farmer's lung" farms were less than six years old compared with seven (78%) from the "other disorder" farms.

(2) <u>The relationships between the month when respiratory signs were first noticed and other factors</u>

From September to December 13 cases (29%) became ill compared with 18 (40%) from January to March and 14 (31%) during April, May and June (Table 19).

The acute and chronic forms of the disease differed in the time of year that respiratory signs were first noticed. Only four acute cases (22%) became ill from September to December whereas eight (44%) and six (33%) did so from January to March and from April to June respectively. On the other hand, a similar number of chronic cases were noticed to be ill throughout the winter, nine (33%) from September to December, ten (37%) from January to March and eight (30%) from April to June.

The geographical area from which these cases came seemed to have had an effect on when they were first seen to be ill. Only one of the Scottish cases (10%) became ill from September to December compared with 12 (34%) from England and eight (29%) from

TABLE 19

The relationships between the month when respiratory disease was first noticed and other epidemiological factors.

Epidemiological Factors	Month Respiratory Disease First Noticed										
	Sept	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	June	Total
No. of Cases	2	2	6	3	6	7	5	5	8	1	45
Form of Disease											
Acute	1	-	2	1	3	3	2	3	3	-	18
Chronic	1	2	4	2	3	4	3	2	5	1	27
Geographical Origin											
England	2	2	5	3	6	4	4	3	5	1	35
Westmorland	2	-	4	2	6	3	3	2	5	1	28
Scotland	-	-	1	-	-	3	1	2	3	-	10
System of Husbandry											
Beef	-	-	3	2	-	1	2	3	1	1	13
Dairy	2	2	3	1	6	6	3	2	7	-	32
Farmer's Reaction to Dust											
No reaction	1	2	4	1	1	1	3	2	4	1	20
Positive reaction	1	-	2	2	5	6	2	3	4	-	25
Farmer's lung	1	-	1	1	4	3	2	-	4	-	16
Other disorder	-	-	1	1	1	3	-	3	-	-	9

Westmorland alone. About 40 per cent of cases from each area were noticed to be ill during January, February and March compared with April to June when five cases (50%) from Scotland, nine cases (26%) from England and eight cases (29%) from Westmorland were noticed to have respiratory disease.

The system of cattle husbandry also appeared to have affected the month of onset of clinical farmer's lung. Fifteen dairy animals (47%) developed respiratory disease during January, February and March but the beef cows became ill regularly throughout the winter.

The farmer's reaction to dust was also associated with the month in which respiratory signs were first observed. On the "no reaction" farms most cases were noticed to be ill either at the beginning (40%) or at the end (35%) of winter, whereas on the "positive reaction" farms, just over half the cases (52%) developed respiratory disease during the middle period of the winter. This peak in incidence from January to March was only a feature on the "farmer's lung" farms on which nine cases (56%) were observed to be ill during these three months with only three cases (19%) during September to December and four cases (25%) from April to June. Cases developed on the "other disorder" farms with equal frequency during the three periods of the winter.

(3) <u>The relationships between the system of cattle husbandry and other factors</u>.

Farmer's lung was diagnosed in 13 beef cows and 32 dairy females (Table 20) and every one was being, or had been, fed hay. The signs of respiratory disease were noticed while these cows were housed, apart from cases A8 and C12 which were first observed to be ill immediately after they went outside at the beginning of the summer grazing period when they developed marked exercise intolerance.

Nine beef cows (70%) and 27 dairy animals (84%) had been tied during the winter making a combined total of 80 per cent. The remaining 20 per cent had been kept in some form of loose-housing.

TABLE 20

The relationship between the system of cattle husbandry and other epidemiological factors.

Epidemiological Factors	System of Cattle Husbandry				Total
	Beef		Dairy		
	Loose	Tied	Loose	Tied	
No. of Cases	4	9	5	27	45
Form of Disease					
Acute	2	4	-	12	18
Chronic	2	5	5	15	27
Geographical Origin					
England	3	8	5	19	35
Westmorland	3	7	-	18	28
Scotland	1	1	-	8	10
Farmer's Reaction to Dust					
No reaction	3	4	5	8	20
Positive reaction	1	5	-	19	25
Farmer's lung	-	2	-	14	16
Other disorder	1	3	-	5	9

The system of cattle husbandry did not appear to affect the form of disease that developed; six beef cows (46%) and 12 dairy animals (38%) presented with the acute disease. Both forms of farmer's lung were more common in tied than in loose-housed cattle and not one of the five loose-housed dairy animals presented with the acute disease.

There was a definite association between the geographical area in which the cattle were kept and their liability to develop farmer's lung. The cattle in Westmorland seemed to be particularly at risk since ten beef cows (77%) and 18 dairy cattle (56%), making a total of 28 cases (62%) overall, came from this county alone.

Nineteen dairy animals (59%) were admitted from "positive reaction" farms compared with only six beef cattle (46%). In addition, there was a definite association between dairy husbandry and the development of farmer's lung in the farmer because 14 dairy cattle (74%) came from "farmer's lung" farms compared with only two beef cows (33%). Similarly, dust-induced respiratory disease in man was associated with keeping cows tied in byres since 24 of the "positive reaction" cases (96%) were tied compared with only 12 (60%) of those from "no reaction" farms.

(4) The relationship between the reaction of farmers to dust and other factors

The farmer's reaction to mouldy hay dust and the animals admitted from each farm are given in Table 21. The cases came from 29 farmers, 15 (52%) of whom suffered an adverse clinical reaction either during or after working with mouldy hay. Farmer's lung had been confirmed by medical consultants in six of these farmers while the nine "other disorder" farmers named their individual respiratory complaints as follows: bronchitis (2), hay fever (2), bad chest (1), choked up (1), feels seedy (1), weak chest (1) and wheezing (1). In addition farmer 2 and his wife both had precipitins to *M. faeni* in their sera and the brother of farmer 27 has had farmer's lung for over 20 years.

When the cases of farmer's lung in cattle were classified according to the individual farmer's reaction to mouldy hay dust, it was found that 25 animals (56%) had developed the disease on

TABLE 21

The cases admitted from each farm and the reaction of the farmer to working with mouldy hay.

Farm	Form of Disease		Farmer's reaction to mouldy hay dust
	Acute	Chronic	
1	A1		No reaction
2	A2		No reaction
3	A3	C1	Farmer's lung
4	A4, A7		No reaction
5	A5		Bronchitis
6	A6		Choked up
7	A8	C20	Farmer's lung
8	A9		Farmer's lung
9	A10		No reaction
10	A11, A15		Farmer's lung
11	A12		No reaction
12	A13		Feels seedy
13	A14		Hay fever
14	A16		No reaction
15	A17		No reaction
16	A18		Wheezing
17		C2	Hay fever
18		C3, C4, C5, C13, C14, C18	Farmer's lung
19		C6	Weak chest
20		C7, C9, C10	Farmer's lung
21		C8, C19	No reaction
22		C11	No reaction
23		C12	No reaction
24		C15	No reaction
25		C16	Bronchitis
26		C17	No reaction
27		C21	No reaction
28		C22, C23, C24, C25, C27,	No reaction
29		C26	Bad chest

farms where the farmer suffered a clinical reaction when he worked with mouldy hay (Table 22). Within this "positive reaction" group, 16 cases (64%) came from "farmer's lung" farms and nine (36%) from "other disorder" farms.

The form of disease that developed was not related to the farmer's reaction to dust since eight (40%) and ten (40%) acute cases came from the "no reaction" and "positive reaction" farms respectively. Within the "positive reaction" group, similar numbers of acute and chronic cases were admitted from "other disorder" farms, whereas most of the animals (69%) from the "farmer's lung" farms were chronic cases.

Eight cases (80%) from Scotland came from "positive reaction" farms compared with 17 (49%) from England and 16 (57%) from Westmorland alone. The occurrence of farmer's lung in cattle and man was closely related only in Westmorland where 11 of the "positive reaction" cases (69%) arose on "farmer's lung" farms compared with only five (44%) in Scotland.

The 18 acute cases came from 16 farms, the 27 chronic cases from 15 farms and only on farms 3 and 7 did one acute and one chronic case each arise. Only a single case was admitted from 21 farms (72%) and these 21 cases represented 47 per cent of the total number. From two to six cases were admitted from the other eight farms. The farmer's reaction to dust did appear to bear some relationship to the number of cases admitted. Although almost equal numbers of single animals came in from the "no reaction" and the "positive reaction" farms, five of the eight multiple admissions came from "positive reaction" farms. Within the "positive reaction" group, only one single case (10%) came from a "farmer's lung" farm compared with all five (100%) of the multiple incident cases. Fourteen acute cases (78%) arose singly compared with only 11 (41%) of the chronic ones.

(5) The relationship between geographical origin and other factors

The location of the 29 farms on which these 45 cases of farmer's lung developed is presented in Figure 3. The ten cases from Scotland came either from the counties of Dumfries (4 cases) or Lanark (6 cases), whilst the other 35 animals were admitted from

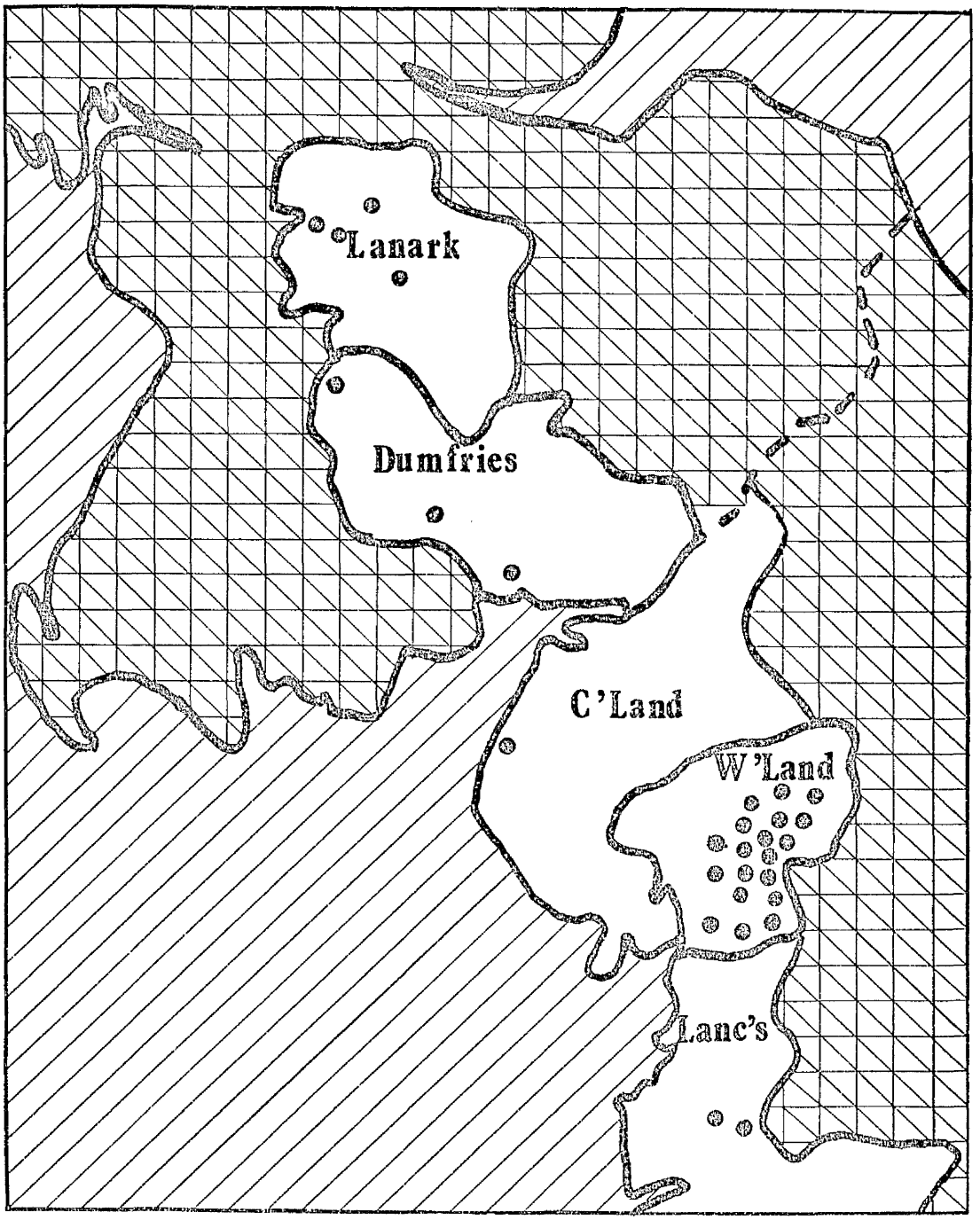
TABLE 22

The relationships between the farmer's reaction to mouldy hay dust and other epidemiological factors.

Epidemiological Factors		Farmer's Reaction to Mouldy Hay Dust				
		No Reaction	Positive Reaction	Farmer's Lung	Other Disorder	Total
No. of Cases		20	25	16	9	45
Form of Disease						
Acute		8	10	5	5	18
Chronic		12	15	11	4	27
Geographical Origin						
England		18	17	11	6	35
Westmorland		12	16	11	5	28
Scotland		2	8	5	3	10
No. of Cases/Farm						
Acute	Single	6	8	3*	5	14
	Multiple	1	1	1	-	2
Chronic	Single	5	6	2*	4	11
	Multiple	2	2	2	-	4

* 1 acute and 1 chronic case were admitted from farms 3 and 7.

FIGURE 3 The geographical locations of the 29 farms from which the 45 cases of farmer's lung were admitted.



three counties in north-west England, 28 from Westmorland, five from Cumberland and two from Lancashire. Acute farmer's lung was proportionally more common in Westmorland (50%) than in either Scotland (30%) or the rest of England (14%) (Table 23).

(6) The relationships between breed and other factors

Almost half (49%) the cases of farmer's lung in this study were Friesian cattle (Table 24), with 12 (67%) having been admitted with the acute disease but only 10 (37%) with the chronic form.

The findings presented above will now be examined following the incorporation of a third variable. The results of these cross tabulations are given below while the tables themselves are in Appendix 1.

(1) Form of disease v Age

The mean age of the acute cases was significantly less than that of the chronic cases.

a) v Month respiratory disease first noticed (Appendix 1 - Table 1)

With both forms of the disease, the younger cows became ill during the second half of the winter while the older cows became ill during the first half.
Therefore, an animal's age was important in determining when it became ill with both acute and chronic farmer's lung.

b) v System of husbandry (Appendix 1 - Table 2) Whereas dairy cattle with acute farmer's lung were significantly younger than those with chronic farmer's lung, there was no such difference with the beef animals. The ratio of dairy to beef cows less than six years old that developed chronic farmer's lung was six to one, while the ratio with the acute disease was three to one.
Therefore, dairy husbandry was associated with the development of clinical farmer's lung in young animals (less than six years old).

c) v Geographical origin (Appendix 1 - Table 3) Overall, the mean age of the acute cases was significantly less than that of the chronic cases but there was no significant difference

TABLE 23

The relationship between the geographical origin of cases and the form of disease.

Epidemiological Factors	Geographical Origin of Cases			Total
	Scotland	England	Westmorland	
No. of Cases	10	35	28	45
Form of Disease				
Acute	3	15	14	18
Chronic	7	20	14	27

TABLE 24

The relationship between breed of cattle and form of disease.

Epidemiological Factors	Breed of Cattle						
	Friesian	Ayrshire	Jersey	A.A.	Galloway	Shorthorn	Total
No. of Cases	22	6	5	4	4	3	45
Form of Disease							
Acute	12	1	-	3	1	1	18
Chronic	10	5	6	1	3	2	27

A.A. - Aberdeen Angus.

in the mean ages between the acute and chronic cases from Westmorland. The mean ages of the acute cases from Westmorland and from the rest of Britain was almost the same, but the chronic cases from Westmorland were significantly younger than those from the rest of Britain. Therefore, chronic farmer's lung developed in young animals (less than six years old) in Westmorland.

d) v Farmer's reaction to dust (Appendix 1 - Table 4) There was a significant difference between the mean ages of the acute and chronic cases from the "no reaction" farms but not from the "positive reaction" farms. There was no difference in the mean ages of the acute cases from the "no reaction" compared with the "positive reaction" farms, but the cases from "farmer's lung" farms were significantly older than those from the "other disorder" farms. The chronic cases from the "no reaction" farms were significantly older than those from the "positive reaction" farms but there was no significant difference in mean age between chronic cases from "farmer's lung" compared with "other disorder" farms.

Therefore, on "no reaction" farms, acute farmer's lung developed in young animals and chronic farmer's lung in older animals. On "positive reaction" farms, the acute and chronic forms of the disease developed in young animals. With the acute disease, cases from "other disorder" farms were younger than those from "farmer's lung" farms.

(2) Form of disease v Month respiratory disease first noticed

There was a peak incidence of acute farmer's lung from January to March, but chronic cases developed with equal prevalence throughout the winter.

a) v System of husbandry (Appendix 1 - Table 5) The January to March peak incidence of acute farmer's lung was a feature of dairy husbandry only and, although there was also a peak of chronic dairy cases from January to March, this was masked by the fact that most beef cases became ill either at the beginning or at the end of winter.

Therefore, with dairy cattle, there was a peak incidence of both acute and chronic farmer's lung during January, February and March.

b) v Geographical origin (Appendix 1 - Table 6) Most acute cases were admitted during January, February and March from Westmorland and Scotland. The number of chronic cases from Westmorland was also greatest from January to March. There was a dramatic decrease in the number of cases, however, admitted from the rest of England during the winter but this was complemented by an increasing incidence of cases from Scotland.

Therefore, with cattle from Westmorland there was a peak incidence of both acute and chronic farmer's lung during January, February and March.

c) v Farmer's reaction to dust (Appendix 1 - Table 7) With the acute form of the disease, the January to March peak incidence was only a "positive reaction" effect but one which was apparent with cases admitted from both "farmer's lung" and "other disorder" farms. There was also a January to March peak incidence of chronic cases from the "positive reaction" farms only, but this was entirely a "farmer's lung" effect. Both acute and chronic cases developed with similar frequency throughout the winter on the "no reaction" farms.

Therefore, on the "positive reaction" farms, there was a peak incidence of both acute and chronic farmer's lung during January, February and March. With the chronic disease, this high incidence was entirely a "farmer's lung" effect.

(3) Form of disease v Farmer's reaction to dust

Most chronic cases came from "farmer's lung" farms.

a) v Geographical origin (Appendix 1 - Table 8) The association between chronic farmer's lung in cattle and farmer's lung in man was evident in both Scotland and Westmorland.

Therefore, chronic cases of farmer's lung in cattle came from "farmer's lung" farms in both major areas studied.

b) v System of husbandry (Appendix 1 - Table 9) The chronic farmer's lung cases from "farmer's lung" farms were all dairy cattle.

Therefore, chronic farmer's lung in cattle is associated

with farmer's lung in man which is closely associated with dairy husbandry.

(4) Form of disease v Geographical origin

Both forms of the disease, but particularly the acute form, were common in Westmorland.

a) v System of husbandry (Appendix 1 - Table 10) With the acute disease, there was no geographical difference in the proportion of beef to dairy cases. However, with the chronic form, most of the beef cases originated from Westmorland where the proportion of beef to dairy animals was one to one, in the rest of England it was zero to six and in Scotland it was one to six.
Therefore, beef cattle in Westmorland were particularly liable to develop chronic farmer's lung.

(5) Form of disease v Breed

Acute farmer's lung was very common in Friesian cattle.

a) v System of husbandry (Appendix 1 - Table 11) With the exception of one case of both acute and chronic farmer's lung, all Friesian cattle were dairy animals.
Therefore, the close association between Friesian cattle and the development of both forms of farmer's lung was almost entirely a dairy husbandry effect.

b) v Age (Appendix 1 - Table 22) There was no difference in the mean age of the Friesian cattle with farmer's lung compared to that of the other breeds. However, with the chronic form, the Friesian animals were significantly younger than those of the other breeds.
Therefore, both acute and chronic farmer's lung affected young (less than six years old) Friesian cattle.

c) v Geographical origin (Appendix 1 - Table 23) All bar two of the Friesian cattle with acute farmer's lung were dairy animals from Westmorland and six of the ten with the chronic form of the disease also came from this county.
Therefore, both forms of farmer's lung, but particularly the acute form, were common in Friesian cattle most of which came from Westmorland.

(6) Month respiratory disease first noticed v Age

During the first half of the winter housing period, most cases were more than six years old whereas in the second half most cases were less than six years of age.

a) v System of husbandry (Appendix 1 - Table 12) The association between the time that clinical signs of respiratory disease were first noticed and the animal's age was related almost wholly with dairy husbandry. Therefore, as the winter housing period progressed, the incidence of clinical farmer's lung increased in dairy heifers and young cows but decreased in older dairy cows.

b) v Geographical origin (Appendix 1 - Table 13) The association between age and the month when respiratory signs first became apparent was only present in the cases from England. With cases less than six years old, this was mainly a Westmorland effect compared with those more than six years of age in which it was more apparent with cases from the rest of England. In Scotland, the number of cases of farmer's lung increased during the winter irrespective of the animal's age.
Therefore, the incidence of farmer's lung in cattle less than six years of age increased in all areas throughout the winter, but the high incidence at the beginning of winter in animals more than six years old was a particular feature of north-west England.

c) v Farmer's reaction to dust (Appendix 1 - Table 14) On the "no reaction" farms, the number of cases in the younger age group increased during the winter while the number in the older group decreased. On the "positive reaction" farms, this was not so evident and there was a January to March peak incidence in the older and particularly in the younger animals. In the older group, this was a "farmer's lung" effect.
Therefore, the number of farmer's lung cases in cattle less than six years old increased as the winter progressed on both the "no reaction" and the "positive reaction" farms. However, with animals more than six years old, there was a high incidence of cases on the "no reaction" farms and this decreased during the winter whereas on the "positive

reaction" farms there was a constant high incidence throughout the winter.

(7) Month respiratory disease noticed v Geographical origin

There was a gradual increase during the winter in the number of farmer's lung cases admitted from Scotland while in Westmorland, the peak incidence was from January to March and in the rest of England, from September to December.

a) v System of husbandry (Appendix 1 - Table 15) The increase in the number of cases from Scotland during the winter was a particular feature of dairy husbandry. Likewise, the January to March peak incidence in Westmorland was a dairy husbandry effect only. In England outside Westmorland, all bar one of the seven cases were dairy animals and so the high incidence at the beginning of winter was also a dairy husbandry effect.
Therefore, the regional differences in the time that farmer's lung cases were first seen to be ill was mainly a dairy husbandry effect.

b) v Farmer's reaction to dust (Appendix 1 - Table 21) In Scotland, the increasing incidence of cases during the winter was mostly evident on the "positive reaction" farms. The January to March peak incidence in cases from Westmorland was entirely a "positive reaction" effect and was almost exclusively confined to cases from "farmer's lung" farms. In the rest of England, since all except one of the cases came from "no reaction" farms, the high incidence of cases at the beginning of winter was a "no reaction" effect.
Therefore, the regional differences in the time that farmer's lung cases arose were due to variations in the numbers of cases from the "positive reaction" farms with the peak incidence during January, February and March in Westmorland coming from "farmer's lung" farms.

(8) Month respiratory disease noticed v System of husbandry

In dairy cattle, there was a peak incidence of farmer's lung from January to March.

a) v Farmer's reaction to dust (Appendix 1 - Table 17) Beef cattle developed farmer's lung with a similar frequency on "no reaction" and on "positive reaction" farms. Most of the "other disorder" cases were first seen to be ill at the end of winter. The January to March peak incidence in dairy cattle cases was entirely a "positive reaction" effect and primarily, a "farmer's lung" effect.
Therefore, the high incidence of farmer's lung in dairy cattle during January, February and March was made up entirely of cases from "positive reaction" farms and these were mainly "farmer's lung" farms.

(9) Farmer's reaction to dust v Age

Cases from "other disorder" farms were significantly younger than those from "farmer's lung" farms.

a) v Geographic origin (Appendix 1 - Table 18) Although a similar proportion of "other disorder" cases from Scotland (67%) and from Westmorland (63%) were less than six years old, the low mean age of this group resulted mainly from the relatively large number of young animals from Westmorland. Therefore, in Westmorland, "bovine" farmer's lung was found to have developed in older animals where the farmer suffered from farmer's lung and in younger cattle when some other reaction was experienced.

b) v System of husbandry (Appendix 1 - Table 19) The vast majority of beef and dairy animals from the "other disorder" farms were less than six years old while those from the "farmer's lung" farms were more than six years of age. Therefore, both beef and dairy cases from "other disorder" farms were younger than those from "farmer's lung" farms.

(10) Farmer's reaction to dust v System of husbandry

Most of the dairy cattle came from "positive reaction" farms and the vast majority of these came from "farmer's lung" farms.

a) v Geographical origin (Appendix 1 - Table 20) The prevalence of farmer's lung in dairy cattle was equally high in both Scotland and Westmorland.
Therefore, the association between dairy farming and the development of farmer's lung in cattle and man was

evident in both major areas studied.

(ii) Age v Geographical origin

There was no significant difference in the mean ages of the cases admitted from different parts of the country.

a) v System of husbandry (Appendix 1 - Table 16) The effect of this variable can be adequately studied only in Westmorland where farmer's lung was more prevalent in beef cattle over six years of age (80%) and in dairy cattle less than six years old (61%) A similar proportion of dairy cases from Scotland were less than six years old (63%) but, from the rest of England, all the dairy animals were more than six years old.
Therefore, the beef cattle that developed farmer's lung in Westmorland were more than six years old while the dairy cattle that became ill were less than six years of age in both Westmorland and Scotland, but more than six years in the other areas studied.

DISCUSSION

Since the number of cases of farmer's lung in cattle increased with age, it can be deduced that the pathological effect of cattle being regularly exposed to mouldy hay dust was cumulative. The mean age of the 45 cases was considerably greater than that of the beef and dairy cattle in Scotland and Westmorland sampled during this and other recent field investigations (Table 25). Because the youngest clinical case was a two-year old heifer which had become ill towards the end of her second winter it would appear, even when mouldy hay is being fed twice daily, that a minimum period of about six months is required for signs of respiratory disease to become obvious.

The epidemiological features of farmer's lung depended upon whether the adult female cattle had been kept for milk production or to rear their own calves. The dairy animals that developed the acute disease were significantly younger than those with the chronic form although no such difference was found with the beef cows. A much higher proportion of dairy cows less than six years old developed chronic farmer's lung than did beef cows. Provided that all breeds

TABLE 25

The mean ages of beef and dairy cattle in Scotland and Westmorland examined during the serological survey together with the mean ages of the acute and chronic cases of farmer's lung.

	Geographical Origin		Farmer's Lung Cases		
Type of Cattle	Scotland	Westmorland	Acute	Chronic	Total
Beef					
No. Sampled	340+	155	5	9	14
Mean Age*	6.5 ± 2.7	5.7 ± 2.6	7.0 ± 2.3	8.3 ± 2.1	7.7 ± 0.6
Dairy					
No. Sampled	640	165	12	20	32
Mean Age*	5.4 ± 2.2	5.2 ± 1.7	6.3 ± 2.5	7.9 ± 1.8	7.3 ± 0.4

\+ Grimshaw, W.T.R. (1977) Personal communication.

* Mean age and standard deviation.

of cattle respond to the inhalation of mouldy hay dust in a similar manner, it can be concluded that dairy cattle had a different periodicity of exposure to mouldy hay than had beef cattle.

In the same area, dairy cattle are housed for a longer period than beef cattle and even when the hay is of equal mouldiness, the dairy animals must have a greater exposure to mouldy hay dust. Some of the differences in the age of animal affected between the two forms of husbandry can be attributed to the fact that lactating dairy cattle are closely observed twice daily whereas beef cattle are at best only "looked at" twice per day. Consequently, the latter animals will only be seen to be ill when the respiratory signs are relatively severe.

The incidence of farmer's lung was higher amongst dairy cattle except in Westmorland where the condition was more prevalent in beef animals. In this county, beef cows are kept from November to April in field-houses (Figure 4) in which their winter's supply of hay is also stored. The fact that these cows are exposed to large amounts of mouldy hay dust twice per day for up to six consecutive months every year undoubtedly influences the probability of their developing farmer's lung. Although parts of the counties of Dumfries and Lanark are topographically similar to Westmorland, the climate is less extreme and so when beef cattle are housed, it is for a much shorter period. The type of housing also differs in that a much higher proportion of the beef animals are loose-housed in the two Scottish counties compared with Westmorland.

There was no significant difference between the mean ages of the animals with the two forms of the disease in Westmorland although overall, the acute cases were significantly younger than the chronic ones. Since the chronic cases from Westmorland were significantly younger than those from the rest of the country and because a very high proportion of the total number of animals came from this part of England, it can be deduced that all cattle in Westmorland are likely to be exposed to comparatively large amounts of mouldy hay dust. The explanation for this is two-fold: firstly, the regular rainfall during the hay-making season means that mouldy hay is likely to be made three years out of every four (215) and secondly, cattle in Westmorland are housed for a longer period than those in the other parts of the country because of the relatively extreme winter climate.

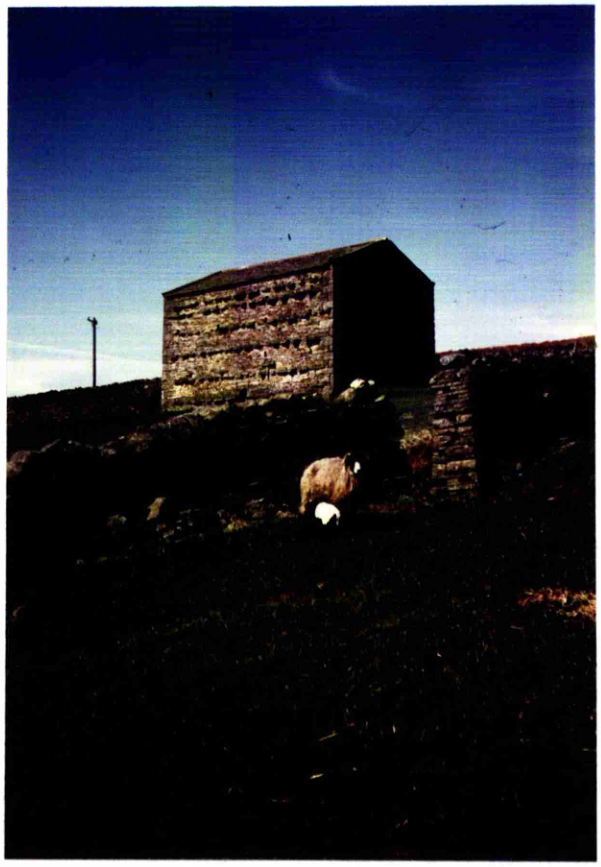


FIGURE 4 A view of a typical field-house in Westmorland.

The large number of animals admitted from Westmorland compared with the counties of Dumfries and Lanark could simply have been a reflection of the greater number of cattle at risk. In fact, the reverse was true (Table 26) and it was found that cattle in Westmorland were about six times more likely to develop farmer's lung than those in the two Scottish counties. That twice as many dairy as beef cattle were affected might also have been a reflection of the numbers at risk but again this was found not to be so. In Dumfriesshire and Lanarkshire, farmer's lung was three times as prevalent in dairy as in beef animals whereas in Westmorland the opposite was seen (Table 26). Dairy cattle were four times more likely and beef cattle 20 times more likely to suffer from farmer's lung in Westmorland than in Dumfriesshire and Lanarkshire. Consequently, the probability of cattle developing this respiratory disorder is dependant upon both geographical and husbandry factors.

It is not unreasonable to speculate that the farmers who were adversely affected by mouldy hay dust had a history of greater exposure than those who were unaffected. Evidence that there had been regular, high levels of exposure on the "positive reaction" farms seemed to be confirmed by the fact that there was no significant difference in the mean age between the acute and chronic cases from these farms. In addition, not only were the chronic cases from the "no reaction" farms significantly older than the acute cases but they were also significantly older than the chronic cases from the "positive reaction" farms. If the development of farmer's lung had been entirely dependant upon the amount of exposure to mouldy hay dust then it might have been expected that the acute cases from the "farmer's lung" farms should have been younger than those from the "other disorder" farms. However, the opposite was found and the acute "other disorder" cases were significantly younger than those from the "farmer's lung" farms. Differences in the frequency and amount of exposure could perhaps explain this rather unexpected finding. It has been suggested that sudden onset episodes of bird fancier's lung result from intermittent (once per week), massive exposure to antigen (pigeon form) while the insidious onset (budgerigar form) was brought on by constant, low-grade antigenic exposure (113). In this investigation it was not possible, even retrospectively, to relate the onset of acute respiratory signs to known sudden changes in exposure to M. faeni, although the fact that only single animals within a herd

TABLE 26 The prevalence of farmer's lung in the total cattle population of Dumfriesshire, Lanarkshire and Westmorland.

Geographical Location	Beef Cattle			Dairy Cattle		
	Total Numbers	Farmer's Lung Cases	Prevalence	Total Numbers	Farmer's Lung Cases	Prevalence
Dumfriesshire	34,615*	1	1/35,000	32,434*	3	1/11,000
Lanarkshire	18,923*	1	1/19,000	37,108*	5	1/7,500
Scotland	53,538	2	1/27,000	69,542	8	1/9,000
Westmorland	14,097+	10	1/1,400	37,973+	18	1/2,100
Total	68,000	12	1/5,666	110,000	26	1/4,320

* Scottish Milk Marketing Board, Paisley.

\+ Milk Marketing Board, Thames Ditton.

were affected at one time might indicate that their pattern of exposure had been different from that of their peers. In Canada (31) and in Finland (187), mouldy hay-induced respiratory disease most commonly affects cows in the standings adjacent to where the hay is thrown down from the loft.

Four acute cases were first seen to be ill soon after they had calved and the owners of Herds 1, 2 and 4 (Chapter 2, Section I) claimed that respiratory disease was frequently first observed a few weeks post-partum. If a post-calving change in exposure to mouldy hay dust had occurred, then it is much more likely to have been a decrease rather than an increase as "dry" cows are usually given the mouldiest hay.

On the other hand, the ability of an individual cow to react to a given exposure of mouldy hay dust might be different soon after calving than at other times during her lactation. Significant amounts of immunoglobulins are transferred from cow to calf only via the colostrum (242) and, during the two to three weeks before parturition, the concentration of IgG-1 in the serum of the dam decreases by more than 50 per cent whereas the concentrations of IgG-2, IgM, IgA and albumin remain unchanged (33, 61). By four weeks after parturition, the concentration of IgG-1 in the dam's serum has returned to a value similar to what it had been before its abrupt fall (33). IgG-1 has been described as the "complement-fixing sub-class of IgG" in cattle and sheep (148) and so is essential for the development of farmer's lung which is thought to be the result of a type III hypersensitivity reaction in the lungs (196). Therefore, the development of clinical farmer's lung a few weeks after parturition may be more a function of the rapid increase in the titre of serum precipitating antibody to M. faeni than of the amount of exposure to mouldy hay dust.

Differences in the M. faeni antigenicity of mouldy hays are known to occur (109, 199), but it is unlikely that they are important with regard to the development of farmer's lung in single animals.

An animal's age and therefore its accumulated history of exposure to mouldy hay was found to be closely associated with the period of the winter when the respiratory signs first became obvious. With both acute and chronic forms of the disease, older animals (more

than six years) became ill mainly during the first half of the winter and younger animals (less than six years) usually during the second half. This is unlikely to be fully explained by variations in the amount of exposure that individual animals have had to mouldy hay dust but is likely to be related to the titre of precipitating antibody to M. faeni at the beginning of winter. The prevalence of precipitins increases with age (Chapter 3, Section II) as does the proportion of animals with a relatively high titre (greater than 1/8). After the summer grazing season, many young animals which had been sero-positive in the spring were found to be sero-negative whereas the precipitins had persisted in the vast majority of the older cows (57). On subsequent exposure to mouldy hay, a much shorter period would then appear to be required for clinical respiratory disease to become obvious.

It was only on the "no reaction" farms that the old cows became ill at the beginning of winter and the young ones towards the end. On the "positive reaction" farms and particularly on the "farmer's lung" farms, there was a peak incidence during January, February and March. A high incidence of farmer's lung during these three months was a feature of the factors which were associated with the development of disease in young animals (the acute form of the disease, dairy husbandry and coming from Westmorland).

Since only a single animal was admitted from 21 of the 29 farms, clinical farmer's lung would appear to affect mainly individual animals. However, in more than three-quarters of these 21 herds, there was clinical evidence of respiratory disease in the other housed cows. It should not be surprising to find that farmer's lung is really a herd disease since it has already been shown that the feeding of mouldy hay twice daily for about 180 consecutive days can produce herd outbreaks of respiratory disease of varying severity (Chapter 2, Section I). In man, farmer's lung (77, 286) and other examples of extrinsic allergic alveolitis (15, 45) can also present as a multiple incidence disease when groups of people have been exposed simultaneously to the exciting dust.

A single case was admitted from only one of the six "farmer's lung" farms and even there another cow, which had been noticed to wheeze during the winter, was found to have chronic farmer's lung when it was purchased two years later (290). If the farmer himself has

developed farmer's lung and if the cattle have been fed mouldy hay, then it is highly probable that they too will have developed farmer's lung. The converse however does not apply; confirmation of farmer's lung in cattle does not mean that the farmer is suffering from the disease since the amount of exposure to which he is subjected depends upon his own husbandry methods. A farmer who feeds hay prior to milking is particularly at risk whereas if the cows are fed hay after milking the amount of exposure to which the farmer is subjected will be very small indeed.

In every case presented in this study, the development of farmer's lung was closely associated with the feeding of mouldy hay. That the probability of contracting farmer's lung is greatest where the possibility of exposure to mouldy hay is highest would appear to be true since farmer's lung was most prevalent in Westmorland in the Lake District of England, an area renowned for its scenic beauty, regular summer rainfall and mouldy hay.

To conclude, farmer's lung in cattle was particularly common in Westmorland, in the upland areas of Lanarkshire and also in Cumberland and Dumfriesshire. The disease was confirmed during the winter housing period or within a few weeks of the animals going out to grass. This was found to be a disease of adult animals (more than two years old) and in particular of cows over six years of age. The older cows tended to become ill towards the beginning of winter and the younger animals towards the end of the winter. Although both beef and dairy cows were affected, the disease was more prevalent overall in dairy animals except in Westmorland where there was a high incidence in beef cows. Acute farmer's lung generally presented as a single animal condition often within the first few weeks post-calving whereas the chronic form of the disease presented as a single incidence or multiple incidence condition.

CHAPTER 3

SEROLOGICAL STUDIES OF FARMER'S LUNG IN CATTLE

GENERAL INTRODUCTION

It was suspected that there could be a farmer's lung-like respiratory disease of cattle when precipitating antibodies to *M. faeni* were found in the serum of a housed cow which had been exposed to mouldy hay and had developed respiratory disease (225). The possibility that acute farmer's lung in man and "indoor" fog fever might have a similar aetiology was investigated by Jenkins and Pepys (1965) who found precipitins to *M. faeni* in 75 per cent of sera from cattle said to have been affected with "indoor" fog fever. This figure is much higher than the prevalence of precipitins in any of the other groups they examined (Table 27). Precipitins to *M. faeni* were also detected in 53 per cent of cattle suffering from an unspecified pulmonary disorder which was also said to have resulted from the feeding of mouldy hay. However, precipitins were not present in serum from the one case of "classical", pasture-associated fog fever examined and so it was postulated that the presence of precipitins could be used to differentiate between the "indoor" form and the "pasture-associated" forms of fog fever (132).

As part of our investigation, serum from every case of acute respiratory disease in adult cattle was examined for precipitins to *M. faeni* and, as a result of finding that precipitins were common in housed cattle with respiratory disease, an investigation was undertaken to determine the prevalence of precipitins to *M. faeni* in adult cattle in this country.

In Section I, the results of the investigation to determine the prevalence of precipitins to *M. faeni* in cases of fog fever are presented.

In Section II, the findings of the survey to determine the prevalence of precipitins to *M. faeni* in adult cattle are discussed.

TABLE 27

The numbers of cattle in selected groups with serum precipitins against extracts of Micropolyspora faeni.

	Groups of Sera	No. of Animals	M. faeni Positive %
No clinical respiratory disease	Not exposed to mouldy hay/ affected with non-respiratory disease	84	10
	Abattoir samples	193	5
	Exposed to mouldy hay	68	24
Clinical respiratory disease	Virus pneumonia	28	4
	Respiratory disease (undiagnosed)	38	37
	Fog fever (diagnosed)	28	75
	Total	439	16

After Jenkins and Pepys (1965).

SECTION I

A STUDY OF THE PREVALENCE OF PRECIPITATING ANTIBODIES TO MICROPOLYSPORA FAENI IN CATTLE AFFECTED WITH FOG FEVER

MATERIALS AND METHODS

(1) Selection of cattle

a) Fog fever group The animals were admitted to the Glasgow Veterinary School during an investigation of acute respiratory disease in adult cattle. A diagnosis of fog fever was made when an animal had become ill during the months of September, October or November after a change to a better pasture and when at least two of the following lesions were present at necropsy; pulmonary oedema and hyaline membranes, pulmonary emphysema and alveolar epithelial hyperplasia. The cases of fog fever admitted during the first two years of this investigation form fog fever (Group A) and those admitted in the three subsequent years comprise fog fever (Group B).

b) Indoors respiratory disease group Serum samples taken by a veterinary practitioner in Westmorland from a number of adult cattle which had developed respiratory disease during the winter (December to May inclusive) were also examined for precipitins to M. faeni and the results have been included for comparison with the fog fever cases. The clinical signs of respiratory disease had been present for several weeks in every case except one which had presented with acute respiratory distress.

(2) Examination of blood samples

Blood was taken from the jugular vein of every animal admitted alive. The samples were kept at $4^{o}C$ overnight and, after being spun at 1300 g for 30 minutes, the serum was taken off and stored at $-20^{o}C$ until examined.

The sera from the fog fever (Group A) and the indoor respiratory disease group were examined for the presence of precipitating antibodies against antigens prepared from the following micro-organisms: Aspergillus candidus, A. fumigatus,

A. nidulans, Humicola stellata, Malbranchea pulchella, M. faeni and a thermophilic Penicillium species.

The sera from the fog fever (Group B) cases were examined for precipitating antibodies against A. fumigatus and M. faeni only.

(3) Preparation of antigens for double diffusion tests

The A. candidus, A. fumigatus and A. nidulans antigens were prepared by culturing the organisms in glucose peptone broth in Roux flasks for six weeks at 28°C. The broth cultures were filtered and the filtrates dialysed against running tap water for 36 hours, concentrated to approximately one-quarter of their volume using carbowax M20 (Searle, High Wycombe, Bucks.) and sterilised by millipore filtration (pore size = 0.45 μm). The filtrate was used unconcentrated for the double diffusion tests.

The other micro-organisms, H. stellata, M. faeni, M. pulchella and the Penicillium species, were grown on nutrient agar for ten to 14 days at 55°C. The plates were frozen and thawed three times, then the fluid exudate was decanted, filtered and the filtrate, after it had been dialysed against running tap water for 36 hours, was concentrated to approximately one-quarter of its volume using carbowax M20 and sterilised by millipore filtration (pore size = 0.45 μm). The filtrate was used unconcentrated for the double diffusion tests.

(4) Double diffusion test procedure

Sera were examined for Aspergillus species antibodies in borate-buffered (pH = 8.6) 1.5 per cent Ionagar No. 2 (Oxoid, London) according to the method of Murray and Mahgoub (1968). The plates were incubated for seven days, then flooded with a citrate solution and left overnight to ensure that the precipitation lines were not the result of a non-specific reaction due to C-reactive protein (196). For the detection of antibodies against the other micro-organisms, the sera were tested in 1.5 per cent Oxoid Ionagar No. 2 prepared with Macilvain's citric acid buffer (pH = 7.2). The pattern used was a central antigen well 4 mm in diameter and five peripheral serum wells 6 mm in diameter; the distance edge to edge between

the central and peripheral wells was 5 mm. The plates, which were kept in a humid chamber at 24°C were examined daily and, when the final reading was made after five days, the number and intensity of the lines were noted. Over a period of three to four days, the plates were washed in two changes of phosphate-buffered saline and once in distilled water. They were then stained with either naphthalene black 12B (amidoschwartz) or azocarmine B.

RESULTS

The results of the double diffusion tests with the individual antigens are set out in Table 28. Precipitating antibodies against the complete test panel of micro-organisms were not detected in any of the sera from the 12 cases of fog fever in Group A. Similarly, precipitins against *A. fumigatus* and *M. faeni* were not detected in the sera from the cases of fog fever in Group B.

With the indoors respiratory disease group, precipitins to *M. faeni* were present in ten samples (91%). Of the other six antigens used, positive precipitation reactions were detected only with *A. candidus*, *A. fumigatus* and *A. nidulans* and it was the same two animals that were positive with each species.

DISCUSSION

In this study which extended over five years, not one of the 33 adult cattle affected with "classical" fog fever had demonstrable levels of serum precipitating antibody to *M. faeni* or to some of the common fungal antigens encountered in mouldy foodstuffs. This was not entirely unexpected since, in the original reports of fog fever, a disease that affected grazing cattle in the autumn had been described (141, 221). Farmer's lung is usually diagnosed in the spring (52, 250) when most cattle in the "farmer's lung" areas of Britain are housed. That over 90 per cent of the cows which developed respiratory disease whilst they were indoors did have precipitins to *M. faeni* was in agreement with the original suggestion made by Jenkins and Pepys (1965) that a respiratory disease similar to farmer's lung could affect cattle. This suggestion was confirmed later when a housed, hay-fed cow which

TABLE 28 The results of double diffusion tests on the sera of cattle with fog fever and indoor respiratory disease using antigens derived from micro-organisms found on mouldy hay.

	M. faeni		A. fumigatus		A. candidus		A. nidulans		A. stellata		M. pulchella		Penicillum sp.	
	No. Tested	No. Pos.	No. Tested	No. Pos.	No. Tested	No. Pos.	No. Tested	No. Pos.	No. Tested	No. Pos.	No. Tested	No. Pos.	No. Tested	No. Pos.
Fog Fever (Group A)	12	0	12	0	12	0	12	0	12	0	12	0	12	0
Fog Fever (Group B)	21	0	21	0	N.E.	-	N.E.	-	N.E.	-	N.E.	-	N.E.	-
Indoor Respiratory Disease Group	11	10	10	2	10	2	10	2	10	0	10	0	10	0

N.E. = Not Examined.

developed an acute respiratory disease diagnosed by the veterinary practitioner as "indoor" fog fever, was found to be suffering from a condition virtually identical to acute farmer's lung in man (207).

In addition to the serological differences between the "indoor form" of fog fever (farmer's lung-like disease) and the "pasture form" ("classical" fog fever), there are obvious epidemiological and histopathological differences (Table 29). As mentioned above, "classical" fog fever occurs when cattle are grazing and consequently, are not being fed hay; the feeding of mouldy hay to cattle is commonly associated with the development of farmer's lung in man (250). None of the characteristic histopathological lesions of acute farmer's lung (mononuclear cellular infiltration of the alveolar septa, bronchiolitis obliterans and epithelioid granulomata) were found in the lungs of the fog fever cases. In cattle, although both farmer's lung and fog fever can present as sudden onset respiratory distress, the epidemiological and histopathological differences are so great that the result of a precipitation test for antibodies to M. faeni is not required in order to differentiate between them.

TABLE 29

A comparison of the major epidemiological and histopathological features of fog fever in cattle and acute farmer's lung in man.

Disease	Epidemiology	Histopathological Lesions
Fog Fever	Autumn (Sept. - Nov.) Cattle outside eating grass.	Pulmonary Congestion. Pulmonary oedema and hyaline membranes. Alveolar epithelial hyperplasia. Interstitial emphysema.
Acute Farmer's Lung	Spring (Jan. - May) Cattle housed eating mouldy hay.	Mononuclear cellular infiltration. Bronchiolitis obliterans. Epithelioid granulomata.

SECTION II

A STUDY OF THE PREVALENCE OF PRECIPITATING ANTIBODIES TO MICROPOLYSPORA FAENI IN ADULT CATTLE

MATERIALS AND METHODS

(1) Selection of cattle

The herds involved in this study were selected for one of the following reasons: because the farmer suffered from farmer's lung - "farmer's lung" herds (FL1 to FL7), or because precipitating antibodies to M. faeni had been detected in serum samples from individual cows which had developed respiratory disease whilst they were indoors - "positive sample" herds (PS1 to PS6), or simply because hay was being fed to the cattle during the winter - "random" herds (R1 to R4). Farmer's lung had been confirmed in the owners of "farmer's lung" herds during the five years prior to this survey and, although the other farmers were not known to be free from the disease, they were not aware of any respiratory symptoms after working with mouldy hay.

Herds FL1 to FL7, PS1 and R1 to R4 were located in the south-west of Scotland while the other herds, PS2 to PS6 and FL8 were in the north-west of England. All were dairy herds apart from PS2, PS3 and PS4 which were single-suckling beef enterprises. All the cattle were tied during the winter except for part of herd PS3 in which 70 of the 98 cows were loose-housed.

This study was continued for a second year on eight of these farms (FL1, FL3, FL5, FL7, PS1, PS6, R1, R2) and also on farm FL8 where farmer's lung was confirmed in the milking cows during the first year of this survey.

(2) Examination of blood samples

The housed adult cattle in the "farmer's lung" and "positive sample" herds were blood sampled on two occasions during the first year of this investigation. The first samples were collected in November or December either just before, or immediately after, the animals had been housed; this is referred to as the first test. The samples for the second test were taken in the late spring immediately after the cattle were put

out to pasture. The four randomly selected herds were only sampled at the end of the winter housing period. During the second year of this study, blood samples were collected from all the housed adult cattle in the eight herds on two occasions.

Blood was collected from the caudal vein using 7 ml draw vacutainers with no additive (Becton, Dickinson and Co., Clarkson, Ontario). The samples were kept at $4^{o}C$ overnight and, after they had been spun at 1300 g for 30 minutes, the serum was taken off and stored at $-20^{o}C$ until required.

(3) Preparation of Micropolyspora faeni antigens for double diffusion tests

Each serum was tested against two antigen preparations of M. faeni, strain IMI 134062 obtained from the Commonwealth Mycological Institute, Kew. The antigens were derived from cultures grown on either nutrient agar or Czapek Dox agar at $55^{o}C$ for seven to ten days. The culture plates were frozen and thawed three times, the liquid drained off and Seitz filtered, dialysed against running tap water for 36 hours and millipore filtered (pore size = 0.45 μm). The filtrate was used unconcentrated for the double diffusion tests.

(4) Double diffusion test procedure

Double diffusion was carried out in 1.5 per cent Oxoid Ion agar No. 2 prepared with Macllvain's citric acid buffer (pH = 7.2). The pattern used was a central antigen well 4 mm in diameter and five peripheral serum wells 6 mm in diameter; the distance edge to edge between the central and peripheral wells was 5 mm. The plates, which were kept in a humid chamber at $24^{o}C$ were examined daily and, when the final reading was made after five days, the number and intensity of the lines were noted.

The detailed results of the examination of the serum samples from the individual animals in each of the herds for precipitating antibodies to M. faeni are given in Appendix 2.

RESULTS

The results of the examination for precipitating antibodies to M. faeni in 13 herds are given in Table 30. At the first test, 33 per cent of the total number of cattle sampled had precipitins, the prevalence in the individual herds ranging from 3 per cent in PS1 to 62 per cent in FL6. At the second test, 47 per cent of the cattle had precipitins in their sera and again the prevalence varied greatly, ranging from 14 per cent in PS2 to 78 per cent in FL5. The increase in the total prevalence of precipitins that had occurred during the winter was very highly significant. Although the proportion of animals with precipitins increased in nine herds, the increase was statistically significant in only three (FL1, PS1, PS3). There was also a small decrease in the incidence of precipitins in three herds.

When the herds were grouped according to the reason for their selection (Table 31), the increase in the incidence of precipitins was highly significant in the "farmer's lung" herds but was not significant in the "positive sample" herds. In the four "random" herds which were only sampled at the end of winter (Table 32), the prevalence of precipitins ranged from 0 per cent in R1 to 51 per cent in R2. In total, 26 per cent of the cattle in the "random" herds were preciptin positive at the second test compared with 33 per cent in the "positive sample" herds and 58 per cent in the "farmer's lung" herds. The difference in the prevalence of precipitins at the second test between the "farmer's lung" herds and the "positive sample" herds was very highly significant whereas the difference between the "positive sample" and "random" herds was not significant.

Since the population of individual animals within a herd can change over a six month period, the results from those cows that were positively identified at both tests have also been presented (Table 33). When the change in the precipitin status of individual animals was closely examined, 40 per cent of the cattle that had been precipitin-negative at the first test were found to be precipitin-positive at the second test. This increase in the number of cattle with precipitins was very highly significant. Within the individual herds, the number of precipitin-negative cattle that became precipitin-positive during the winter was very highly significant in four (FL1, FL3, FL5, PS3) and significant in two (PS1, PS6). It was also discovered that 20 per cent of the animals that had been precipitin-positive at the first

TABLE 30

The results of the examination of sera from housed adult cattle in selected herds for precipitating antibodies to *Micropolyspora faeni*.

Herd	First Test			Second Test			Significant Change
	No. Animals Tested	No. Animals Positive	% +ve	No. Animals Tested	No. Animals Positive	% +ve	
FL1	35	3	9	34	26	76	VHS
FL2	39	10	26	38	11	29	-
FL3	88	26	30	82	41	50	-
FL4	30	13	43	32	13	41	-
FL5	80	41	51	79	62	78	-
FL6	76	47	62	75	45	60	-
PS1	32	1	3	33	10	30	S
PS2	39	5	13	43	6	14	-
PS3	98	17	17	93	31	34	S
PS4	33	13	39	32	8	25	-
PS5	19	9	47	15	8	53	-
PS6	26	13	50	26	18	69	-
Total	595	198	33	582	279	47	VHS
FL7*	63	0	0	59	1	2	-

* Only silage fed.

TABLE 31 The prevalence of precipitating antibodies to Micropolyspora faeni in herds grouped according to the reason for their selection.

Reason for Selection	First Test			Second Test			Significant Change	
	No. Animals Tested	No. Animals Positive	% +ve	No. Animals Tested	No. Animals Positive	% +ve		
"Farmer's lung" herds	348	140	40	340	198	58	HS	VHS
"Positive sample" herds	247	58	23	242	81	33	-	-
"Random" herds	-	-	-	249	64	26		

TABLE 32

The results of the examination of sera from housed adult cattle in herds selected at random for precipitating antibodies to Micropolyspora faeni.

Herd	Roughage	Second Test		
		No. Animals Tested	No. Animals Positive	% +ve
R1	Good hay	75	0	0
R2	Poor hay	51	26	51
R3	Variable hay	71	18	25
R4	Poor hay and silage	52	20	38
Total		249	64	26

TABLE 33 The results of the examination of sera from positively identified, hay-fed cattle in selected herds for precipitating antibodies to Micropolyspora faeni.

Herd	No. Animals Tested	First Test		Second Test			Change in Precipitin Status					
		No. Animals Positive	% +ve	No. Animals Positive	% +ve	Significant Change	No. Animals Gained	% Gain	Significant Change	No. Animals Lost	% Loss	Significant Change
FL1	29	3	10	22	76	HS	19	73	VHS	0	0	-
FL2	17	4	24	5	29	-	3	23	-	2	50	-
FL3	57	14	25	34	60	S	22	51	VHS	2	14	-
FL4	24	11	46	11	46	-	3	23	-	3	27	-
FL5	51	20	39	42	82	S	23	74	VHS	1	5	-
PS1	26	0	0	9	27	S	9	35	S	0	0	-
PS2	20	3	15	4	20	-	1	6	-	0	0	-
PS3	82	16	20	27	33	-	16	24	VHS	5	31	-
PS4	15	6	40	4	27	-	1	11	-	3	50	-
PS5	15	7	47	8	53	-	2	25	-	1	14	-
PS6	22	10	45	15	68	-	7	58	S	2	20	-
Total	358	94	26	181	51	VHS	106	40	VHS	19	20	-

test were precipitin-negative at the second. However, this decrease in the incidence of precipitins and that which occurred in the individual herds were not statistically significant.

When the positively identified cattle were grouped according to the reason for their selection (Table 34), it was found that the prevalence of precipitins had increased significantly from the first to the second test in both the "farmer's lung" and the "positive sample" herds. In addition to there being a very highly significant increase in the number of precipitin-negative cattle that developed precipitins during the winter in both groups of animals, significantly more "farmer's lung" cattle developed precipitins than did "positive sample" animals. Only 15 per cent of the precipitin-positive cattle in the "farmer's lung" herds became precipitin-negative during the winter compared with 26 per cent in the "positive sample" herds. Neither of these changes achieved statistical significance.

At the first test, there was a significant positive correlation ($r = +0.98$) between age and the percentage of cattle with precipitins (Table 35: Figure 5). This correlation was significant in both the "farmer's lung" herds ($r = +0.95$) and the "positive sample" herds ($r = +0.81$) (Table 36). However, there was no significant correlation between age and the total number of animals that developed precipitins during the winter nor between age and the numbers that became precipitin-positive in either the "farmer's lung" herds or the "positive sample" herds. The only marked difference between the "farmer's lung" and the "positive sample" herds was in the two-three year old age group in which 82 per cent came from "farmer's lung" herds compared with 61 per cent from four-five year old, 59 per cent from six-seven year old and 60 per cent in the eight year old and above group. Of the total number of animals that gained precipitins, 41 per cent were less than six years old compared with 40 per cent more than six years of age.

Too few animals became precipitin-negative during the winter for meaningful conclusions to be drawn. Of the animals that did become precipitin-negative, 17 per cent were less than six years old and 24 per cent were more than six years of age. Fifty per cent came from "farmer's lung" herds and fifty per cent from "positive sample" herds.

TABLE 34 The prevalence of precipitating antibodies to Micropolyspora faeni in positively identified, hay-fed cattle in selected herds grouped according to the reason for their selection.

Reason for Selection	No. Animals Tested	First Test		Second Test			Change in Precipitin Status					
		No. Animals Positive	% +ve	No. Animals Positive	% +ve	Significant Change	No. Animals Gained	% Gain	Significant Change	No. Animals Lost	% Loss	Significant Change
"Farmer's lung" herds	178	52	29	114	64	VHS	70	56	VHS	8	15	-
"Positive sample" herds	180	42	23	67	37	S	36	26	VHS	11	26	-
Total	358	94	26	181	51	VHS	106	40	VHS	19	20	-

TABLE 35

The relationship between age and the prevalence of precipitating antibodies to Micropolyspora faeni in hay-fed cattle at the first test.

Age (Years)	No. Animals Tested	No. Animals Positive	% +ve
2-3 (2.5) *	127	29	23
4-5 (4.5) *	189	56	30
6-7 (6.5) *	142	56	39
8 and above (10.5) *	104	49	47
Total	562	190	

* Ages used in calculating coefficient of correlation.

$r = +0.98$. $y = 16.66 + 3.01x$

where x = age of animals

y = number (%) of animals.

FIGURE 5 The relationship between the age of the cattle sampled during the serological survey and the prevalence of precipitating antibodies to Micropolyspora faeni.

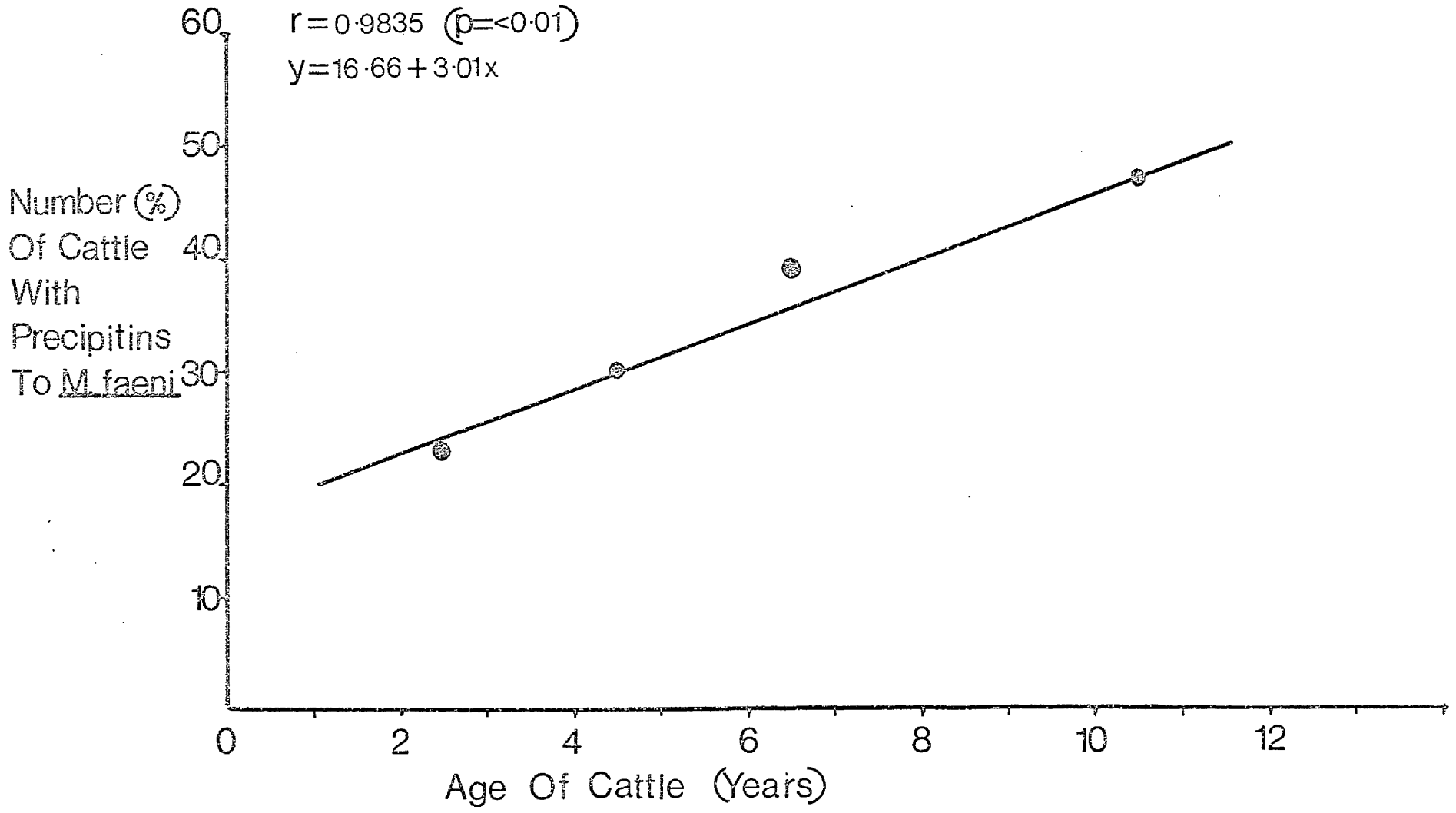


TABLE 36

The relationship between age and the prevalence of precipitating antibodies to Micropolyspora faeni at the first and second tests in positively identified hay-fed cattle grouped according to the reason for the selection of the herd.

Reason for Selection	Precipitin Status		Age of Cattle (Years)								
	First Test	Second Test	2-3	(%)	4-5	(%)	6-7	(%)	8 and above	(%)	Total
"Farmer's Lung" Herds	+	+	7		20		8		9		44
	+	-	2		2		3		1		8
	Total Positive at First Test		9	(15)	22	(33)	11	(33)	10	(50)	52
	-	-	27		16		9		4		56
	-	+	23	(46)	28	(64)	13	(59)	6	(60)	70
Total Number Tested			59		66		33		20		178
"Positive Sample" Herds	+	+	3		15		3		8		29
	+	-	2		3		3		2		10
	Total Positive at First Test		5	(18)	18	(22)	6	(17)	10	(33)	39
	-	-	18		47		20		16		101
	-	+	5	(22)	18	(28)	9	(31)	4	(20)	36
Total Number Tested			28		83		35		30		176
Total Number Gained Precipitins			28	(38)	46	(42)	22	(43)	10	(33)	106
Total Number "Lost" Precipitins			4	(29)	5	(13)	6	(35)	3	(15)	18

Ages used in calculating coefficients of correlation were 2.5 years, 4.5 years, 6.5 years and 10.5 years.

TABLE 36 (Cont'd.)

(1) Correlation between age and number of cattle with precipitins at the first test in the "farmer's lung" herds.
$r = +0.95$. $y = 8.84 + 3.99x$ (HS)

(2) Correlation between age and number of cattle with precipitins at the first test in the "positive sample" herds.
$r = +0.81$. $y = 12.04 + 1.74x$ (S)

(3) Correlation between age and the total number of precipitin-negative cattle at the first test that were precipitin-positive at the second test.
$r = -0.56$. $y = 43.46 - 0.74x$

(4) Correlation between age and the number of precipitin-negative cattle at the first test in the "farmer's lung" herds that were precipitin-positive at the second test.
$r = +0.53$. $y = 49.96 + 1.21x$

(5) Correlation between age and the number of precipitin-negative cattle at the first test in the "positive sample" herds that were precipitin-positive at the second test.
$r = -0.26$. $y = 27.56 - 0.39x$.

where x = age of animals
y = number (%) of animals.

Not one animal with clinical respiratory disease was referred from any of these farms during the first winter of the serological survey (1970-71). However, in herd FL3 a five year old cow (No. 53) developed acute respiratory distress and was culled without a diagnosis having been made. Despite the marked increase in the prevalence of precipitins that had developed throughout the winter, regular coughing was the only clinical evidence that the animals in herds FL1 and PS1 could have been suffering from a respiratory disorder. None of the farmers complained about the general health or milk production of their cows.

At the second test, the number of coughs was recorded over a ten minute period and quantified per unit of 50 cows (Table 37). There was a very highly significant difference in the prevalence of precipitins between the + group compared with the ++ group and a highly significant difference in the prevalence of precipitins between the ++ group and the +++ group. From Figure 6, it is obvious that there was a close correlation between the frequency of coughing and the mean number of cows with precipitins in each group.

The details of the hay-making, the farmer's assessment of the dustiness and quality of the total crop together with the daily amounts fed per cow are set out in Table 38. Hay had been made from permanent grass (more than six years old) on 11 farms, from temporary leys (less than six years old) on two farms and from both types of grass on the other three farms. The grass had usually been cut during July or at the beginning of August although, on farm PS4 in 1970, the hay had been made in June. On every farm it was attempted to cure the hay in the field and, after a variable amount of mechanical handling, it was baled using a pick-up baler. Although every effort was made to store the crop inside as soon as possible after baling, from 50 to 90 per cent of the bales were said to have been soaked by rain on each of the farms.

The tied cattle ate their hay off troughs on the ground while the 70 loose-housed cows in herd PS3 ate from hay-racks. Hay was given to the dairy cows after milking except on farm PS1 where it was given beforehand.

The daily hay ration was invariably expressed as the number of bales per group of cattle. Therefore, in order to compare the

TABLE 37

The relationship between the frequency of coughing at the second test and the prevalence of precipitating antibodies to *Micropolyspora faeni*.

Frequency of Coughing	Herd	Number of Animals			Confirmed Farmer's Lung in Cattle
		Tested	Positive	% +ve	
+	PS2	43	6	14	Yes
	PS3	93	31	34	Yes
	R1	75	0	0	No
	R3	71	18	25	No
++	FL1	34	26	76	No
	FL2	38	11	29	No
	FL3	82	41	50	No
	PS1	33	10	30	Yes
	PS4	32	8	25	Yes
	PS5	15	8	53	Yes
	R2	51	26	51	Yes
	R4	52	20	38	No
+++	FL4	32	13	41	No
	FL5	79	62	78	Yes
	FL6	75	45	60	Yes
	PS6	26	18	69	Yes

Frequency of Coughing	Total Numbers of Animals			Significant Difference
	Tested	Positive	% +ve	
+	282	55	20)	VHS) HS
++	337	150	45)	
+++	212	138	65)	

\+ = 0-5 coughs in 10 minutes per 50 cows.
++ = 6-10 coughs in 10 minutes per 50 cows.
+++ = 11 or more coughs in 10 minutes per 50 cows.

FIGURE 6 The relationship between the frequency of coughing in the individual herds at the end of the winter housing period and the prevalence of precipitating antibodies to Micropolyspora faeni.

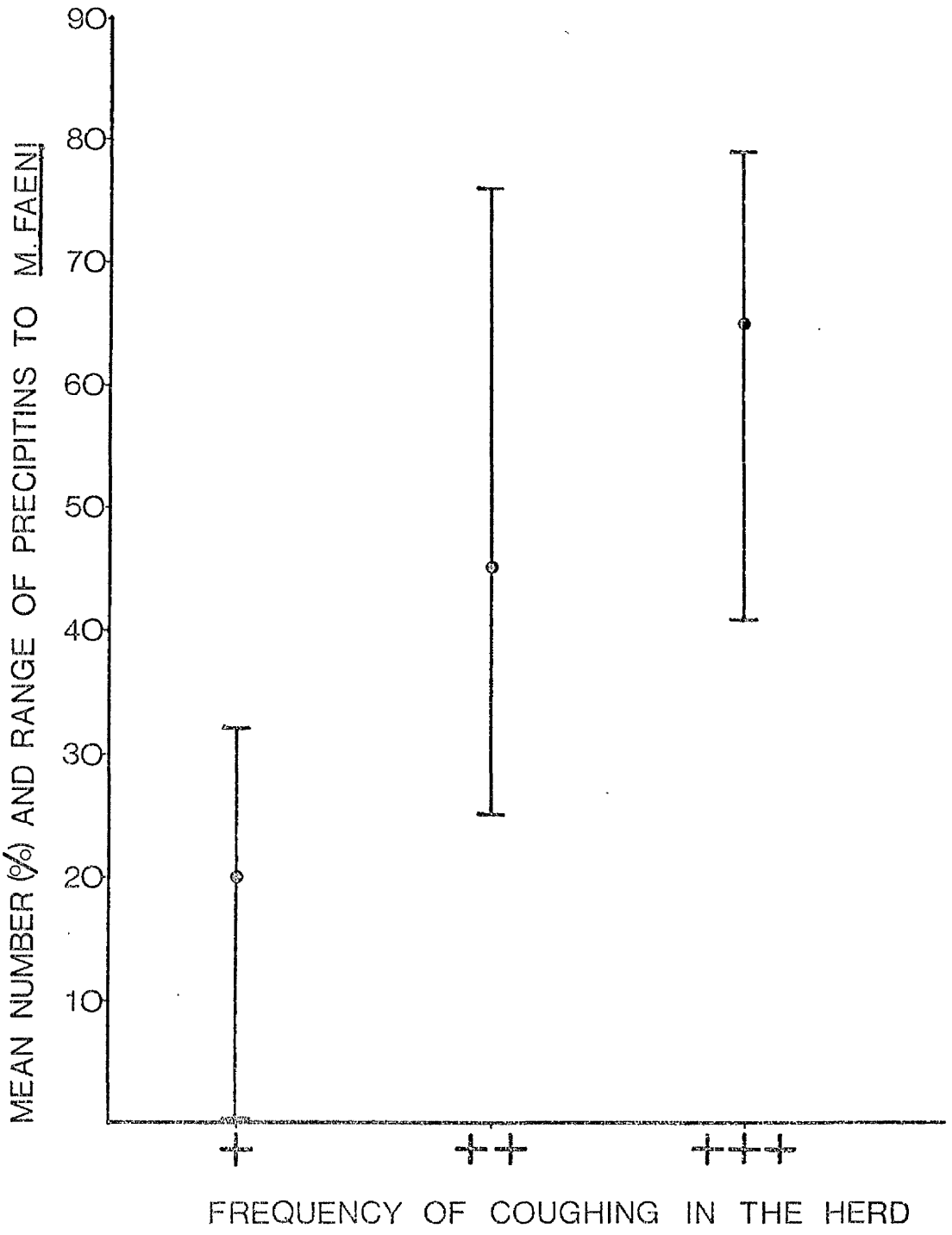


TABLE 38 The details of the hay-making on the individual farms in 1970 and the daily amounts fed per cow.

Herd	Type of Grass	Month when Grass Cut	Farmer's Assessment of		Daily Rate of Feeding		
			Dustiness	Quality	Bales per Group	(per Cow)	lb/Cow +
FL1	Permanent	July/August	Moderate	Fair to poor	3/10 cows	(0.30)	11
FL2	Permanent	July	Moderate	Mixed	2/6 cows	(0.33)	12
FL3	Perm./Temp.	July	Moderate	Mixed	1/5 cows	(0.20)	7*
FL4	Permanent	July/August	Moderate	Mixed	2/6 cows	(0.33)	12
FL5	Permanent	July	None	Good	3/6 cows	(0.50)	19
FL6	Permanent	July/August	Moderate	Fair to poor	30/80 cows	(0.38)	14
PS1	Permanent	July	Slightly	Mixed	2/6 cows	(0.30)	11
PS2 (B)	Permanent	July	Moderate	Mixed	2/4 cows	(0.50)	19
PS3 (B)	Permanent	July	Slightly	Good	18/30 cows	(0.60)	22
PS4	Perm./Temp	June	Slightly	Mixed	2/14 cows	(0.14)	5*
PS5 (B)	Permanent	July/August	Moderate	Fair to poor	3/4 cows	(0.75)	28
PS6	Permanent	July	Moderate	Mixed	2/6 cows	(0.33)	12
R1	Perm./Temp.	July	None	Good	2/6 cows	(0.33)	12
R2	Temporary	July/August	Moderate	Mixed	14/50 cows	(0.28)	10
R3	Permanent	July	Slightly	Good	2/8 cows	(0.25)	9
R4	Temporary	July	Moderate	Mixed	7/50 cows	(0.14)	5*

(B) = Beef farm. * - Silage fed also. + - Assuming mean bale weight of 37 lb. and rounded off to nearest lb.

daily amounts given to the individual animals on the various farms, it was first necessary to find out the average weight of a bale of hay. The mean weight of 100 unselected bales taken from the Glasgow Veterinary School hay shed was found to be 37 $\pm$ 6 lb (Table 39) and so the daily hay rations per cow were calculated assuming that every bale on each farm weighed 37 lb. The smallest amounts were fed to the animals in herds FL3 (7 lb), PS4 (5 lb) and R4 (5 lb) because silage was also made on these farms. The largest amounts were fed to herds FL5 (19 lb), which was a dairy herd, and to PS2 (19 lb), PS3 (22 lb) and PS5 (28 lb) which were all beef herds. On average, beef cattle (23 lb) were offered about twice as much hay as dairy cattle (11 lb).

Since farmer's lung is associated with the feeding of mouldy hay, 42 mouldy bales were also weighed and their mean weight was found to be 42 $\pm$ 5 lb (Table 39). Mouldy hay had been fed on five of the six farms where the farmer was known to have farmer's lung disease and on five of the nine farms where clinical farmer's lung had been confirmed in the cattle (Table 37).

After the owner of herd FL7 (Table 30) contracted farmer's lung, he fed only silage to the milking cows. However, a few acres of hay were still made and given to the heifers and a few "dry" cows which were housed together in a small byre some distance from the main animal accommodation. Precipitins were not detected in any of the cows at the first test but by the end of the winter, one cow had become precipitin-positive although she had never been fed hay. Nonetheless, as a milking cow, she had been given rolled, wet-stored barley twice per day every day during the winter housing period.

The results of the serological examinations at the beginning and at the end of the 1971 grazing season are presented in Table 40. The decrease in the total number of cattle with precipitins from 53 per cent in the spring to 29 per cent in the autumn was very highly significant. The falls in the incidence of precipitins in the "farmer's lung" herds and in the other herds considered as one group were also very highly significant. In five of the eight herds examined, decreases of varying statistical significance occurred in the incidence of precipitins.

Results from the animals that were positively identified are given in Table 41. Since the numbers were much smaller, fewer of the

TABLE 39

The weights of 100 unselected and 42 mouldy bales of hay.

Weight (lb)	Number of Bales		Weight (lb)	Number of Bales	
	Unselected	Mouldy		Unselected	Mouldy
23	1	-	41	4	2
24	1	-	42	1	6
25	1	-	43	4	4
26	-	-	44	4	6
27	1	-	45	-	2
28	-	1	46	-	3
29	2	-	47	1	1
30	1	-	48	1	1
31	1	-	49	-	1
32	6	3		-	-
33	3	-	51	-	1
34	6	1	52	-	-
35	14	-	53	-	-
36	14	-	54	2	1
37	6	1	55	-	-
38	11	2	56	-	-
39	2	4	57	1	-
40	11	2	58	-	-
			59	-	-
			60	-	-
			61	1	-

Type of Bale	Number	Mean Weight (lb)	S.D.	S.E.
Unselected	100	37.42	5.91	0.59
Mouldy	42	41.76	5.16	0.80

TABLE 40

The results of the examination of sera from adult cattle in selected herds for precipitating antibodies to Micropolyspora faeni at the beginning and at the end of the 1971 summer grazing season.

Herd	Spring 1971			Autumn 1971			Significant Change
	No. Animals Tested	No. Animals Positive	% +ve	No. Animals Tested	No. Animals Positive	% +ve	
FL1	34	26	76	37	12	32	S
FL3	82	41	50	82	7	9	VHS
FL5	79	62	78	80	61	76	-
FL8	54	45	83	59	26	44	S
PS1	33	10	30	34	9	26	-
PS6	26	18	69	27	3	11	HS
R1	75	0	0	76	0	0	-
R2	51	26	51	48	9	19	S
Total	434	228	53	443	127	29	VHS
"Farmer's Lung" Herds	249	174	70	258	106	41	VHS
Other Herds	185	54	29	185	21	11	VHS
FL7*	59	1	2	66	0	0	-

* Only silage fed.

TABLE 41 The results of the examination of sera from positively identified, adult cattle in selected herds for precipitating antibodies to Micropolyspora faeni at the beginning and at the end of 1971 summer grazing season.

		Spring, 1971		Autumn, 1971			Change in Precipitin Status					
Herd	No. Animals Tested	No. Animals Positive	% +ve	No. Animals Positive	% +ve	Significant Change	No. Animals Gained	% Gain	Significant Change	No. Animals Lost	% Loss	Significant Change
FL1	20	16	80	7	35	-	0	0	-	9	56	-
FL3	38	20	53	2	5	VHS	0	0	-	18	90	HS
FL5	31	23	74	25	81	-	5	63	S	3	13	-
FL8	43	35	81	23	53	-	0	0	-	12	34	-
PS1	25	8	32	9	36	-	2	12	-	1	13	-
PS6	22	15	68	3	14	S	0	0	-	12	80	S
R1	64	0	0	0	0	-	0	0	-	0	0	-
R2	22	10	45	6	27	-	1	8	-	5	50	-
Total	265	127	48	75	24	HS	8	6	HS	60	47	HS
"Farmer's lung" herds	132	94	71	57	32	S	5	13	-	42	45	HS
Other herds	133	33	25	18	14	-	3	3	-	18	55	S

total changes in incidence achieved statistical significance. Although a number of precipitin-positive cows in every herd except R1 became precipitin-negative during the summer, the change was significant only in FL3 and PS6. Therefore, it was surprising to find that a highly significant number of precipin-negative cattle in herd FL5 had become precipitin-positive during the same period.

The animals that became precipitin-negative during the grazing season have been grouped according to their age in Table 42. Although it was mainly cattle less than six years old that "lost" their precipitins (57%), the correlation with age did not quite achieve statistical significance ($r = -0.79$).

The results of the serological examinations from the herds sampled at the beginning and at the end of the second winter housing period (1971-72) are presented in Table 43. A statistically significant increase in the prevalence of precipitins did not occur in any of the groups studied nor in any of the eight individual herds, although an increase was recorded in five of them. A significant number of positively identified, precipitin-negative animals became precipitin-positive in herds FL1, FL3 and FL8 (Table 44). The total number of precipitin-negative cattle that developed precipitins was also significant as was the change in the "farmer's lung" herds and the other herds grouped separately.

Although not one case of acute respiratory disease was referred from any of these farms during the second winter, several cows in a few herds were noticed to be hyperpnoeic and/or coughing while they were being blood sampled. Six of these animals were later purchased and they have already been discussed as part of the chronic farmer's lung group (Chapter 2, Section II). The farmers were unanimous that the hay was of much better quality and far less dusty than it had been during the first year of this investigation. However, the frequency of coughing in the individual herds was not recorded at the end of the second winter housing period.

Details concerning the rainfall on the individual farms is contained in Appendix 2 as follows: the monthly rainfall during June, July and August, 1970 (Table 1), the monthly rainfall during June, July and August, 1971 (Table 2), the long-term (1941-70) average monthly rainfall during June, July and August (Table 3), the total number of raindays in June, July and August, 1970 (Table 4) and the total number

TABLE 42

The relationship between age and the number of precipitin-positive cattle that became sero-negative for precipitating antibodies to Micropolyspora faeni during the 1971 summer grazing season.

Age (Years)	No. Animals Tested	No. Animals Positive	No. Animals "Lost" Precipitins	% "Lost" Precipitins
2-3 (2.5)*	41	15	7	47
4-5 (4.5)*	88	57	34	60
6-7 (6.5)*	50	39	14	36
8 and above (10.5)*	15	15	4	27

* Ages used in calculating coefficient of correlation.

$r = -0.79$: $y = 62.21 - 3.29x$

where x = age of animal

y = number (%) of animals.

TABLE 43

The results of the examination of sera from hay-fed adult cattle in selected herds for precipitating antibodies to Micropolyspora faeni at the beginning and at the end of the 1971-72 winter housing period.

Herd	First Test			Second Test			Significant Change
	No. Animals Tested	No. Animals Positive	% +ve	No. Animals Tested	No. Animals Positive	% +ve	
FL1	37	12	32	32	21	66	-
FL3	82	7	9	52	6	12	-
FL5	80	61	76	63	48	76	-
FL8	59	26	44	44	33	75	-
PS1	34	9	26	32	2	6	-
PS6	27	3	11	25	3	25	-
R1	76	0	0	72	0	0	-
R2	48	9	19	44	11	25	-
Total	443	127	29	364	124	34	-
"Farmer's Lung" Herds	258	106	41	191	108	57	-
Other Herds	185	21	11	173	16	9	-
FL7*	66	0	0	67	0	0	-

* Only silage fed.

TABLE 44 The results of the examination of sera from positively identified, hay-fed adult cattle in selected herds for precipitating antibodies to Micropolyspora faeni at the beginning and at the end of the 1971-72 winter housing period.

		First Test		Second Test			Change in Precipitin Status					
Herd	No. Animals Tested	No. Animals Positive	% +ve	No. Animals Positive	% +ve	Significant Change	No. Animals Gained	% Gain	Significant Change	No. Animals Lost	% Loss	Significant Change
FL1	23	6	26	15	65	-	9	53	HS	0	0	-
FL3	33	4	12	4	12	-	2	7	-	2	50	-
FL5	51	38	75	39	76	-	5	38	S	4	11	-
FL8	38	17	45	30	79	-	14	67	VHS	1	6	-
PS1	26	6	23	2	8	-	0	0	-	4	67	-
PS6	24	2	8	3	13	-	1	5	-	0	0	-
R1	70	0	0	0	0	-	0	0	-	0	0	-
R2	28	6	21	7	25	-	4	18	-	3	50	-
Total	293	79	27	100	34	-	35	16	VHS	14	18	-
"Farmer's lung" herds	145	65	45	88	61	-	30	38	VHS	7	11	-
Other herds	148	14	10	12	8	-	5	4	S	7	50	-

of raindays in June, July and August, 1971 (Table 5).

In 1970, June was a comparatively dry month on 65 per cent of the farms (Table 45), July was wetter than average on 82 per cent of the farms and August was particularly dry on all 17 farms. In 1971 (Table 45), the rainfall in June was less than average on all eight farms studied, but in July and August 63 per cent and 88 per cent of the farms respectively had a higher than average rainfall. When the figures for June and July were added together, 59 per cent of the farms had less than the average rainfall in 1970 compared with 88 per cent in 1971.

No significant difference was found in 1970 in the mean monthly rainfall on the farms on which slightly mouldy hay compared with moderately mouldy hay had been made (Table 46). In 1971, the hay made on all eight farms was slightly mouldy and, when the 1970 and 1971 results were combined, it was found that there had been significantly less rain in June and in June and July together on the farms that had made slightly mouldy compared with moderately mouldy hay (Table 47). On the other hand, August was significantly wetter on the farms on which slightly mouldy hay had been made.

There was very little difference between the mean number of raindays in 1970 on the farms that had made slightly mouldy compared with moderately mouldy hay (Table 48). When the results for the two years were combined, there were significantly more raindays in July and in June and July together on the farms on which moderately mouldy hay rather than slightly mouldy hay had been made (Table 49). In June and in August slightly mouldy hay would appear to have been made in wetter conditions than the moderately mouldy hay.

Since mouldy hay was the only major source of farmer's lung antigens on these farms, the association between the feeding of mouldy hay and the development of precipitating antibodies to M. faeni was investigated (Table 50). At the end of the 1970 winter housing period, there was a highly significant difference between the prevalence of precipitins in cattle that had been fed slightly mouldy compared with moderately mouldy hay. The difference was highly significant when the 1970 and 1971 results were considered together. There was no significant difference between the two types of hay in the numbers of positively identified, precipitin-negative cattle that developed precipitins during the 1970 winter (Table 51). However, over the

TABLE 45

The difference between the rainfall during the summer months of 1970 and 1971 and the monthly long-term average (1941-70).

	1970				1971			
Herd	June	July	Aug.	June + July	June	July	Aug.	June + July
FL1	-23.9	+25.5	-24.7	+ 1.6	-28.2	-57.0	-44.6	-85.2
FL2	+23.0	+73.5	-39.1	+96.5	-	-	-	-
FL3	-16.1	+10.9	-28.2	- 5.2	-31.9	+16.7	+33.7	+15.2
FL4	-16.1	+10.9	-28.2	- 5.2	-	-	-	-
FL5	-17.9	+ 5.2	-40.3	-12.7	- 8.5	+16.6	+33.5	+ 8.1
FL8	-34.8	+24.8	-46.2	-10.0	-22.7	-32.8	+51.3	-55.5
PS1	-16.1	+10.9	-28.2	- 5.2	-31.9	+16.7	+33.4	-15.2
PS2	+ 0.4	+21.0	-25.9	+21.4	-	-	-	-
PS3	+ 0.4	+21.0	-25.9	+21.4	-	-	-	-
PS4	+ 0.4	+21.0	-25.9	+21.4	-	-	-	-
PS5	+ 0.4	+21.0	-25.9	+21.4	-	-	-	-
PS6	+ 0.4	+21.0	-25.9	+21.4	-13.5	-13.3	+58.2	-26.8
R1	- 5.5	- 2.5	-17.7	- 8.0	-34.0	+25.7	+10.4	- 8.3
R2	-16.1	+10.9	-28.2	- 5.2	-31.9	+16.7	+33.4	-15.2
R3	- 6.0	- 6.4	-23.1	-12.4	-	-	-	-
R4	- 8.1	-15.3	-19.3	-23.4	-	-	-	-

TABLE 46

The relationship between the monthly summer rainfall in 1970 and the mouldiness of the hay.

Mouldiness of Hay	Herd	Total Monthly Rainfall					
		June	July	Aug.	June + July	July + Aug.	June + July + A.
Slightly Mouldy	FL5	40	78	44	118	122	162
	PS1	56	102	81	158	183	239
	PS3	59	94	70	153	164	224
	PS4	59	94	70	153	164	224
	R1	65	83	83	147	166	230
	R3	61	84	80	145	160	221
	Mean	57	89	71	146	160	217
	S.D.	9	9	15	14	20	28
Moderately Mouldy	FL1	67	143	99	210	242	309
	FL2	94	177	73	271	249	343
	FL3	56	102	81	158	183	239
	FL4	56	102	81	158	183	239
	FL6	61	73	51	134	125	185
	FL8	58	130	82	188	212	270
	PS2	59	94	70	153	164	224
	PS5	59	94	70	153	164	224
	PS6	59	94	70	153	164	224
	R2	56	102	81	158	183	239
	R4	71	79	91	150	169	240
	Mean	63	108	77	171	185	249
	S.D.	11	30	13	39	36	44
Significant Difference		-	-	-	-	-	-

TABLE 47

The relationship between the monthly summer rainfall in 1970 and 1971 and the mouldiness of the hay.

Mouldiness of Hay		Rainfall (mm)					
		June	July	Aug.	June + July	July + Aug.	June + July + Au.
Slightly Mouldy	Mean	52	89	107	141	196	248
	S.D.	11	17	40	15	45	42
Moderately Mouldy	Mean	63	108	77	171	185	249
	S.D.	11	30	13	39	36	44
Significant Difference		S	-	S	S	-	-

TABLE 48

The relationship between the number of raindays* in the summer of 1970 and the mouldiness of the hay.

Mouldiness of Hay	Herd	Number of Raindays					
		June	July	Aug.	June + July	July + Aug.	June + July + A.
	PS1	12	23	11	34	34	46
	PS3	9	20	11	29	31	40
	PS4	9	20	11	29	31	40
Slightly	R1	13	22	14	35	36	49
Mouldy	R3	10	19	11	29	30	40
	Mean	10.6	20.8	11.6	31.4	32.4	43
	S.D.	1.8	1.6	1.3	3.2	2.5	4.2
	FL1	9	21	9	30	30	39
	FL3	12	23	11	35	34	46
	FL4	12	23	11	35	34	46
	FL6	12	16	11	28	27	39
	FL8	10	18	12	28	30	40
Moderately	PS2	9	20	11	29	31	40
Mouldy	PS5	9	20	11	29	31	40
	PS6	9	20	11	29	31	40
	R2	12	23	11	35	34	46
	R4	11	24	12	35	36	47
	Mean	10.5	20.8	11.0	31.3	31.8	42.3
	S.D.	1.4	2.5	0.8	3.2	2.7	3.4
Significant Difference		-	-	-	-	-	-

* Rainday is a day when there was more than 0.25 mm (0.01 inches) rain.

TABLE 49

The relationship between the number of raindays in the summers of 1970 and 1971 and the mouldiness of the hay.

Mouldiness of Hay		Number of Raindays					
		June	July	Aug.	June + July	July + Aug.	June + July + Au.
Slightly Mouldy	Mean	12.8	14.8	15.6	27.6	30.4	43.2
	S.D.	2.3	5.0	3.5	3.8	2.3	2.7
Moderately Mouldy	Mean	10.5	20.8	11.0	31.3	31.8	42.3
	S.D.	1.4	2.5	0.8	3.2	2.7	3.4
Significant Difference		S	HS	VHS	S	-	-

TABLE 50

The relationship between the prevalence of precipitating antibodies to Micropolyspora faeni in cattle at the end of the winter housing period and the mouldiness of the hay they were fed.

Slightly Mouldy Hay			Moderately Mouldy Hay			
Herd	No. Animals Tested	No. Animals Positive	Herd	No. Animals Tested	No. Animals Positve	Significant Change
FL5	79	62	FL1	34	26	
PS1	33	10	FL2	38	11	
PS3	93	31	FL3	82	41	
PS4	32	8	FL4	32	13	
R1	75	0	FL6	75	45	
R3	71	18	PS2	43	6	
			PS5	15	8	
			PS6	26	18	
			R2	51	26	
			R4	52	20	
Total	383	129		448	214	
1970-71	383	129		448	214	HS
1971-72	364	124		0	0	
Total	747	253		448	214	HS

TABLE 51

The relationship between the number of precipitin-negative cattle that developed precipitating antibodies to Micropolyspora faeni during the winter housing period and the mouldiness of the hay they were fed.

Slightly Mouldy Hay				Moderately Mouldy Hay				
Herd	No. Animals Tested	No. Animals Negative	No. Animals Gained	Herd	No. Animals Tested	No. Animals Negative	No. Animals Gained	Significant Change
FL5	51	31	23	FL1	29	26	19	
PS1	26	26	9	FL2	17	13	3	
PS3	82	66	16	FL3	57	43	22	
PS4	15	9	1	FL4	24	13	3	
				PS2	20	17	1	
				PS5	15	8	2	
				PS6	22	12	7	
Total	174	132	49		184	132	57	
1970-71	174	132	49		184	132	57	-
1971-72	293	214	35		-	-	-	
Total	467	346	84		184	132	57	HS

two winter housing periods, significantly more precipitin-negative cattle developed precipitins when fed moderately mouldy hay compared with slightly mouldy hay.

There was an association between the frequency of coughing at the second test in 1970 and the mouldiness of the hay fed (Table 52). Slightly mouldy hay had been fed to 75 per cent of the + coughing herds, to 25 per cent of the ++ coughing herds and to 20 per cent of the herds in which there was frequent coughing (+++). In the cattle, farmer's lung had been confirmed more often in the coughing herds that had been fed moderately mouldy hay in 1970-71. Only one of the farmers with confirmed farmer's lung (FL5) had fed slightly mouldy hay and his cows were coughing frequently. In addition to the mouldiness, the amount of hay fed might also have affected the development of precipitins to M. faeni. A significant correlation was not established between the amount of slightly mouldy or moderately mouldy hay fed and either the incidence of precipitins at the second test or the number of positively identified, precipitin-negative animals that became precipitin-positive during the winter housing period (Table 53).

It has already been established that there was a close association between the frequency of coughing at the second test in 1970-71 and the prevalence of precipitins (Table 37). Although there was a significant difference between the + and ++ groups in the number of positively identified, precipitin-negative animals that developed precipitins during the winter, the difference between the ++ and the +++ groups was not significant (Table 54).

The prevalence of precipitins in herds in which farmer's lung had been confirmed in the cattle was significantly greater at the end of the 1970-71 winter than the prevalence in herds in which farmer's lung had not been confirmed (Table 55). However, significantly less positively identified, precipitin-negative animals developed precipitins in the herds in which farmer's lung had been confirmed than in the other herds (Table 56).

Significant correlations were established between the number of raindays in July and in June and July together and the number of precipitin-negative cattle that developed precipitins during the winters of 1970-71 and 1971-72 (Table 57). No significant correlations were present between the monthly rainfall and either the incidence of

TABLE 52

The relationship between the frequency of coughing and the presence of confirmed farmer's lung in cattle during the winter of 1970-71 and the mouldiness of the hay they were fed.

	Slightly Mouldy Hay		Moderately Mouldy Hay	
Frequency of Coughing	Farmer's Lung Confirmed	Farmer's Lung Not Confirmed	Farmer's Lung Confirmed	Farmer's Lung Not Confirmed
+	PS3	R1 R3	PS2	
++	PS1 PS4		PS5 R2	FL1 FL2 FL3 R4
+++	FL5		FL6 FL8 PS6	FL4

TABLE 53 The relationships between the amount of slightly and moderately mouldy hay fed, the prevalence of precipitating antibodies to Micropolyspora faeni at the end of the winter housing period and the number of precipitin-negative animals that developed precipitins during the winter housing period.

	Slightly Mouldy Hay				Moderately Mouldy Hay		
Herd (1970-71)	Amount Hay Fed (lb)	Total Precipitins (%)	Gained (%)	Herd (1970-71)	Amount Hay Fed (lb)	Total Precipitins (%)	Gained (%)
FL5	19	78	74	FL1	11	76	73
PS1	11	30	35	FL2	12	29	23
PS3	22	34	24	FL3	7	50	51
PS4	5	25	11	FL4	12	41	23
R1	12	0	-	FL6	14	60	-
R3	9	25	-	PS2	19	14	6
				PS5	28	53	25
				PS6	12	69	58
				R2	10	51	-
				R4	5	38	-
(1971-72)							
FL5	19	76	38				
PS1	11	8	0				
R1	12	0	0				

TABLE 53 (Cont'd.)

(1) The correlation between the amount of slightly mouldy hay fed in 1970-71 and the prevalence of precipitins at the second test.

$r = +0.51$. $y = 5.36 + 2.05x$.

(2) The correlation between the amount of slightly mouldy hay fed in 1970-71 and 1971-72 and the prevalence of precipitins at the second test.

$r = +0.60$. $y = -11.32 + 3.15x$

(3) The correlation between the amount of slightly mouldy hay fed in 1970-71 and the number of animals that developed precipitins during the winter housing period.

$r = +0.51$. $y = 10.33 + 1.80x$.

(4) The correlation between the amount of slightly mouldy hay fed in 1970-71 and 1971-72 and the number of animals that developed precipitins during the winter housing periods.

$r = +0.55$. $y = 8.04 + 2.41x$.

(5) The correlation between the amount of moderately mouldy hay fed in 1970-71 and the prevalence of precipitins at the second test.

$r = -0.10$. $y = 51.85 - 0.29x$.

(6) The correlation between the amount of moderately mouldy hay fed in 1970-71 and the number of animals that developed precipitins during the winter housing period.

$r = -0.52$. $y = 62.65 - 1.78x$.

where x = amount of hay fed

y = number (%) of animals with precipitins.

TABLE 54

The relationship between the frequency of coughing at the second test and the number of precipitin-negative animals that developed precipitating antibodies to Micropolyspora faeni during the winter housing period of 1970-71.

Frequency of Coughing	Herd	Number of Animals		
		Tested	Negative	Developed Precipitins
+	PS2	20	17	1
	PS3	82	66	16
++	FL1	29	26	19
	FL2	17	13	3
	FL3	57	43	22
	PS1	26	26	9
	PS4	15	9	1
	PS5	15	8	2
+++	FL4	24	13	3
	FL5	51	31	23
	PS6	22	12	7

Totals	Significant Change	No. Tested	No. Negative	No. Developed
+	S	102	83	17
++	-	159	125	56
+++		97	56	33

TABLE 55

The relationship between the presence of confirmed farmer's lung in cattle and the prevalence of precipitating antibodies to Micropolyspora faeni at the second test n 1970-71.

Farmer's Lung Confirmed			Farmer's Lung not Confirmed			
Herd	No. Animals Tested	No. Animals Positive	Herd	No. Animals Tested	No. Animals Positive	Significant Change
FL5	79	62	FL1	34	26	
FL6	75	45	FL2	38	11	
PS1	33	10	FL3	82	41	
PS2	43	6	FL4	32	13	
PS3	93	31	R1	75	0	
PS4	32	8	R3	71	18	
PS5	15	8	R4	52	20	
PS6	26	18				
R2	51	26				
Total	447	214		384	129	HS

TABLE 56

The relationship between the presence of confirmed farmer's lung in cattle and the number of animals that developed precipitating antibodies to Micropolyspora faeni during the winter housing period (1970-71).

Farmer's Lung Confirmed			Farmer's Lung not Confirmed			
Herd	No. Animals Negative	No. Animals Developed Precipitins	Herd	No. Animals Negative	No. Animals Developed Precipitins	Significant Change
FL5	31	23	FL1	26	19	
PS1	26	9	FL2	13	13	
PS2	17	1	FL3	43	22	
PS3	66	16	FL4	13	3	
PS4	9	1				
PS5	8	2				
PS6	12	7				
Total	169	59		95	57	S

TABLE 57

The relationship between the number of raindays per month and the prevalence of precipitating antibodies to Micropolyspora faeni at the end of the winter housing periods (1970-71 and 1971-72) and the number of precipitin-negative cattle that developed precipitins during the winter.

1970-71	No. Raindays per Month			Incidence of	No. Animals Gained
Herd	June	July	June + July	Precipitins (%)	Precipitins (%)
FL1	9	21	30	76	73
FL2	-	-	-	29	23
FL3	12	23	35	50	51
FL4	12	23	35	41	23
FL5	-	-	-	78	74
FL6	12	16	28	60	-
FL8	10	18	28	83	-
PS1	12	23	35	30	9
PS2	9	20	29	14	1
PS3	9	20	29	34	16
PS4	9	20	29	25	1
PS5	9	20	29	53	2
PS6	9	20	29	69	7
R1	13	22	35	0	-
R2	12	23	35	51	-
R3	10	19	29	25	-
R4	11	24	35	38	-
1971-72					
FL1	14	12	26	66	9
FL3	15	11	26	12	2
FL5	14	11	25	76	5
FL8	16	11	27	75	14
PS1	15	11	26	6	0
PS6	12	10	22	25	1
R1	13!	11	24	0	0
R2	15	11	26	25	4

(1) The relationship between the number of raindays in June, 1970 and 1971 and the prevalence of precipitating antibodies to Micropolyspora faeni at the end of the winter housing periods of 1970-71 and 1971-72.
$r = -0.15$. $y = 60.26 - 1.66x$.

(2) The relationship between the number of raindays in June, 1970 and 1971 and the number of precipitin-negative animals that developed precipitins during the winter housing periods of 1970-71 and 1971-72.
$r = -0.24$. $y = 33.39 + 0.44x$.

(3) The relationship between the number of raindays in July, 1970 and 1971 and the prevalence of precipitating antibodies to Micropolyspora faeni at the end of the winter housing periods of 1970-71 and 1971-72.
$r = +0.09$. $y = 33.39 + 0.44x$.

(4) The relationship between the number of raindays in July, 1970 and 1971 and the number of precipitin-negative animals that developed precipitins during the winter housing periods of 1970-71 and 1971-72.
$r = +0.47$. $y = -16.49 + 1.79x$. (S)

(5) The relationship between the combined number of raindays in June and July, 1970 and 1971 and the prevalence of precipitating antibodies to Micropolyspora faeni at the end of the winter housing periods of 1970-71 and 1971-72.
$r = +0.01$. $y = 37.76 + 0.10x$.

(6) The relationship between the combined number of raindays in June and July, 1970 and 1971 and the number of precipitin-negative animals that developed precipitins during the winter housing periods of 1970-71 and 1971-72.
$r = +0.50$. $y = -62.01 + 2.64x$. (S)

where x = number of raindays
y = incidence of precipitins or number of animals that developed precipitins.

precipitins at the end of the winter or the numbers of precipitin-negative cattle that developed precipitins throughout the winter (Table 58).

Although there was a very highly significant relationship between the number of raindays and the total rainfall per month, there was great variation in the amount of rain that actually fell per day (Table 59).

DISCUSSION

Most of the herds involved in this study were selected because the farmers suffered from farmer's lung or because precipitating antibodies to M. faeni had been detected in the serum of a cow with respiratory disease. With one exception (FL7), hay was fed to every herd and for this reason alone the "random" herds were selected. There was a close association between the number of cattle with precipitins to M. faeni at the end of winter and the mouldiness of the hay that had been fed. Throughout the winter housing period, significantly more precipitin-negative cattle developed precipitins in herds that had been fed moderately mouldy compared with slightly mouldy hay. Consequently, at the end of winter, the total prevalence of precipitins was significantly greater in the cattle that had been fed moderately mouldy compared with slightly mouldy hay. However, there was no difference in the prevalence of precipitins at the second test between the three herds that were fed both hay and silage and the other herds. This confirms that the mouldiness of the hay is the most important factor in determining whether or not cattle will develop precipitins to M. faeni and, under farm conditions, that the amount of hay fed is of minor importance.

It is very likely that the farmers who suffered from farmer's lung had developed the disease because they had made mouldy hay more often than the other farmers. Therefore, it was not surprising to find that, at the beginning of both winter housing periods, the prevalence of precipitins to M. faeni was significantly higher in the "farmer's lung" herds than in the "positive sample" herds. When the farmers were asked for their assessment of the mouldiness of their 1970-71 hay crop, 83 per cent of the "farmer's lung" herds had been fed moderately mouldy hay compared with only 50 per cent of both the

TABLE 58

The relationship between the monthly rainfall (mm) and the prevalence of precipitating antibodies to Micropolyspora faeni at the end of the winter housing periods (1970-71 and 1971-72) and the number of precipitin-negative cattle that developed precipitins during the winter.

1970-71	Monthly Rainfall		Incidence of	No. Animals
Herd	June	June + July	Precipitins (%)	Gained Preciptins (%)
FL1	67	210	76	73
FL2	94	271	29	23
FL3	56	158	50	51
FL4	56	158	41	23
FL5	40	118	78	74
FL6	61	134	60	-
FL8	58	188	83	-
PS1	56	158	30	9
PS2	59	153	14	1
PS3	59	153	34	16
PS4	59	153	25	1
PS5	59	153	53	2
PS6	59	153	69	7
R1	65	147	0	-
R2	56	158	51	-
R3	61	145	25	-
R4	71	150	38	-
1971-72				
FL1	63	123	66	9
FL3	40	148	12	2
FL5	50	139	76	5
FL8	70	143	75	14
PS1	40	148	6	0
PS6	46	105	25	1
R1	36	147	0	0
R2	40	148	25	4

(1) The relationship between the rainfall in June, 1970 and 1971 and the prevalence of precipitating antibodies to Micropolyspora faeni at the end of the winter housing period of 1970-71 and 1971-72.
$r = +0.21$. $y = 16.02 + 0.43x$.

(2) The relationship between the rainfall in June, 1970 and 1971 and the number of precipitin-negative animals that developed precipitins during the winter housing periods of 1970-71 and 1971-72.
$r = +0.16$. $y = 1.24 + 0.28x$.

(3) The relationship between the combined rainfall in June and July, 1970 and 1971, and the prevalence of precipitating antibodies to Micropolyspora faeni at the end of the winter housing periods of 1970-71 and 1971-72.
$r = +0.03$. $y = 37.58 + 0.03x$.

(4) The relationship between the combined rainfall in June and July, 1970 and 1971, and the number of precipitin-negative animals that developed precipitins during the winter housing periods of 1970-71 and 1971-72.
$r = +0.24$. $y = -8.77 + 0.16x$.

where x = monthly rainfall
y = incidence of precipitins or number of animals that developed precipitins.

TABLE 59

The relationship between the monthly rainfall and the number of raindays per month on 17 farms.

Monthly No. of Raindays	Monthly Rainfall (mm)
9	59.1: 59.4: 59.4: 59.4: 59.4: 67.1: 99.3.
10	58.2: 61.0.
11	51.1: 70.1: 70.1: 70.1: 70.1: 70.1: 75.9: 80.8: 80.8: 80.8: 80.8.
12	55.9: 55.9: 55.9: 55.9: 60.7: 81.8: 90.7.
13	64.5.
14	83.3.
16	73.5.
18	129.8.
19	83.6.
20	94.0: 94.0: 94.0: 94.0: 94.0.
21	142.5.
22	82.5
23	101.9: 101.9: 101.9: 101.9.
24	78.7.

$r = +0.69$. $y = 39.83 + 2.72x$. VHS

where x = number of raindays per month

y = monthly rainfall (mm).

"positive sample" and the "random" herds. Significantly more precipitin-negative cattle developed precipitins during the winter in the "farmer's lung" than in the "positive sample" herds. Consequently, by the end of the winter, the prevalence of precipitins in the "farmer's lung" herds was significantly greater than in either the "positive sample" or the "random" herds. However, there was no significant difference between the number of cattle with precipitins in the "positive sample" herds compared with the "random" herds at that time.

From the above findings it can be deduced that regular exposure to mouldy hay dust had a cumulative effect. This was substantiated by the good positive correlation between the prevalence of precipitins to M. faeni and the age of the animals sampled. In a previous, much smaller survey, Harbourne and others (1970) had failed to find any relationship between the prevalence of precipitins and the age of cattle sampled.

It is interesting that, during both winter housing periods, about 20 per cent of the cattle that had been precipitin-positive at the first test were precipitin-negative at the second. In some of these cows, the titre of precipitating antibody may have dropped below the minimal level of detection by the double diffusion test because these cows were approaching parturition. For a period of several weeks before and after parturition in the cow, there is a hypogammaglobulinaemia which results from the concentration of maternal antibodies into the colostrum (33, 61). On the other hand, it is also possible that somehow or other, these animals had inhaled insignificant amounts of M. faeni antigens. This may have been because they had been housed in buildings away from the other cows particularly when they were not lactating. Consequently, their exposure to mouldy hay dust could have been less than that of the milking cows. Against this, "dry" cows were deliberately fed the dustiest hay on virtually all the farms.

A high incidence of precipitins at the second test not only reflected the mouldiness of the hay that had been fed during that winter but was also closely associated with the frequency of coughing in the herd. An exception was herd FL1 in which precipitins were present in 76 per cent of the cows and yet frequent coughing was not heard. Although the amount and duration of exposure to M. faeni had been sufficient for precipitins to develop in a large proportion

of the precipitin-negative animals during the winter (67%), presumably it had not been sufficient for signs of clinical disease to become obvious. Nonetheless, the farmer himself experienced a severe relapse of acute farmer's lung in February, 1971 and was hospitalised for several weeks.

No acute clinical cases of farmer's lung developed during the two winter housing periods of this study but several cows were seen to be hyperpnoeic, tachypnoeic and/or coughing at the time the blood samples were being taken. Some of these animals were subsequently shown to be suffering from chronic farmer's lung (Chapter 2, Section II). The first confirmed case of farmer's lung in cattle (207) arose in herd PS4 during the winter prior to the commencement of this investigation and yet, at the first test, the prevalence of precipitins was only 39 per cent. This apparent anomoly can be explained by the fact that this was a "flying" herd and so many of the milking companions of that first case had been sold.

Hay was the only possible source of M. faeni antigens on every farm except FL7 and FL5 on which barley could also have been involved. Despite the milking cows in herd FL7 being fed only silage, a single cow did develop precipitins. However, she had been fed rolled, wet-stored barley twice daily. The farmer said that, if he did not wear a mask, he experienced a recurrence of some of his previous symptoms (headaches, sweating and a "tightness across the chest") several hours after he had worked with barley that had lain for four to six days after it had been rolled. On this farm barley was confirmed as the source of the M. faeni. In contrast, the owner of herd FL5 suffered no adverse clinical reaction after he had fed his cows rolled, wet-stored barley and so a significant amount of M. faeni antigens were unlikely to have been present on his grain. In the past, working with mouldy grain has often been held responsible for the development of farmer's lung in man (250, 258). Recent evidence would suggest that M. faeni may not provide the allergens that cause this form of the disease at the present time because precipitins to M. faeni were not detected in the sera from four grain-induced cases (112).

Just as exposure to mouldy hay dust during the winter resulted in a significant increase in the number of cattle with precipitins to M. faeni so the lack of exposure during the summer resulted in a significant decrease in the prevalence of precipitins.

This decrease was greatest in the youngest age group but the relationship between age and the number of animals that "lost" precipitins was not quite statistically significant. The precipitin-positive younger cattle had relatively low precipitin titres which had become undetectable by the end of the summer whereas the older cows had higher precipitin titres which persisted throughout the grazing period (57). Therefore, the precipitins that can be detected at the beginning of a winter housing period have almost certainly resulted from exposure to mouldy hay during the previous winter.

Although a statistically significant decrease in the prevalence of precipitin-positive animals had occurred in two herds during the summer, a significant increase in the number of precipitin-positive animals had occurred in herd FL5. This was due to the cows having been fed hay while they were housed only at night for two to three weeks. The farmer considered that the cows had been housed for the winter when they did not go outside at all and it was after this that their precipitin status was assessed at the first test.

Farmer's lung in man is most common in the western, upland parts of Britain (250) where hay can be dried adequately under field conditions about one year in every four (215). Consequently, it has been stated that the incidence of farmer's lung in man during the winter is related directly to the amount of rainfall the previous summer (89, 250, 286). The assumption that an apparently "wet" summer invariably results in the making of mouldy hay throughout the whole country is a gross over simplification because only the rain that falls while the hay is actually being made directly affects the mouldiness of the crop. The hay-making season varies greatly from area to area and extends from June in southern England to late August in some parts of western Scotland. During the two years of this study the total rainfall and number of raindays in July were found to be closely associated with the mouldiness of the hay. This was to be expected since almost all the hay had been made in July. It was also found that there had been significantly more rain during June and August on the farms on which slightly mouldy hay had been made compared with the farms on which moderately mouldy hay had been made. This supports the view that summer monthly rainfall figures can be misleading unless the specific time that the hay had been made within a particular area is also known.

The total monthly rainfall is likely to be of less importance than the number of raindays in affecting the mouldiness of the hay because a small amount of rain halts hay-making as effectively as a thunder storm. The frequency of the raindays is also important since eight to ten successive dry days is sufficient for hay to dry in the field. The subsequent rainfall, even if it were to be ten times the average, would not then affect the probability of the hay becoming mouldy. Nevertheless, the large number of clinical cases of bovine farmer's lung that were diagnosed during the 1974-75 winter does confirm that a very high regular rainfall during the summer does significantly influence the incidence of farmer's lung in cattle the following winter.

In many instances, the moisture which initiates heating and moulding will not have come from the clouds but from the cell sap within the grass. It is the forecast of rain that so often pressurises a farmer into baling hay while the moisture is still above 25 per cent. However, it is preferable to bale hay too early even though it does become mouldy, because cattle will eat mouldy hay but they will totally reject baled rotten grass.

The examination of climatic data, either nationwide or local, ignores completely the important role that the individual farmer has in the making of mouldy hay. At the end of two successive winter housing periods not one of 70 cows in herd R1 had precipitins to M. faeni in its sera whereas over 50 per cent of the cows in many other herds in the same area had precipitins in their sera. In complete contrast, some farmers in the west of Scotland still managed to make mouldy hay during the summers of 1975 and 1976 when virtually no rain fell for ten consecutive weeks (292).

The amount of rain that falls during the hay-making season largely determines the mouldiness of the hay crop and this in turn determines the proportion of cattle which develop precipitins to M. faeni during the winter housing period. The longer the period which cows are continually exposed to M. faeni, the higher will be the prevalence of precipitins, the more frequent will be the coughing and eventually, clinical cases of farmer's lung will develop. However, a high prevalence of precipitins to M. faeni in a herd confirms that the cattle have been fed mouldy hay for several months but does not confirm, only suggests strongly, that a number of the cows could be suffering from farmer's lung disease.

CHAPTER 4

THE DIAGNOSIS OF FARMER'S LUNG IN CATTLE

Crofton and Douglas (1969) have stated that "the diagnosis of farmer's lung depends on clinical history, clinical examination, x-ray appearance, lung function tests and serological tests". The disease in cattle is diagnosed in a similar manner although the individual diagnostic procedures vary in their usefulness. Since positive patient participation is required during most of the tests of lung function, it has not been possible to use these procedures during the investigation of the bovine disease. On the other hand, individual cases of farmer's lung in cattle can be bought and a full post-mortem examination undertaken. In this way, a complete range of pathological lesions can be itemised and an excellent correlation achieved between the extent of these lesions and the severity of the clinical signs.

The diagnosis of farmer's lung in cattle will be discussed in the light of experience gained during the investigation of the 45 cases discussed in Chapter 2 and with specific reference to the use of:

(i) Clinical history and clinical examination
(ii) Serology
(iii) Radiology
(iv) Skin testing
(v) Pathology.

SECTION I

THE USE OF CLINICAL HISTORY AND CLINICAL EXAMINATION IN THE DIAGNOSIS OF FARMER'S LUNG IN CATTLE

INTRODUCTION

The diagnosis of disease often depends as much upon the clinical history of the case as upon the abnormalities detected during a detailed clinical examination. When considering the differential diagnosis of respiratory disease in adult cattle, it is important to consider whether or not the condition has developed suddenly or insidiously, whether the animals are housed or grazing and whether an individual animal or group of animals is affected.

DISCUSSION

In this study, farmer's lung was only confirmed in cattle from the western, mainly upland areas of this country. This does not mean that the disease does not occur elsewhere, only that it has not yet been reported. From the fact that the youngest confirmed case developed towards the end of the its second winter inside together with the findings of previous investigations into respiratory diseases of immature cattle (292), it can be deduced that farmer's lung does not affect young cattle. The source of the farmer's lung antigens was almost invariably mouldy hay although mouldy rolled barley was considered to have been responsible for one cow becoming sensitised to M. faeni. Therefore, for clinical farmer's lung to develop, affected animals will almost certainly need to have been fed mouldy hay during two winter housing periods. Although farmer's lung is typically a disease of housed cattle, some long-standing severe cases may first be seen to be ill only after they have developed exercise intolerance when, at the beginning of the grazing season, they suddenly have to undertake a long walk to and from the milking parlour twice daily.

Acute farmer's lung has only been confirmed in single animals in a herd at any one time in contrast to the chronic form which can present either as a single animal or as a group disease.

The clinical signs of acute farmer's lung and those of other

common sudden onset respiratory conditions are presented in Table 60. Irrespective of the specific disorder, cattle affected with acute respiratory disease are anorexic, and if lactating, there is an abrupt decrease in their milk production. The most common causes of acute respiratory disease in housed adult cattle are bacterial bronchopneumonia and farmer's lung. With the former disease, there is obvious dullness and evidence of toxaemia but respiratory distress does not usually develop until the terminal stages. On the other hand, cases of acute farmer's lung are alert even although they are severely dyspnoeic. A degree of thoracic pain can usually be detected with acute bacterial bronchopneumonia but thoracic percussion is not resented with acute farmer's lung. Pyrexia, which is present in virtually every case of acute bronchopneumonia, will not be detected as often with acute farmer's lung. Occasional coughing, tachypnoea and, in some cases, fine crackles antero-ventrally are findings common to both conditions. The rate of recovery following appropriate therapy is likely to be different in that most cases of farmer's lung were said by the owner to be "normal" within 24-48 hours, whereas clinical recovery from an acute bacterial pneumonic episode can take up to one week and even then complete recovery may not have taken place.

In a small number of cases, there is severe dullness of sudden onset, anorexia, agalactia, marked thoracic pain, pyrexia (up to 107°F) and infrequent soft coughing. At necropsy, these cases have usually been found to be suffering from a necrotising bronchopneumonia. It has been stated that pneumonic pasteurellosis (264) presents in a similar manner.

Toxaemia is absent from animals with milk allergy and lung tumours. Milk allergy, which has been shown to be a type I hypersensitivity reaction mainly to alpha-casein (42), can affect susceptible heifers and cows at any time during their lactation if milking has been delayed for any reason. As well as their being dyspnoeic, affected animals dribble saliva and urine and develop generalised urticaria. Soon after the onset of milking there is an obvious decrease in the severity of the clinical signs. Within the last six years, the one case of pulmonary neoplasia that presented with acute respiratory distress was diagnosed at necropsy.

It is more difficult to differentiate between chronic farmer's lung and chronic suppurative pneumonia (Table 61) than it is to differentiate between their respective acute forms.

TABLE 60 The differentiation of acute farmer's lung from other causes of acute respiratory disease in housed adult cattle.

Clinical Signs	Acute Farmer's Lung	Acute Bronchopneumonia	Pneumonic Pasteurellosis	Necrotising Bronchopneumonia	Milk Allergy	Lung Tumour
Dyspnoea	++	-	-	-	++	±
Hyperpnoea	++	±	-	-	++	++
Coughing	+	±	±	±	+	±
Tachypnoea	++	++	++	++	++	++
Thoracic Pain	-	++	+++	+++	-	-
Adventitious Lung Sounds - crackles	+	±	±	±	+	-
- rhonchi	-	-	-	-	-	-
Dullness	±	++	+++	+++	±	±
Pyrexia	+	+++	+++	+++	-	-
Particular Features	Fed mouldy hay	-	Associated with movement	Halitosis	Follows hefting. Urticaria. Dribbles urine.	-

±)
\+)
++) indicates frequency of occurrence of clinical sign.
+++)

TABLE 61 The differentiation of chronic farmer's lung from other causes of chronic respiratory disease in housed adult cattle.

Clinical Signs	Chronic Farmer's Lung	Chronic Suppurative Pneumonia	Embolic Pneumonia	Lung Tumour	Tuberculosis	Parasitic Bronchitis Patent	Parasitic Bronchitis Reinfection
Dyspnoea	-	-	-	-	-	-	-
Hyperpnoea	++	+	+	±	++	++	++
Coughing	++	+	+	±	+	++	+++
Tachypnoea	++	+	+	±	++	++	+++
Thoracic Pain	-	+	++	-	+	-	-
Adventitious Lung Sounds - crackles	+	±	-	-	+	++	-
- rhonchi	+	±	+	-	+	++	-
Dullness	-	+	++	±	+	±	-
Pyrexia	-	±	+	-	±	-	-
Particular Features	Fed mouldy hay. Weight loss.	Previous acute episodes	Posterior vena cava thrombosis.	Loss of thoracic resonance.	Diagnosis at necropsy.	Exposed to massive infection. Husk in calves.	

±) +) ++) +++) indicates frequency of occurrence of clinical sign.

This is due to the great variation in the range of clinical signs in both chronic disorders and also because one animal can be affected with both conditions simultaneously. Cases of chronic farmer's lung generally cough much more frequently, are more hyperpneoic and more tachypnoeic than animals suffering from chronic suppurative pneumonia. In addition, most cases of chronic suppurative pneumonia are slightly or moderately dull, they usually resent thoracic percussion and their rectal temperature is often slightly elevated. With embolic pneumonia, which is a more severe condition than either chronic farmer's lung or chronic suppurative pneumonia, there may be a history of relapsing acute pneumonic episodes or evidence of co-existing suppurative disease such as arthritis, mastitis or metritis. Thoracic pain is frequently one of the major presenting signs of this condition. The source of the pulmonary emboli is usually a thrombus in the posterior vena cava and such cases almost invariably develop haemoptysis terminally (235).

During the six years of the respiratory disease survey, tuberculosis was suspected once at necropsy and confirmed after bacteriological and microscopical examination of the lesions. The clinical signs were typical of a chronic suppurative pneumonia apart from the fact that there appeared to be an excessive amount of thoracic pain.

A lung tumour that was causing chronic respiratory disease was diagnosed when a large area of decreased thoracic resonance was detected during a routine physical examination. Pulmonary neoplasia is usually found during routine post-mortem examination.

Parasitic bronchitis has been included in Table 61 as both the patent and the re-infection forms can affect housed individual animals. However, after a detailed history has been obtained, there should be little difficulty in differentiating between farmer's lung and parasitic bronchitis. With the latter condition, the coughing is much more frequent, often being paroxysmal, and the tachypnoea more severe than with the former condition (292).

The chronic form of farmer's lung has been confirmed as affecting several dairy animals in the same herd simultaneously. The only other disease that has been reported as producing a similar syndrome (tachypnoea, hyperpnoea, frequent coughing, weight loss and decreased milk production) in Britain is one of the forms of parasitic

bronchitis (128, 130, 168, 237). The re-infection syndrome has been encountered more often in this area than the patent disease but both forms have invariably occurred in the autumn. Therefore, when a respiratory syndrome characterised by tachypnoea, hyperpnoea, frequent coughing, weight loss and decreased milk production occurs in the autumn the cause will be parasitic bronchitis and when the syndrome occurs in the spring in housed cattle, it will be farmer's lung.

The only occasion when these two conditions are likely to be confused is in the early winter when the respiratory signs are noticed only after the cows are housed, such as happened with herd 4 (Chapter 2, Section 1). Parasitic bronchitis must be the obvious diagnosis but for adult cattle to develop obvious clinical signs of disease they must be subjected to a massive larval challenge. In practice, this means that affected cows must have been grazing on fields which had been grazed previously by young stock suffering from clinical parasitic bronchitis. The absence of this type of history means that parasitic bronchitis is extremely unlikely although it should not be ruled out entirely. Farmer's lung may be suspected only if very mouldy hay is being fed and most of the affected animals are more than six years old.

In order to diagnose a particular disease, the clinician must first be aware that it has been reported and secondly, be familiar with the major if not the full range of clinical signs. Farmer's lung should be suspected if mouldy hay is being fed to housed adult cattle which are suffering from obvious respiratory disease, although a thorough clinical examination of affected individuals is still desirable to eliminate the possibility of other disorders.

SECTION II

THE USE OF SEROLOGY IN THE DIAGNOSIS OF FARMER'S LUNG IN CATTLE

INTRODUCTION

The presence of precipitating antibodies against "farmer's lung hay" antigens in the sera of patients with farmer's lung was the first laboratory evidence that this was a hypersensitivity disease (142, 201). When human volunteers inhaled mouldy hay dust, extracts of mouldy hay or extracts of M. faeni, only those with serum precipitins developed clinical symptoms similar to farmer's lung (16, 199, 287). These findings indicated that precipitins against "farmer's lung hay" antigens were closely associated with the clinical disease. That the results of precipitation tests should be interpreted with caution was stressed by Parish (1963) who stated that the presence of precipitating antibodies might only be an indication of exposure to "farmer's lung hay" antigens and that they might not be necessary for the development of clinical disease. As a result of more recent work, it is generally accepted that precipitins to M. faeni confirm exposure to the organism but do not confirm the presence of clinical farmer's lung in man (102, 109, 111, 198).

In an effort to improve upon the efficiency of the double diffusion precipitation test, immuno-electrophoresis (198), latex agglutination (175), complement fixation (211), immuno-osmophoresis (127) and a fluorescent antibody test (194) have all been developed. However, none would appear to hold any significant advantage over the double diffusion test with the possible exception of the fluorescent antibody technique which was not only more sensitive but also gave some indication as to the antibody titre.

DISCUSSION

When the survey of acute respiratory disease in adult cattle began in 1969, it was decided to use the double diffusion precipitation test in agar gel for the detection of serum precipitating antibody to M. faeni because the test procedure was simple, the results were easy to interpret and large numbers of sera could be examined simultaneously. Initially, a comparison was made between the macro-technique and the

micro-technique and it was found that a positive precipitation reaction was detected in about twice as many sera with the former technique compared with the latter (59). Consequently, the conventional macro-technique of double diffusion was adopted for all routine serological investigations.

Since farmer's lung in cattle can present as either a herd disease (Chapter 2, Section I) or an individual animal condition (Chapter 2, Section II), the diagnostic significance of precipitins to M. faeni will be discussed in both contexts.

The prevalence of precipitins in the four herds in which farmer's lung presented as a group disease was significantly higher at the end of the winter housing period than the incidence in the herds, sampled during the serological survey, in which farmer's lung had presented as an individual animal disease (Table 62). Also at the end of winter, the prevalence of precipitins in every herd in the serological survey in which farmer's lung had been confirmed was significantly higher than that in the rest of the herds. Therefore, it would appear that when a large proportion of the adult cattle in a herd (70%+) have precipitins to M. faeni in their sera at the end of winter, some animals are likely to be suffering from clinical farmer's lung. On the other hand, the prevalence of precipitins was also very high in herd FL1 (76%) in which farmer's lung had not been confirmed and in herd PS6 (69%) in which the condition presented as a single animal disease. However, coughing was frequent in both of these herds which had been fed very mouldy hay during the whole winter of the serological survey. The close association between the prevalence of precipitins and the frequency of coughing in the individual herds has already been noted (Chapter 3, Section II). Considering the herd as a whole, a high proportion of animals with precipitins to M. faeni confirms that they have recently been fed very mouldy hay and that a few animals are likely to be suffering from farmer's lung although this may not be apparent while the cattle are tied up.

The precipitin titres were estimated to ascertain whether they could provide a better correlation with the status of clinical farmer's lung in the individual herds. Precipitin titres in excess of 1/8 were found in 35 per cent and 44 per cent of the sera from herds FL6 and FL8 respectively in which farmer's lung had presented as a group disease. On the other hand, 27 per cent of the titres in herd

TABLE 62 The incidence of precipitating antibodies to Micropolyspora faeni in herds in which farmer's lung presented as an individual animal disease compared with the incidence in herds in which farmer's lung presented as a group disease.

Farmer's Lung - Individual Animal Disease			Farmer's Lung - Group Disease			Significant Difference
Herd	No. Animals Sampled	No. Animals Positive	Herd	No. Animals Sampled	No. Animals Positive	
PS1	33	10	1	75	45	
PS2	43	6	2	54	45	
PS3	93	31	3	24	16	
PS4	32	8	4	69	30	
PS5	15	8				
PS6	26	18				
FL5	79	62				
R2	51	26				
Total	372	169 (45%)		222	136 (61%)	S

FLI were also greater than 1/8 and farmer's lung had not even been confirmed in that herd. It would appear that estimating the titre of precipitating antibody does not really differentiate between widespread clinical farmer's lung and massive recent exposure to M. faeni.

Although all 45 clinical cases discussed in Chapter 2 of this study had serum precipitins to M. faeni, a large number of cows which are precipitin-positive do not show overt signs of respiratory disease. In individual animals, the presence of precipitins does not confirm clinical disease only previous exposure to M. faeni which meant that every one of the clinical cases had been fed mouldy hay. In experimental calves constantly exposed to mouldy hay dust (Chapter 5, Experiments 1 and 4), precipitins developed and microscopic lesions of farmer's lung were found at necropsy although clinical signs of respiratory disease were absent. Therefore, precipitins to M. faeni do not only confirm previous exposure to this micro-organism but also that the animal has become sensitised.

That cows have been or are being fed mouldy hay and have precipitins to M. faeni in their sera does not in any way prevent other respiratory disorders from arising. In several cows with precipitins, the major respiratory disease was chronic suppurative pneumonia although lesions of farmer's lung were also found at necropsy. Another animal developed traumatic pericarditis with sudden onset dullness, anorexia and groaning respirations; again lesions of farmer's lung were found at post-mortem examination.

In herds in which farmer's lung has been confirmed, an average of 22 per cent of the cattle with precipitins had titres greater than 1/8 compared with 11 per cent in herds in which farmer's lung had not been confirmed (57). Titres in excess of 1/32 were only found in animals from herds in which farmer's lung had been clinically and pathologically confirmed and so titres greater than 1/32 could perhaps be of diagnostic significance in an individual animal.

In the human form of the disease the titre of precipitating antibody to M. faeni is considered to be merely an indication of the amount of exposure to mouldy hay dust and to bear no relationship to the severity of the clinical symptoms (111, 216). When cattle of known M. faeni precipitin titre were exposed to mouldy hay and/or to M. faeni antigens under controlled conditions, a marked clinical

response developed in only one cow (A1) which had a titre of 1/64 (207). A mild but nevertheless obvious clinical reaction was produced in one of four experimental calves given a massive exposure to mouldy hay dust (Chapter 5, Experiment 4) and this particular animal (EA20) had the highest antibody titre in the group (1/16). However, on being exposed to mouldy hay dust for a second time, calf EA20 did not develop a detectable clinical response despite its titre remaining at 1/16. It would appear that in cattle the higher the precipitin titre to M. faeni the greater the probability of a severe clinical response developing on further exposure to mouldy hay dust.

Precipitating antibody to M. faeni has also been detected in sera from calves less than four weeks of age but this antibody will have been acquired from the dam by way of the colostrum. Serum samples from one calf were examined regularly and the precipitins became undetectable when the calf was eight weeks old (292). This rate of decline in colostral derived antibody is similar to that of Parainfluenza 3 virus in calves (58). Since lesions of farmer's lung disease have never been found in the lungs of the multitude of calves less than three months of age examined at necropsy at the Glasgow Veterinary School (292), it can be stated that these calves did not become sensitised following the inhalation of mouldy hay dust.

The presence of precipitins to M. faeni does not confirm clinical farmer's lung in cattle and neither does their absence indicate freedom from the disease. Farmer's lung has been diagnosed clinically and typical lesions found at necropsy in several cows in which demonstrable levels of precipitins to M. faeni were not found (292). In one incident involving 26 milking cows, precipitins against 15 extracts prepared from the various foodstuffs, five species of Aspergillus and M. faeni were not detected in any of the sera. It may have been that the double diffusion test was not sufficiently sensitive to detect the very low titres of antibody present. However, if the titres were so low as to be undetectable then it is likely that that specific antigen was not involved in the aetiology of the syndrome. Although precipitins to M. faeni can become undetectable following a period of six months without exposure to the allergens (Chapter 3, Section II), the sera referred to above were examined while the animals were ill.

For routine serological diagnostic work at least two standard

antigenic preparations of M. faeni should be used since the method of antigen preparation can lead to considerable differences in the numbers of sera considered to be positive (59). This variation in antigenicity does not appear to be due to strain differences since Edwards (1972) found very little antigenic variation between strains isolated in four different countries. It may be due to variations in the enzyme content of the various antigenic fractions since it has been shown that most M. faeni antigens have enzymatic activity (29). Ideally, reference antigen preparations and positive bovine sera should be available, so that results obtained from different laboratories can be compared and evaluated. This is necessary because the antigenic preparations best suited for routine diagnostic work with human sera were not those ideally suited for work with bovine sera (59).

The obvious explanation for a negative M. faeni precipitation reaction is that some other micro-organism is responsible for the respiratory signs. As yet only the role of M. faeni has been investigated extensively in cattle (185, 205, 206, 291), although three species of thermophilic actinomycete (T. vulgaris, Thermonospora viridis and Acinobifida dichotomica) in addition to M. faeni have been associated with farmer's lung in man (145). There is every reason to suppose, therefore, that M. faeni is not the sole cause of farmer's lung in British cattle. Wenzel and others (1974) have recently reported that 39 per cent of their positive sera from human patients would have been considered negative had M. faeni alone been used to examine the sera. Hence, they advocated that a panel of antigens be used for routine serological investigative work.

Some clinical cases of farmer's lung may not produce a positive precipitation reaction with M. faeni antigens because of variation in the affinity of the antibodies. It is known that this can affect the pathogenesis of disease in other systems (276).

Finally, some cattle could develop clinical signs of farmer's lung after massive exposure to mouldy hay because they possess a very labile alternative pathway of complement activation as has been suggested with pigeon fancier's lung in man (28). It has already been confirmed that dust alone can induce the onset of clinical symptoms in M. faeni precipitin-negative farmer's lung patients by stimulating the alternative pathway (98).

The examination of sera for precipitins to M. faeni is the only laboratory test in routine use for the diagnosis of farmer's lung in cattle. However the result of the precipitin test should not be the sole criterion on which the diagnosis of farmer's lung is made although the presence or absence of precipitins can assist a clinician in possession of relevant clinical and epidemiological details to make a diagnosis.

SECTION III

THE USE OF RADIOLOGY IN THE DIAGNOSIS OF FARMER'S LUNG IN CATTLE

INTRODUCTION

Radiology has been an important aid in the diagnosis of farmer's lung in man since the condition was first described (40, 75, 202). These early workers reported that the radiological changes, which ranged from fine stippling to course granular mottling, were most intense in the basal areas near the hilum. In severe cases, there was an overall increase in opacity which faded to a fine granular mottling around the periphery of the lung fields (251). With continued exposure, there was evidence of pulmonary fibrosis, pulmonary emphysema and even of pulmonary hypertension (86).

The interpretation of thoracic radiographs is much more difficult in the bovine than in the human because lateral exposures only can be taken and so the depth of tissue through which the x-rays have to penetrate is relatively massive. The antero-ventral parts of both lung fields are totally obscured by the heart and by the bone and muscle shadows of the fore-limbs. Consequently, only the dorsal and posterior parts of the lungs can be studied. A further complication is the superimposition of lesions present in one lung on those of the other lung.

In spite of these difficulties, radiographs from 21 of the 45 cases in this series were taken in order to ascertain whether changes could be seen in the lungs and also to find out whether this technique might be of use in the diagnosis of farmer's lung in cattle.

MATERIALS AND METHODS

Standing lateral radiographs of the thorax were taken with the x-ray beam centred over the sixth rib, mid-way between the posterior angle of the scapula and the olecranon process of the ulna. This provided a good projection of the diaphragmatic lobes and the dorsal parts of the cardiac lobes in most instances.

Positioning was greatly facilitated by the use of a linked x-ray tube and image intensifier suspension system (Siemen 3D

Suspension System, Siemens Aktiengesellschaft, Karlsruhe, West Germany), which was fitted with a cassette holder (149). This allowed the x-ray tube to be positioned accurately while the cassette remained centred on the x-ray beam.

Par speed 35.6 x 43.2 cm film and screens (Kodak Ltd., London) were used in conjunction with a focused grid (grid ratio 10:1, 44 lines/cm). Although exposure factors varied with individual animals, initially they were within the range 45-55 kV and 80-130 mAs at a film focus distance of 100 cm. However, in some subjects respiratory movement was a problem and radiographic contrast tended to be excessive. The use of a higher kV (70-75 kV) in subsequent examinations allowed the mAs to be reduced (32-40 mAs); this lessened the risk of movement blur and gave an improved latitude in radiographic contrast.

Radiographs of six cases of acute farmer's lung, 15 cases of chronic farmer's lung and one cull cow were taken.

RESULTS

Normal cow (Figure 7)

It can be seen that only the diaphragmatic lobes and the dorsal parts of the apical and cardiac lobes can be meaningfully examined. Compared with man, cattle have a very obvious broncho vascular pattern and the main diaphragmatic bronchus can be identified easily as it passes dorso-caudally in the dorsal third of the diaphragmatic lobe. As the bronchi and pulmonary vessels run together, the vessels cannot be distinguished individually. The broncho-vascular sub-divisions can be seen radiating over the lung field in a fan-like manner from the main bronchus and they can generally be traced to the second or third branch. The aorta, posterior vena cava and trachea can also be identified.

Cull 10 (Figure 8)

This case had not been treated for any respiratory disorder but had been losing weight during two successive winter housing periods. On admission in May, she was slightly tachypnoeic (Resp. Rate = 30/minute), slightly hyperpnoeic and she coughed occasionally.

FIGURE 7 A lateral radiograph of a healthy cow in which the main diaphragmatic bronchus (DB), the aorta (A), posterior vena cava (PVC), trachea (T) and rumen (R) can be seen.

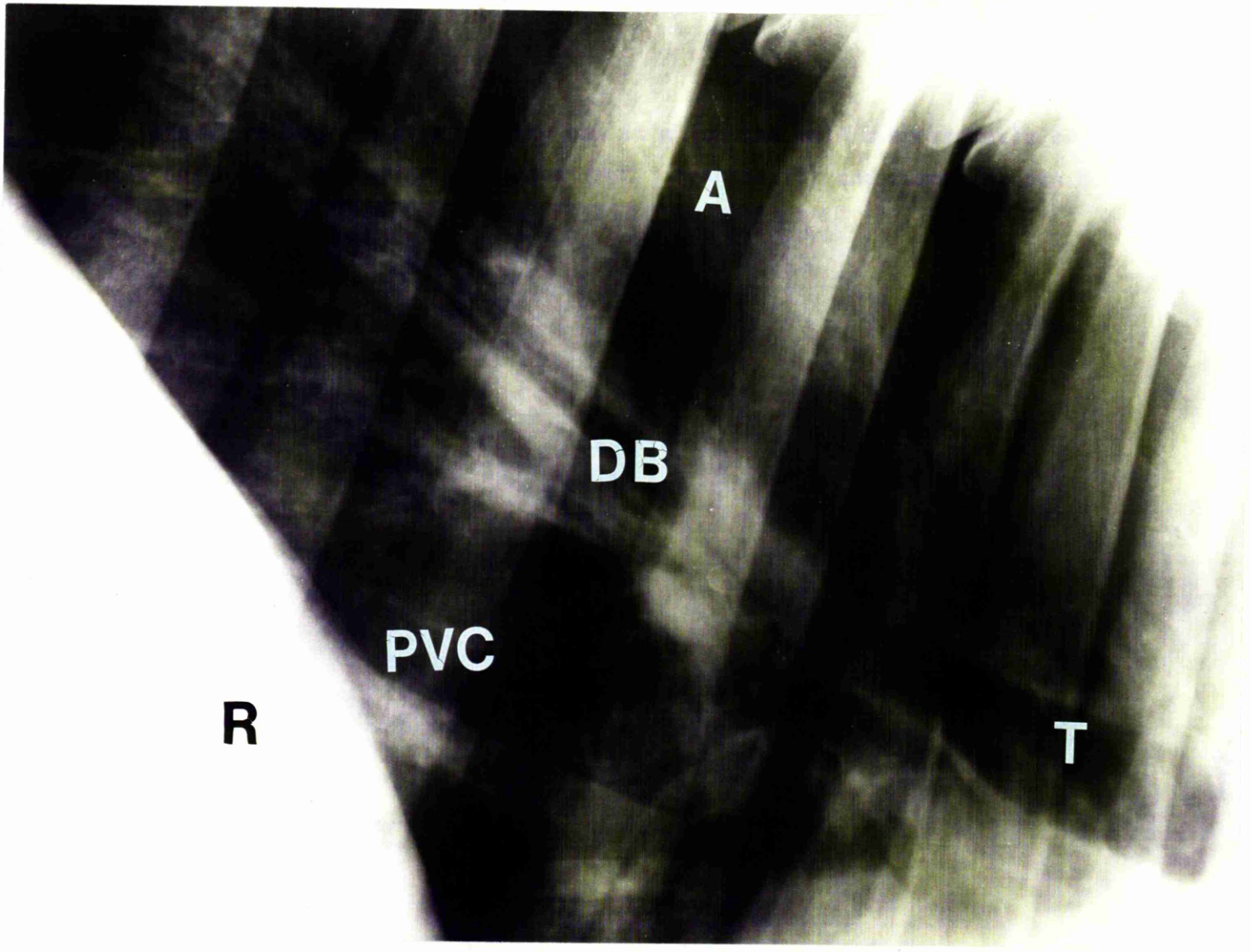
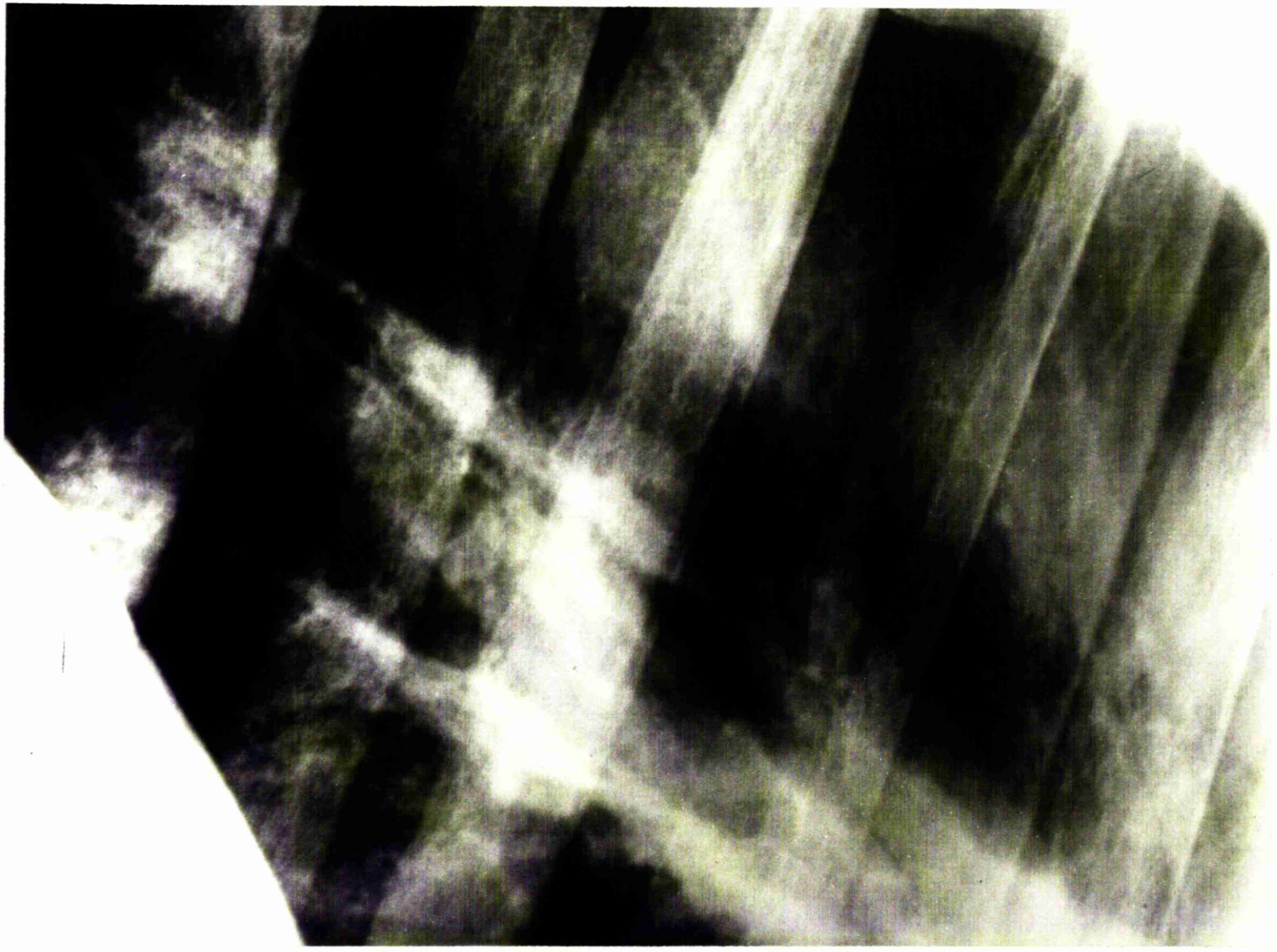


FIGURE 8 An increase in the peribronchial reaction can be appreciated as well as some loss of radiolucency towards the antero-ventral parts of the lung-field.



There is an increase in the peribronchial reaction compared with the radiograph taken of the healthy cow. There is some loss of radiolucency in the antero-ventral parts of the diaphragmatic lobes and more obviously, around the dorsal part of the cardiac lobes.

Case C10 (Figure 9).

This case had not been treated for any respiratory disorder and in May, during the serological survey, she was noticed to be hyperpnoeic and coughing. On admission in October, she was not tachypnoeic (Resp. Rate = 25/minute) but she was slightly hyperpnoeic and she had an occasional non-productive cough.

Some decrease in radiolucency can be seen at the antero-ventral parts of the plate and the peri-bronchial reaction is more obvious than with Cull 10. As well as an increased number of small bronchioles, there is some evidence of mottling especially dorsally and what also appears to be small nodules.

Case A8 (Figure 10)

This case developed sudden onset respiratory distress which appeared to be brought on by exercise soon after she was put out to graze in the early summer. On admission three months later, she was tachypnoeic (Resp. Rate = 50/minute), grossly hyperpnoeic and she had a frequent productive cough. Bilateral crackles and rhonchi were heard antero-ventrally.

There is generalised loss of radiolucency especially around the bifurcation of the trachea. The radiating small bronchi and bronchioles are very obvious as is the granular, generalised mottling over the whole lung field. There would appear to be several distinct nodules in the dorsal, posterior parts of the diaphragmatic lobes.

Case C20 (Figure 11)

This case had not been treated for respiratory disease but the farmer recognised that "she was going the same way as her stall-mate", case A8. On admission in October, she was tachypnoeic (Resp. Rate = 50/minute), grossly hyperpnoeic and she had a frequent, harsh productive cough. Bilateral crackles could be heard but rhonchi could only be detected on the right side.

There is complete and generalised loss of radiolucency,

FIGURE 9 There is evidence of mottling at the posterior aspects of the diaphragmatic lobes and a still greater loss in radiolucency antero-ventrally.

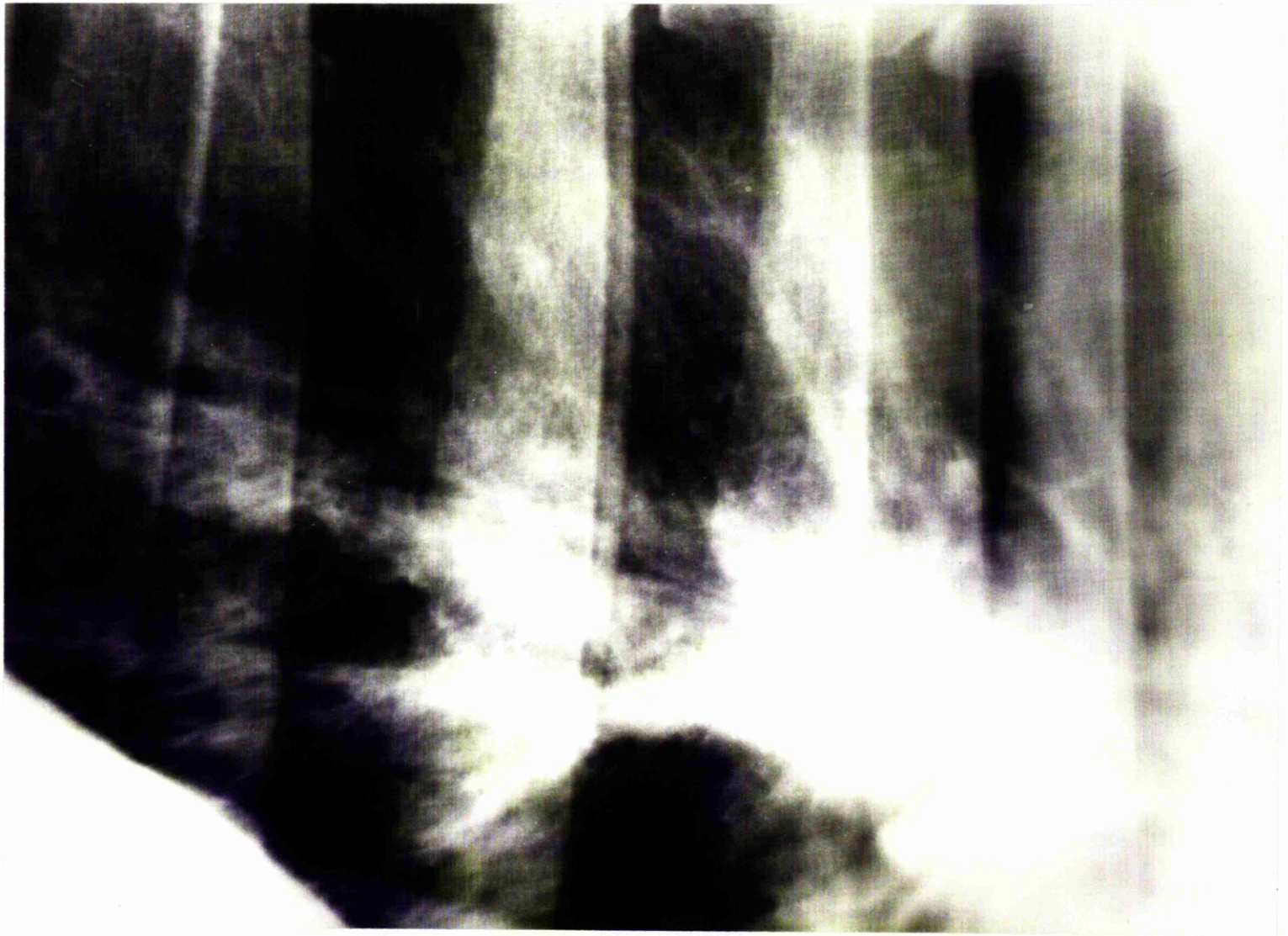


FIGURE 10 There is a generalised loss of radiolucency and a granular mottling over the whole of the visible lung-field.

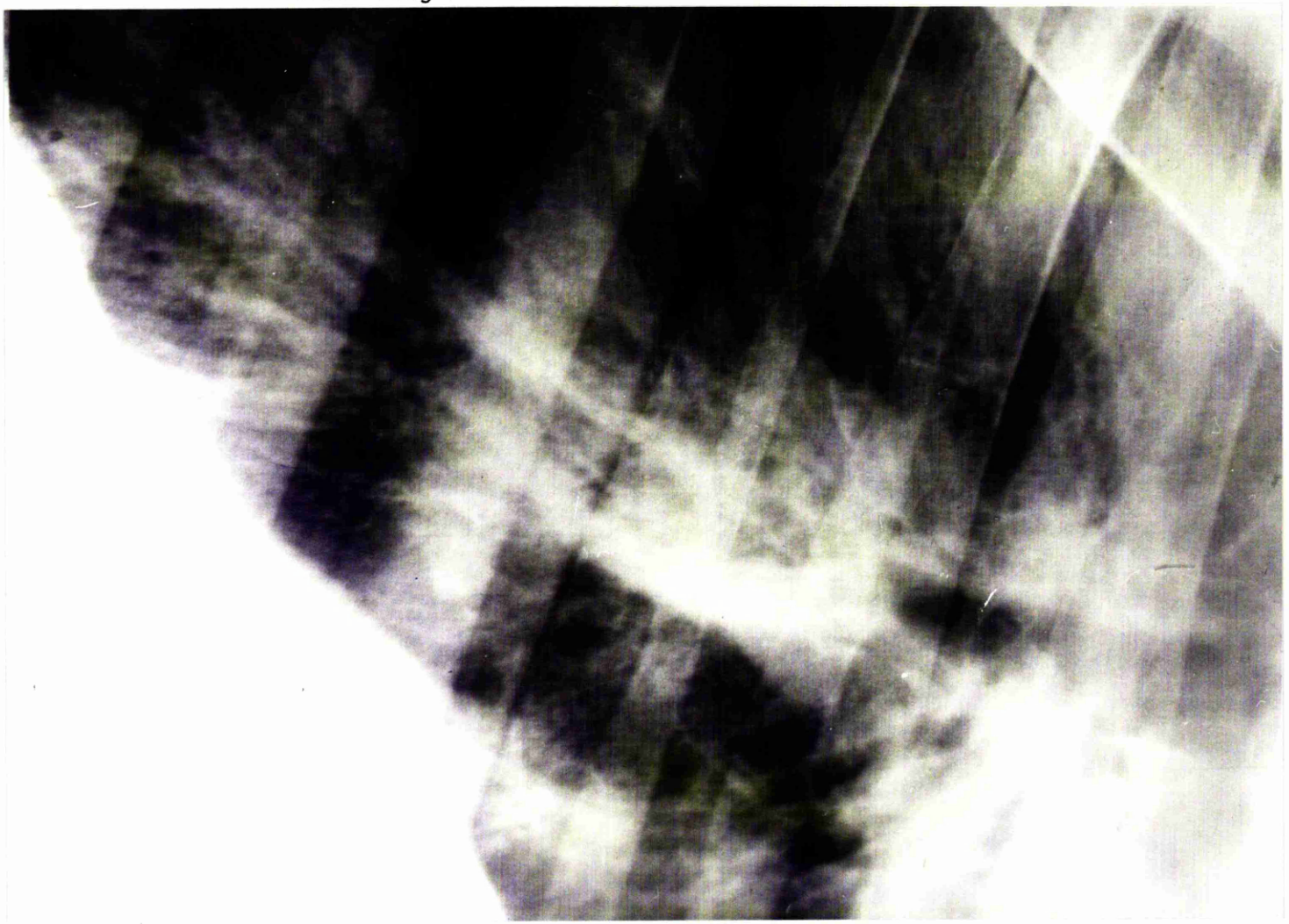
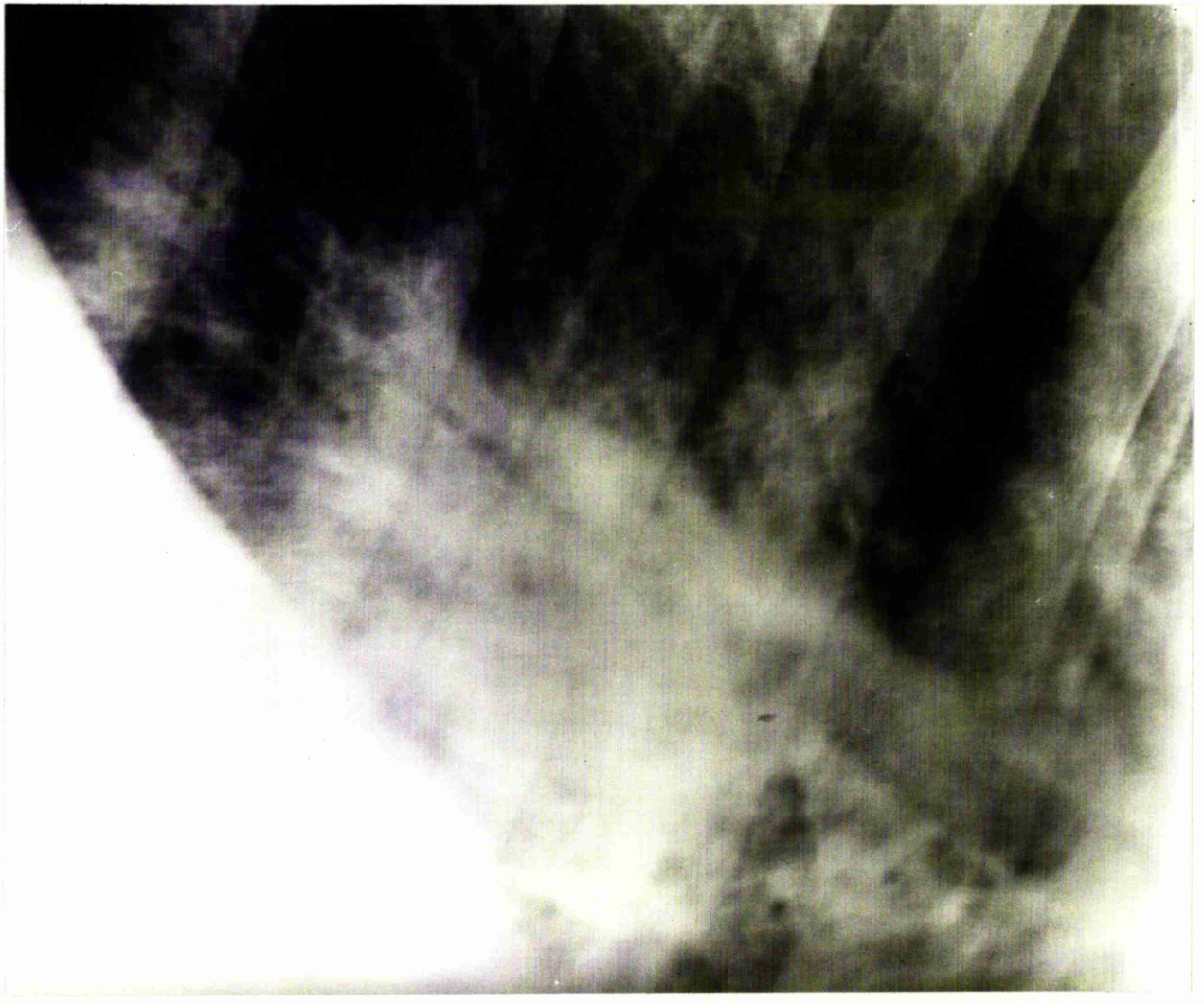


FIGURE 11 There is an almost complete loss of radiolucency around the bronchi and vessels in the mid-chest area and there is coarse mottling over the rest of the lung-field.



especially around the bronchi and pulmonary vessels in the mid-chest area. This change becomes progressively less obvious towards the posterior of the diaphragmatic lobes. There is extensive coarse mottling and one or two nodules appear to be present in the caudal areas of the diaphragmatic lobes.

Case A15 (Figure 12)

This was an old cow which developed acute respiratory distress in March. On admission, she was tachypnoeic (Resp. Rate = 40/minute), moderately hyperpnoeic and she had an occasional, non-productive cough.

The radiograph was taken 5 days after the acute episode. The most striking feature is the widespread uniform granular mottling. There is also an increased peri-bronchial reaction.

Case A17 (Figure 13)

This was the youngest case, a two year old heifer, which had experienced two acute farmer's lung episodes in a three week period in April. On admission, she was slightly tachypnoeic (Resp. Rate = 30/minute), slightly hyperpnoeic and she had an occasional non-productive cough. Bilateral rhonchi were detected antero-ventrally but crackles were only heard on the left side. The radiograph was taken three days after the acute episode. There has been some loss of radiolucency over the whole visible lung field, but especially anterior and ventral to the major diaphragmatic bronchus. There is also evidence of an intense peri-bronchial reaction which appears to be most severe in the middle of the plate. Some mottling can also be appreciated in the antero-ventral parts of the diaphragmatic lobes.

The severity of the radiological changes in the individual cases was assessed as either mild, moderate or severe and then compared to the severity of disease as judged by the clinical signs (Table 63). There was a good correlation between the degree of radiological change and the severity of the clinical signs in two of the acute cases (30%) and in eight chronic cases (53%). The radiographs indicated the presence of a less severe respiratory condition than was suspected by clinical examination in eight of the remaining 11 animals (73%) and a more severe disease in the other three. Diffuse pulmonary fibrosis was suspected in cases A15, A17, C20 and C25 because of the generalised loss of radiolucency.

FIGURE 12 Widespread, uniform coarse granular mottling can be seen as well as an increased peribronchial reaction.

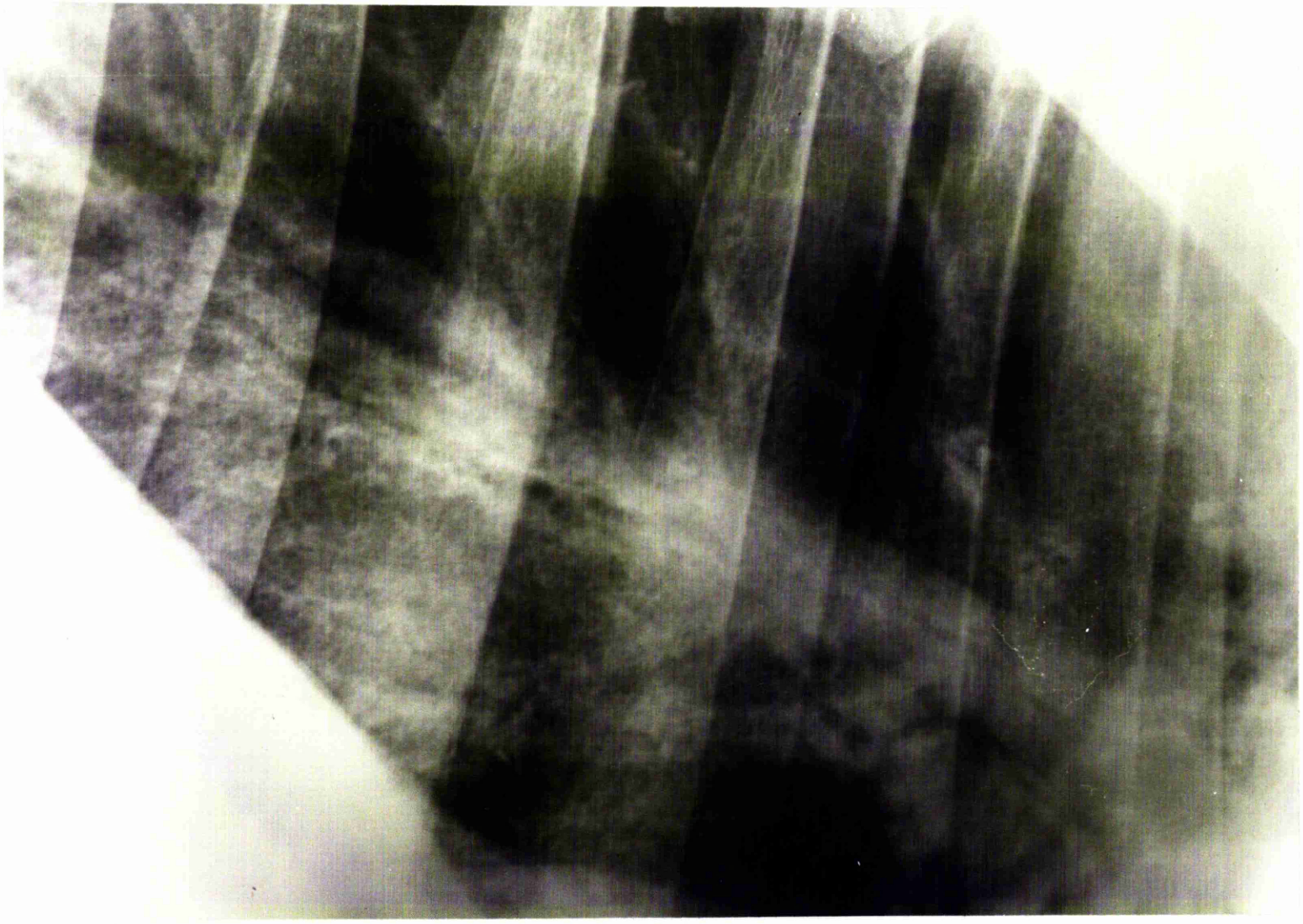


FIGURE 13 Some loss of radiolucency has occurred over the whole lung-field especially anterior and ventral to the main diaphragmatic bronchus. An intense peribronchial reaction can be seen particularly in the mid-chest area.

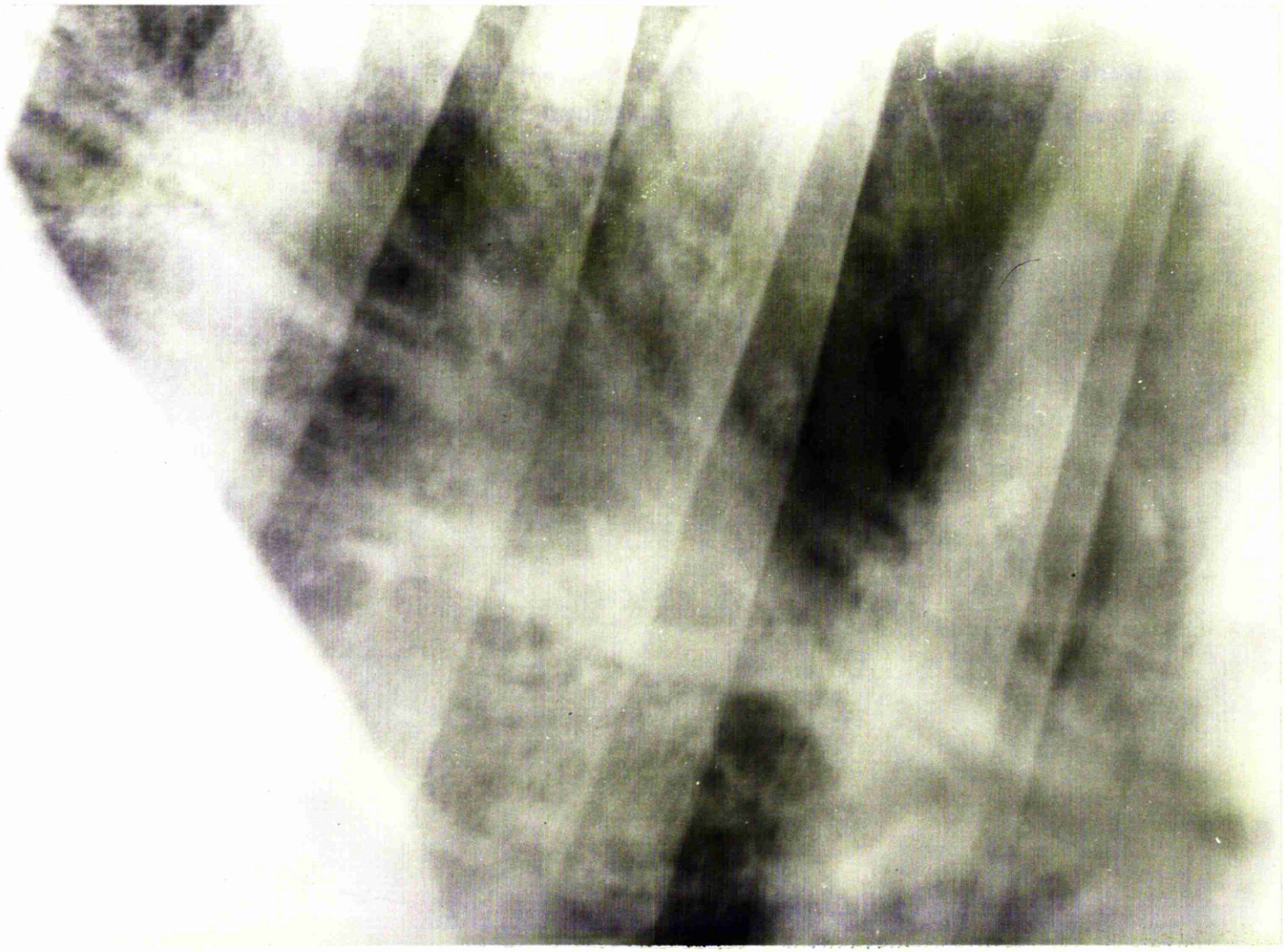


TABLE 63

A comparison of the severity of farmer's lung in cattle as assessed by radiology and by clinical examination.

Case No.	Radiological Score	Comments	Clinical Score
A8	++	Early cor pulmonale	+++
A9	++		+
A10	++		++
A15	++	Diffuse fibrosis?	+
A16	+	Cor pulmonale	+++
A17	++	Diffuse fibrosis?	++
C6	++		++
C9	++		++
C10	+		+
C11	+		±
C12	++		++
C13	+		++
C14	+		++
C15	+		++
C16	++		++
C20	+++	Diffuse fibrosis?	+++
C21	++	Cor pulmonale	+++
C23	+		++
C25	+	Diffuse fibrosis?	++
C26	+		+
C27	+		+
Cull 10	+		+

\+ mild
++ moderate
+++ severe

DISCUSSION

The earliest appreciable radiological change was an increase in the degree of peri-bronchial thickening and the delineation of many small airways which are not normally visible. The peri-bronchial reaction was the result of an intense cellular infiltration which was found at necropsy to be one of the major pathological features of the cases in this series (Chapter 4, Section V). As the severity of the clinical disease increased, the mottling became widespread and also more granular. In the most severely affected cases, there was an overall increase in the radio-opacity which was most obvious around the major bronchi and vessels.

It has been suggested that the widespread, fine mottling which is so characteristic of the acute stage of farmer's lung in man results from the presence of granulomata (86, 247). Although reference has been made to apparent "nodules" on some of the radiographs in this series, it is most unlikely that they correspond to the small granulomata (1-2 mm in diamter) which were seen throughout the lungs at necropsy. The "nodules" seen on these radiographs were more likely to have been pulmonary vessels viewed end-on. On the other hand, the very coarse, granular mottling seen in case A15 (Figure 12) was almost certainly produced by the very large number of "asteroid bodies" (2-5 mm in diameter) throughout the lungs. Large numbers of these "asteroid bodies" can be seen just under the pleura of the lungs of case A15 (Figure 12).

In man, the radiological abnormalities may have cleared within three weeks of a single acute attack (109, 169), although physiological abnormalities can still remain and the patient can still feel breathless (60). However, in case A17 (Figure 13) which had experienced two acute episodes in the three weeks prior to her being admitted, fine crackles were heard on auscultation antero-ventrally where the loss of radiolucency was greatest. There was also an intense peri-bronchial reaction in this case. These clinical and radiological findings indicate that case A17 was probably in the sub-acute stage of the disease.

Only in the chronic form of the disease was there a fairly good correlation between the radiological and clinical findings whereas in man, the clinical symptoms and radiological findings correlate closely only in the acute stage (109, 213). The

radiological changes detected in severe cases of chronic farmer's lung were similar to those of diffuse fibrosing alveolitis in cattle (209). Although this is also true in the human, differentiation can be made because pulmonary fibrosis occurring as a result of extrinsic allergic alveolitis (farmer's lung) tends to be most severe in the dorsal parts of the lungs, whereas pulmonary fibrosis as a result of diffuse (cryptogenic) fibrosing alveolitis is most severe in the ventral parts (52, 112). At present, it is not certain whether the distribution of pulmonary fibrosis in cattle is disease dependent. But even if it were, the limited area of the lungs which can be examined properly precludes any differentiation between extrinsic allergic alveolits and diffuse fibrosing alveolitis being attempted by radiological examination alone.

Many of the original human patients with farmer's lung were initially diagnosed as suffering from puimonary tuberculosis (75, 202, 251) because of the clinical and radiological similarity between these two conditions. Recently at this veterinary school, a diagnosis of diffuse fibrosing alveolitis was made after the examination of a radiograph from a cow with chronic respiratory disease. However, at necropsy, she was found to have widespread pulmonary tuberculosis.

It has been possible to detect significant radiological changes in cases of farmer's lung in cattle despite the obvious limitations of the technique. Abnormalities have also been detected in other pulmonary diseases of cattle (149) but it is too early to know whether radiology will ever be useful in the differential diagnosis of bovine respiratory disease.

SECTION IV

THE USE OF SKIN TESTS IN THE DIAGNOSIS OF FARMER'S LUNG IN CATTLE

INTRODUCTION

Farmer's lung was initially thought to be a true pulmonary mycosis (75, 76) and, at that time, suspected cases of broncho-mycosis were routinely injected intra-dermally with fungal material (76). It appeared that fungi were indeed responsible for the development of farmer's lung since Fawcitt (1938) reported that positive intra-dermal tests had been produced with preparations of Mucor species and Penicillium species. Subsequently, Fuller (1953), Studdert (1953) and Williams (1963) were unable to differentiate patients with farmer's lung from those with other respiratory diseases after both groups had been injected intra-dermally with extracts of different hays and fungi because of the non-specific irritant effect of the preparations used. For this reason, skin testing has never been used extensively as an aid to the diagnosis of farmer's lung in man (275).

It was decided to investigate whether an intra-dermal injection of M. faeni antigens could produce a detectable skin reaction in cases of farmer's lung in cattle and if so, to ascertain whether this reaction was specific.

MATERIALS AND METHODS

(a) Selection of animals

Skin tests were performed on nine cattle which had precipitating antibodies to M. faeni in their sera. Eight of these animals (A1, A2, A3, A4, C1, C3, C4, C5) were admitted to the Veterinary School because they were suffering from a respiratory disease considered to be farmer's lung. The ninth cow (Cull 1) had been culled from the same herd as case A2 but on admission, no evidence of clinical respiratory disease was detected.

A series of 12 adult cattle (PNC1-12) free from clinical signs of respiratory disease and lacking detectable M. faeni were each used as controls. These animals were used for one experiment only.

(b) Preparation of Micropolyspora faeni antigens

The four antigenic preparations of M. faeni were derived from strain IMI 134062 (Commonwealth Mycological Institute, Kew). The methods of preparation of the different antigens are given in Table 64. After extraction Ag 42, Ag 113 and Ag 117 were Seitz filtered, dialysed against running tap water for 36 hours and millipore filtered (pore size = 0.45 μm). All antigenic preparations were freeze-dried and reconstituted with sterile saline immediately before use.

(c) Procedure for skin testing

A tuberculin syringe was used to deliver 0.1 ml of M. faeni solution into the shaven skin on the dorsal part of the animal's thorax. The dilutions of antigen, the number of injections and the size of the subsequent skin reactions are given in the table referring to that particular experiment. In addition to the M. faeni injections, every animal was given duplicate intradermal injections of sterile normal saline. When a skin reaction developed, the edge of the swelling was marked and the diameter of the reaction recorded. The size of the skin reactions was recorded at 15 minutes, at hourly intervals for six or seven hours and at 24, 48 and 72 hours post-injection apart from the first experiment with Ag 42 when the reactions were examined at five hours post-injection only because this was a preliminary study.

(d) Procedure for skin biopsies

The time post-injection that the skin biopsies were removed and the animals from which they were taken are given in Table 65. The specimens were fixed in Bouin's fluid, embedded in paraffin wax, sectioned at 8 microns and stained with haematoxylin and eosin.

(e) Estimation of titre of precipitating antibody to Micropolyspora faeni

The method of M. faeni antigen preparation and the immunodiffusion technique were as described in Chapter 3, Section II. Doubling dilutions of serum were made in the peripheral wells of the agar plates and the highest dilution at which a precipitation line was still visible was taken as the antibody titre.

TABLE 64

The method of preparation of the Micropolyspora faeni antigens used for the skin testing of cattle.

Antigen	Cultural Details	Method of Preparation
Ag 42	16 days at 55°C	CS* culture on horse serum dextrose agar. Removed and immersed in Coca's for 7 days.
Ag 41	16 days at 55°C	Horse serum dextrose agar from preparation of Ag 42. Freeze-thawed x 3.
Ag 113	11 days at 55°C	CS* culture on half nutrient agar. Removed and immersed in Coca's for 10 days.
Ag 117	13 days at 55°C	CS* culture on Czapek-Dox agar. Removed and immersed in Coca's for 36 days.

* CS = cellophane supported.

TABLE 65

The individual cattle from which biopsies were removed following the intra-dermal injections of Micropolyspora faeni antigens and saline.

Antigen	Time of Biopsy (Hours)	Source of Biopsy Material
Ag 42	5-6	A1, A2, A3, A4, PNC5, Cull 1
	24	-
	72	A1, A2
Ag 117	6	C5
	24	C3, C4
	72	-
Sterile Saline	4	A1, PNC5
	24	- -
	72	A1, -

RESULTS

(a) Antigen 42 (Ag 42)

Experiment 1 Animals C1, PNC1, PNC2, PNC3 and PNC4 were injected with three dilutions (1/1, 1/10, 1/1,000) of Ag 42. By five hours post-injection a definite skin reaction had developed at every one of the 1/1 injection sites (Table 66). The largest reaction (35 mm) was on C1, the only animal with precipitins to M. faeni. Reactions which were just detectable were produced with the 1/10 antigen dilution at one site only on PNC2 and PNC4. Detectable reactions were not produced following the injections of either the 1/1,000 dilution of antigen or the saline.

Experiment 2 Animals A1 and PNC5 were injected with one dilution (1/1) of Ag 42 (Table 67). The obvious skin reactions, which were first detected on A1 at three hours post-injection, achieved their maximum size one hour later. Their size and appearance remained the same for a further hour after which time they became less prominent and lost their well-demarcated edge. This meant that the diameter of the reactions could not be measured accurately. The site of the largest reaction (site 1) was removed after six hours. Although the remaining two reactions could not be seen at 24, 48 and 72 hours post-injection, small pea-sized swellings of around 10 mm in diameter could still be palpated in the skin.

Measurable reactions did not develop at any of the antigen sites on PNC5 or at any of the saline sites on either animal.

Experiment 3 Animals A2, A3 and PNC6 were injected with two dilutions (1/2, 1/10) of Ag 42 (Table 68). Obvious reactions were detected at the 1/2 sites one hour post-injection. These reactions reached their maximum diameter three hours post-injection, remained the same size for another hour and then became less prominent. Measurable reactions were still present at 24 hours post-injection but at 48 and 72 hours they had decreased in size and so were no longer visible although they remained easy to palpate. Two biopsies were taken from A2 at six hours and a third at 72 hours post-injection while one biopsy only was taken from A3 at six hours.

TABLE 66

The diameter of the reactions following the intra-dermal injection of Micropolyspora faeni antigens (Ag 42).

Antigen Dilution	Diameter of Skin Reactions (mm)									
	C1		PNC1		PNC2		PNC3		PNC4	
1/1	15	35	20	25	20	25	12	15	20	20
1/10	10	10	10	10	10	11	10	10	10	12
1/1000	10	10	10	10	10	10	10	10	10	10

TABLE 67

The diameter of the reactions following the intra-dermal injection of Micropolyspora faeni antigens (Ag 42).

	Diameter of Skin Reactions (mm)					
Time (Hr)	A1			PNC5		
0.25	10	10	10	10	10	10
1	10	10	10	10	10	10
2	10	10	10	10	10	10
3	25	30	15	10	10	10
4	45 x 20	32	30	10	10	10
5	No Change			No Change		
6	Less Prominent			No Change		
24		+	+		-	-
48		+	+		-	-
72		+	+		-	-
Biopsy	6 Hr	72 Hr		6 Hr		

+ = palpable skin thickening.

TABLE 68 The diameter of the reactions following the intra-dermal injection of Micropolyspora faeni antigens (Ag 42).

	Diameter of Skin Reactions (mm)											
	A2						A3					
Time (Hr)	1/2 Dilution			1/10 Dulution			1/2 Dilution			1/10 Dilution		
0.25	10	10	10	10	10	10	10	10	10	10	10	10
1	10	13	13	10	10	10	16	14	14	10	10	10
2	20	24	23	14	15	10	22	20 x 16	20	12	12	10
3	24	30 x 25	30 x23	14	19	10	27 x 23	23 x 17	30 x 20	11	14	11
4	No Change			No Change			No Change			No Change		
5	Less Prominent			Less Prominent			Less Prominent			Less Prominent		
6	Less Prominent			Less Prominent			Less Prominent			Less Prominent		
24	11			-	-	-	10	10		-	-	-
48	+			-	-	-	+	+		-	-	-
72	+			-	-	-	+	+		-	-	-
Biopsy	72 Hr	6 Hr	6 Hr						6 Hr			

TABLE 68 (Cont'd.)

Time (Hr)	Diameter of Skin Reactions (mm)					
	PNC6					
	1/2 Dilution			1/10 Dilution		
0.25	10	10	10	10	10	10
1	10	12	14	10	10	10
2	11	12	14	11	10	13
3	20 x 15	16	19	12	10	13
4		No Change			No Change	
5		Less Prominent			Less Prominent	
6		Less Prominent			Less Prominent	
24	±	±	±	-	-	-
48	-	-	-	-	-	-
72	-	-	-	-	-	-

Small reactions developed with the 1/10 dilution after two hours but, when they reached their maximum size after three hours, they were much smaller than the 1/2 dilution reactions. No reactions could be palpated at 24 hours, 48 hours and 72 hours post-injection.

With PNC6 small skin reactions were detected one hour post-injection and they too achieved their maximum size within three hours. They became less prominent and at 24 hours post-injection, small thickenings could be appreciated in the skin but by 48 hours and 72 hours, no skin thickenings were detected.

Detectable skin reactions were not produced in any of these animals as a result of the saline injections.

Experiment 4 Animals A4 and Cull 1 were injected with two dilutions (1/2, 1/10) of Ag 42 but PNC7 was injected with the 1/2 dilution only (Table 69). Skin reactions were detected with both dilutions after one hour in Cull 1 and after two hours in A4. On both these animals the reactions achieved their greatest size four hours post-injection. After five hours, a 1/2 reaction site was removed from A4 and at six hours from Cull 1. The remaining 1/2 sites were palpable on both animals at 24 hours, 48 hours and 72 hours as were the 1/10 sites on Cull 1.

Small reactions developed on PNC7 with the 1/2 dilution at three hours post-injection. These reactions became less prominent and small thickenings only could be detected after 24 hours but at 48 hours and 72 hours no thickenings were present.

Detectable skin reactions were not produced in any of these animals following the saline injections.

(b) Antigen 41 (Ag 41)

Twelve weeks after they had been injected with Ag 42 (Experiment 2), animals A2 and A3 along with PNC8 and PNC9 were given two injections of a standard (1/1) solution of Ag 41 (Table 70). PNC9 was examined only at two, five and six hours post-injection because she was difficult to handle. The large oedematous swellings which were easily detected even after 15 minutes on the three cows examined, achieved their greatest diameter at three to five hours post-injection. Afterwards,

TABLE 69 The diameter of the reactions following the intra-dermal injection of *Micropolyspora faeni* antigens (Ag 42).

	Diameter of Skin Reactions (mm)																	
	A4						Cuil 1						PNC7					
Time (Hr)	1/2 Dilution			1/10 Dilution			1/2 Dilution			1/10 Dilution			1/2 Dilution					
0.25	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10			
1	10	10	10	10	10	10	18	30 x 22	30 x 27	20 x 18	15 x 10	20	10	10	10			
2	15 x 10	18 x 15	10	10	11	10	32 x 20	36 x 28	40 x 32	28 x 25	19 x 15	25 x 22	10	10	10			
3	30 x 20	20	22 x 20	10	13	10	34 x 27	40	42 x 40	30 x 26	20 x 18	30 x 24	12	11	10			
4	30 x 20	20	20	10	14	12	Diffuse	41 x 40	48 x 42	30	22 x 18	30 x 25	12	12	10			
5	No Change			No Change			No Change			No Change			No Change					
6	Less Prominent			Less Prominent			No Change			No Change			Less Prominent					
24	+	+		-	-	-	÷	15		10	10	10	±	±	±			
48	+	+		-	-	-	÷	10		÷	÷	÷	-	-	-			
72	+	+		-	-	-	÷	÷		÷	÷	÷	-	-	-			
Biopsy	5 Hr						6 Hr											

TABLE 70

The diameter of the reactions following the intra-dermal injection of Micropolyspora faeni antigens (Ag 41).

Time (Hr)	Diameter of Skin Reactions (mm)							
	A2		A3		PNC8		PNC9	
0.25	37 x 27	26 x 19	32 x 27	40 x 37	25 x 24	20	N/E	N/E
1	52 x 40	30 x 25	40 x 35	40 x 38	30 x 24	31 x 27	N/E	N/E
2	65 x 60	48 x 38	55 x 45	40 x 34	35 x 30	35 x 30	37	37
3	70 x 65	48 x 38	60 x 45	40 x 34	45	45	N/E	N/E
4	Diffuse	50 x 40	Diffuse		Diffuse		N/E	N/E
5	Diffuse	40 x 25	Diffuse		Diffuse		50	60
6	Diffuse		Diffuse		Diffuse		Diffuse	
24	+	+	+	+	+	+	+	+
48	+	+	+	+	±	±	±	±
72	±	±	±	±	-	-	-	-

they became diffuse and their exact size could not be measured accurately. Reactions were palpated at every injection site after 24 hours but at 72 hours, slight skin thickenings were detected only on A2 and A3.

Detectable skin reactions were not produced in any of these four cows following the injections of saline.

(c) Antigen 113 (Ag 113).

Triplicate injections of a standard (1/1) solution of Ag 113 were given to A2 and A3 four weeks after they had been given the Ag 41 antigen and to A4 and Cull 1 12 weeks after they had been injected with Ag 42 (Experiment 3). The control cow was PNC10. A measurable amount of reaction had developed at one or more sites on each of the four animals with precipitins to M. faeni after only 15 minutes (Table 71). On A2 and A3 the antigen had been injected into non-pigmented skin but no evidence of the typical wheal and flare response was seen. The reactions gradually increased in diameter until their maximum size was reached at three hours (A3, A4) and four hours (A2, Cull 1) post-injection. While the size of the reactions remained unchanged over the next three hours on A3, they became less prominent on the other three cows. The reactions, which could be palpated at every site 24 hours after injection, were especially marked on A3. However, after 72 hours slight skin thickenings were palpated only on A2 and A3.

The small reactions which developed on PNC10 reached their maximum size by two hours post-injection, remained unchanged for the next two hours and had almost completely disappeared by six hours post-injection. No skin thickenings were palpated subsequently at any of the sites on this cow.

No detectable reactions developed on A4, Cull 1 and PNC10 following the injections of saline. However, reactions had developed after 15 minutes on A2 and A3 and, over the next four to five hours, they became less pronounced. No detectable skin thickenings were found at any of the sites on A2 or A3 at 24, 48 and 72 hours post-injection.

TABLE 71 The diameter of the reactions following the intra-dermal injection of Micropolyspora faeni antigens (Ag 113) and saline.

	Diameter of Skin Reactions (mm)											
	A2						A3					
Time (Hr)	Ag 113			Saline			Ag 113			Saline		
0.25	20 x 18	16	20 x 18	14	17	20 x 17	13	15	16	12	15	13
1	40	35	42 x 40	14	17	20 x 17	13	15	17	No Change		
2	45 x 40	40 x 35	48 x 45	18	20	21	16 x 15	20	22 x 20	No Change		
3	50 x 45	40 x 35	52	No Change			16	22 x 20	22	Less Prominent		
4	50 x 45	40 x 35	55 x 50	No Change			No Change			Less Priminent		
5	Less Prominent			Less Prominent			No Change			10	10	10
6	Less Prominent			Less Prominent			No Change			10	10	10
24	+	+	+	-	-	-	++	++	++	-	-	-
48	±	±	±	-	-	-	+	+	+	-	-	-
72	±	±	±	-	-	-	±	±	±	-	-	-

TABLE 7I (Cont'd.)

Time (Hr)	Diameter of Skin Reactions (mm)								
	A4			Cull 1			PNC10		
	Ag 113			Ag 113			Ag 113		
0.25	10	14 x 12	15	10	10	15	10	10	10
1	24	18 x 14	25 x 22	15	15 x 13	22	10	10	10
2	25 x 22	18 x 15	23 x 22	15	23	30	12	15	14
3	25	18 x 15	23 x 22	15	25 x 23	32 x 30		No Change	
4		No Change		24 x 18	31 x 28	38 x 36		No Change	
5		Less Prominent			Less Prominent			Less Prominent	
6		Less Prominent			Less Prominent			Less Prominent	
24	±	±	±	+	+	+	-	-	-
48	-	-	-	±	±	±	-	-	-
72	-	-	-	-	-	-	-	-	-

(d) Antigen 117 (Ag 117)

Experiment 1 Animals C3 and C4 were injected in triplicate with a standard (1/1) and a 1/10 dilution of Ag 117 and PNC11 was given three injections of the standard solution only. Reactions were first detected on C3 and C4 with the standard solution after one hour and they reached their maximum size after five hours (Table 72). Twenty-four hours post-injection, all bar one of these reactions could still be measured. A biopsy of a 1/1 solution reaction was taken from C3 and C4 at this time. After 72 hours, palpable reactions were still present at every remaining injection site. With the 1/10 dilution, the reactions were also first detected one hour post-injection but they reached their maximum size after two or three hours. Slight skin thickenings were palpated at every site after 24 hours but none could be detected subsequently.

At every standard and 1/10 antigen injection sites on C3, which was a predominantly white cow, small red areas developed; these were not wheal and flare reactions. The red areas had increased in size after one hour but by two hours, the colour disappeared from the 1/10 sites. On Figure 14 which was taken six hours post-injection, the dark red colour at the 1/1 injection sites can be easily appreciated. The circular broken lines indicate the periphery of the oedematous skin reactions. After 24 hours, the red colour had changed to deep purple and by 48 hours the injection sites were blue-black in colour. This change in the colour at the reaction sites can be seen when Figure 14 is compared with Figure 15, which was taken 72 hours post-injection.

Small reactions which reached their maximum size three hours post-injection developed on PNC11. Very slight thickenings could still be palpated up to 24 hours post-injection.

Detectable skin reactions were not produced in any of these animals following the injections on saline.

Experiment 2 Eighteen weeks after they had been injected with Ag 113, A2, A3, A4 and Cull 1 were given triplicate injections of the standard (1/1) solution of Ag 117 while C5, which had come from the same farm as C3 and C4, was given triplicate injections of both standard and 1/10 dilutions of antigens (Table 73). The

TABLE 72 The diameter of the reactions following the intra-dermal injection of Micropolyspora faeni antigens (Ag 117).

	Diameter of Skin Reactions (mm)							
	C3							
Time (Hr)	1/1 Dilution					1/10 Dilution		
0.25	10	10	10	10	10	10	10	10
1	15 x 12	15 x 10	15 x 12	12 x 11	10	24 x 22	24	22
2	20	18 x 14	18	20 x 18	25	28 x 27	30 x 28	25
3	25 x 22	22 x 17	25 x 17	20		No Change		
4	27 x 25	26 x 21	24 x 20	21 x 20		No Change		
5	31 x 26	30 x 21	30 x 21	29		Less Prominent		
6		No Change				Less Prominent		
24	30	30 x 26	27 x 22	20	+	+	+	+
48	+		+	+	-	-	-	-
72	+		+	+	-	-	-	-
Biopsy		24 Hr						

TABLE 72 (Cont'd.)

	Diameter of Skin Reactions (mm)										
	C4								PNC11		
Time (Hr)	1/1 Dilution					1/10 Dilution			1/1 Dilution		
0.25	10	10	10	10	10	10	10	10	10	10	10
1	12	13	13	13	10	10	10	10	10	10	10
2	19 x 14	15	20	22 x 18	20	17	15	15	13	12	14
3	17 x 15	22 x 18	22 x 20	25 x 22	22	22 x 20	20 x 18	17 x 15	16	18	18
4	20	28 x 22	25 x 22	30 x 26		No Change				No Change	
5	20 x 19	25 x 22	27 x 25	33 x 28		Less Prominent				Less Prominent	
6		No Change				Less Prominent				Less Prominent	
24	25 x 21	30 x 27	Diffuse	18 x 17	±	+	+	±	±	±	±
48	+		+	+	-	-	-	-	-	-	-
72	+		+	+	-	-	-	-	-	-	-
Biopsy		24 Hr.									

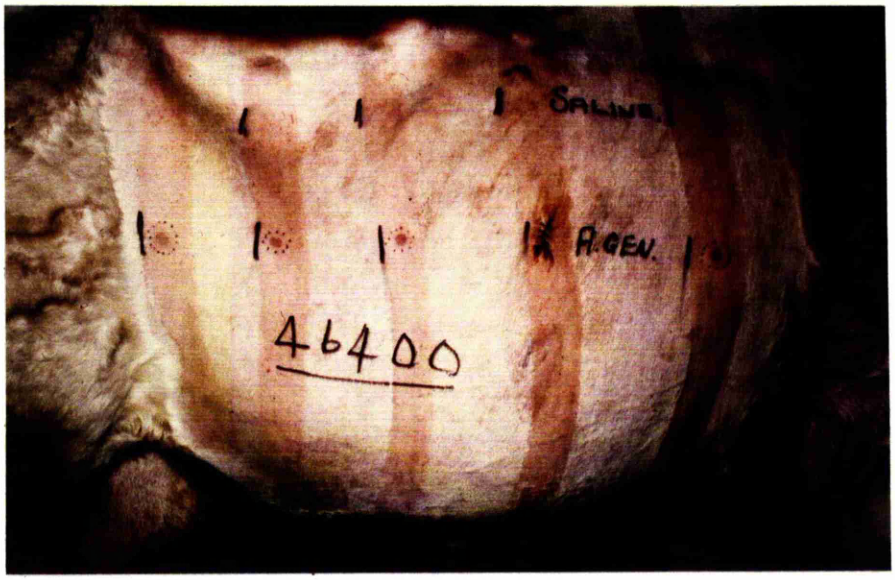


FIGURE 14 View of the right side of case C3 taken 6 hours after the intra-dermal injection of antigens derived from Micropolyspora faeni.

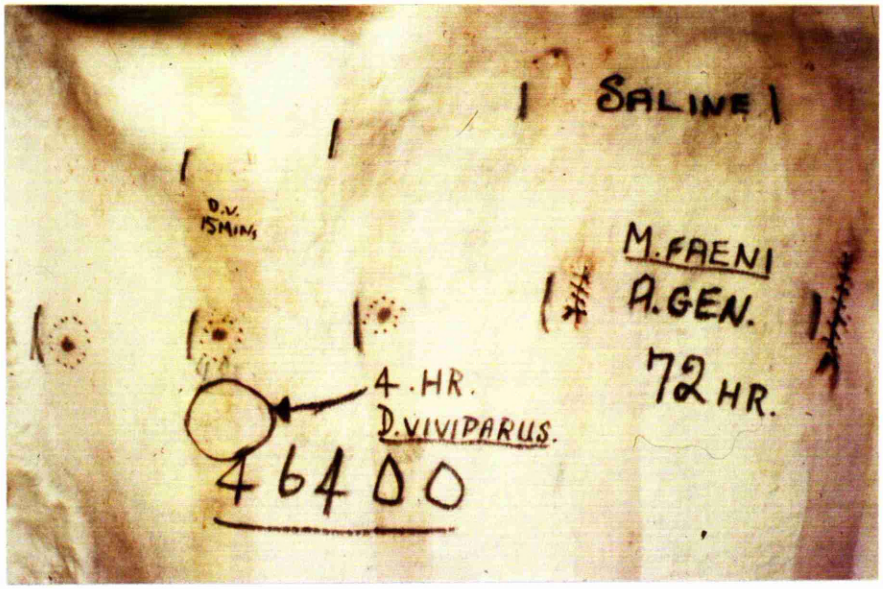


FIGURE 15 View of the right side of case C3 taken 72 hours after the intra-dermal injection of antigens derived from Micropolyspora faeni.

TABLE 73 The diameter of the reactions following the intra-dermal injection of Micropolyspora faeni antigens (Ag 117).

	Diameter of Skin Reactions (mm)														
	C5								A2						
Time (Hr)	1/1 Dilution					1/10 Dilution			1/1 Dilution			Saline			
0.25	10	10	10	10	10	10	10	10	20	34 x 26	30 x 24	21	24	21	
1	12	15	15	17	15	10	15	10	48 x 39	68 x 50	55 x 38	27	34 x 27	26 x 23	
2	14	20 x 19	20	25	19	15	20	10	52 x 37	68 x 50	62 x 50	Less Prominent			
3	23	27	27	30	20	22	28	10	No Change			Diffuse			
4	30 x 25	32 x 30	35 x 30	35 x 30	26 x 22	24	30	10	Less Prominent			Very Diffuse			
5	30 x 25	32 x 30	35 x 30	Diffuse	26 x 22	25	30	10	Less Prominent			+	+	+	
6	No Change					No Change			Less Prominent			-	-	-	
24	+			+	+	+	+	+	+	+		-	-	-	
48	+			+	±	±	±	±	±	±		-	-	-	
72	+			+	-	-	-	-	-	-		-	-	-	
Biopsy		6 Hr	6 Hr												

TABLE 73 (Cont'd.)

	Diameter of Skin Reactions (mm)											
	A3			A4			Cull 1			PNC12		
Time (Hr)	1/1 Dilution			1/1 Dilution			1/1 Dilution			1/1 Dilution		
0.25	10	10	10	12	12	18	10	10	10	10	10	10
1	20 x 17	20	19 x 17	17	20 x 17	30	10	10	15	10	10	10
2	30 x 25	25	22 x 20	27 x 21	25 x 20	32 x 30	15	20 x 18	22 x 20	10	12	12
3	36 x 28	26 x 25	29 x 26	38 x 30	26 x 20	45 x 32	26 x 20	22 x 20	27 x 25	17	16	16
4	No Change			No Change			No Change			No Change		
5	Less Prominent			Less Prominent			Less Prominent			No Change		
6	Less Prominent			Less Prominent			Less Prominent			Less Prominent		
24	+	+	+	±	±	±	+	+	+	+	±	±
48	±	±	±	±	±	±	±	±	±	±	±	±
72	±	±	±	-	-	-	-	-	-	±	±	±
Biopsy												

control animal, PNC12, was given triplicate injections of the standard solution of Ag 117 only. With the standard antigen solution, reactions first became obvious after 15 minutes (A2, A4) or after one hour (A3, Cull 1, C5). These reactions achieved their maximum size at two hours post-injection (A2), or at three hours (A3, A4, Cull 1) or at four hours (C5). The reactions on A2 were particularly large. After staying at their maximum size for about one hour, the reactions then became less prominent. Two skin biopsies of standard solution reactions were taken from C5 six hours post-injection. Skin thickenings were palpated after 24 hours at every remaining site but, at 72 hours post-injection, palpable skin thickenings were only detected on A3 and C5.

The majority of the reactions which had developed with the 1/10 dilution on C5 did so after two hours and they became maximal after five hours. Some skin thickening could still be palpated up until 48 hours post-injection.

With PNC12, the small reactions which developed after two hours and which were maximal at three hours post-injection could still be palpated after 72 hours.

Following the triplicate injections of saline, detectable reactions were not produced on any of these cows with the exception of A2. The obvious reactions which were detected on this animal after 15 minutes, reached their greatest size after one hour and then became increasingly diffuse until by six hours post-injection, no skin thickenings could be appreciated.

Experiment 3 Since reactions had developed on A2 following the injections of saline given at the same time as the Ag 113 and Ag 117 injections, it was decided to study the effect of mepyramine maleate (Anthisan: May and Baker, Dagenham, Essex) on the subsequent development of skin reactions to both saline and to Ag 117.

The day following Experiment 2 (Ag 117) described above, saline and a standard (1/1) solution of Ag 117 were injected in triplicate on the left side of A2. The saline reactions, which developed within 15 minutes, were maximal after one hour, remained the same size for two hours and then became less prominent until

by seven hours post-injection, they were very diffuse (Table 74). Slight skin thickenings were present only at 24 hours post-injection. The Ag 117 reactions, which also developed within 15 minutes, achieved their greatest size after two hours and by seven hours post-injection, they too had become very diffuse. However, some skin thickening was detected at 24 hours and 48 hours post-injection.

Two and a half hours after the above six injections had been given, one gram of Anthisan was injected intra-muscularly into A2. After a period of 30 minutes, a further three saline and five Ag 117 standard solution injections were given on the right side of A2. At the saline injection sites, only very small reactions developed within 15 minutes on this occasion and after one hour, only one reaction was 20 mm in diameter compared with all three immediately before the Anthisan had been given. The reactions quickly became diffuse and by six hours post-injection they could not be seen although distinct skin thickenings could still be palpated. These thickenings could not be detected after 24 hours. The Ag 117 reactions were also much smaller after 15 minutes and their maximum size was reached at six hours post-injection compared with two hours before the Anthisan had been given. The maximum diameter of the reactions was slightly less than before although there was little difference in their persistence; skin thickenings were detected after 48 hours but not at 72 hours post-injection.

Two of the five Ag 117 injections had been given into non-pigmented skin and, at the 15 minute observation period, it was noticed that the hairs in the centre of the reactions were erect. Around these erect hairs there was a raised circular plaque of intensely white skin at the periphery of which there was a dark red ring. These changes were still present after one hour although they did show signs of regression. By two hours post-injection, the blanching had disappeared and the centres of the reactions were uniformly red in colour. At the other three sites, which were on pigmented skin, the hairs were also noticed to be erect but obviously no colour change was appreciated. This was the only time that a true wheal and flare reaction was observed in any of the cows used for the intra-dermal injection of M. faeni antigens.

TABLE 74 The diameter of the reactions on A2 following the intra-dermal injection of saline and *Micropolyspora faeni* antigens (Ag 117) together with the effect on their development of the prior administration of mepyramine maleate*.

Time (Hr)	DIAMETER OF SKIN REACTIONS (mm)													
	Before Mepyramine Maleate						After Mepyramine Maleate							
	Saline			Ag 117			Saline			Ag 117				
0.25	21 x 17	19 x 17	14	19	19 x 18	19 x 18	10	12	12	10	12	10	10	12
1	28 x 20	20	20 x 14	28 x 24	35 x 32	30 x 27	14	13	20 x 15	12	13	17	14 x 12	20 x 15
2	No Change			29 x 26	40 x 36	35 x 27	No Change			22	13	26 x 22	25 x 22	26 x 22
3	No Change			No Change			Less Prominant			27 x 26	13	28 x 26	32 x 25	30 x 30
4	Less Prominant			Less Prominant			Diffuse			27 x 26	25 x 23	28 x 26	32 x 35	34 x 30
5	Less Prominant			Less Prominant			More Diffuse			27 x 26	27 x 25	29 x 28	32 x 26	38 x 32
6	Diffuse			Diffuse			+	+	+	27 x 26	30 x 28	30	Diffuse	47 x 35
7	More Diffuse			More Diffuse										
24	±	±	±	+	+	+	-	-	-	+	+	+	+	+
48	-	-	-	±	±	±	-	-	-	±	±	±	±	±
72	-	-	-	-	-	-	-	-	-	-	-	-	-	-

* Mepyramine Maleate (Anthisan: May & Baker, Dagenham, Essex.)

(e) Histopathology of skin biopsies

The microscopic changes in the skin biopsies taken at four-six hours, 24 hours and 72 hours post-injection from the cows with precipitins to M. faeni and injected with M. faeni antigens, were very similar and so representative sections only will be described in detail.

Six hour biopsy (Case A1) Close examination of the skin reaction immediately after it had been removed from the cow revealed that the swelling was due mostly to a localised collection of oedema fluid deep in the dermis. In Figure 16, it is possible to see the oedematous connective tissue in which there are numerous neutrophils. In addition, neutrophils can also be seen in the lumen and accumulating in the wall of a small blood vessel.

Twenty-four hour biopsy (Case C3) This biopsy was removed from the cow in Figure 14. Superficial dermal necrosis can be seen at the right hand side of Figure 17 and between this and the normal dermis there is a well defined accumulation of neutrophils. At the bottom left of the Figure there is a thrombosed small arteriole around which a few neutrophils can be seen. Slight connective tissue oedema is also present.

Seventy-two hour biopsy (Case A1) Very little connective tissue oedema can be seen in Figure 18. The cell population is markedly different from that in Figure 16 in that almost all the cells surrounding the small blood vessels are mononuclear in type; they are mainly plasma cells or lymphocytes and eosinophils with only a very small number of neutrophils.

Saline reactions (Case A1) No microscopically detectable changes were present in the biopsies from the saline injection sites taken at four and 72 hours post-injection.

Precipitin-negative control group No microscopic lesions were detected at four and 72 hours post-injection in biopsies from either the M. faeni antigen sites or the saline injection sites on PNC5.

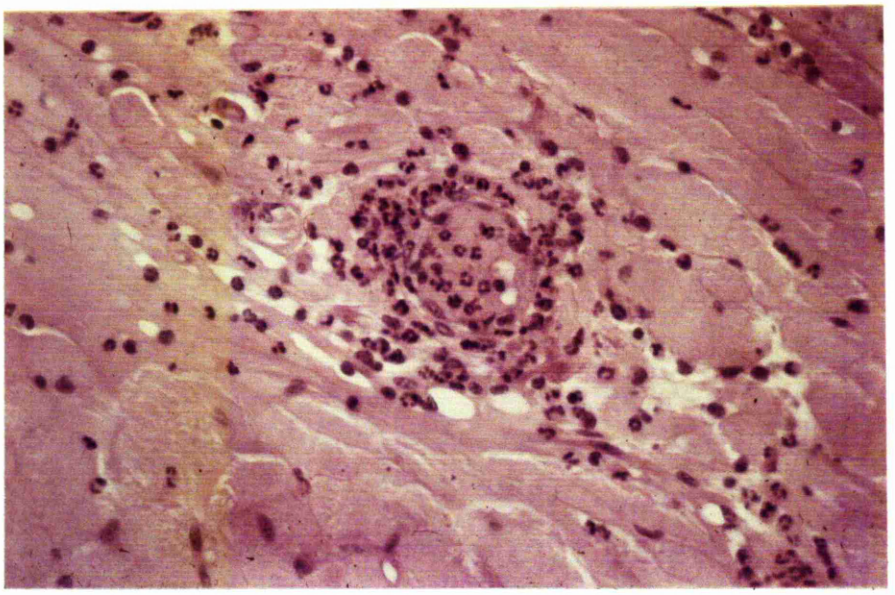


FIGURE 16 Skin biopsy from case A1 taken 4 hours after the intradermal injection of antigens derived from Micropolyspora faeni. There is oedema of the dermal connective tissue and a large number of neutrophils can be seen around and also within a small blood vessel (H & E x 250).

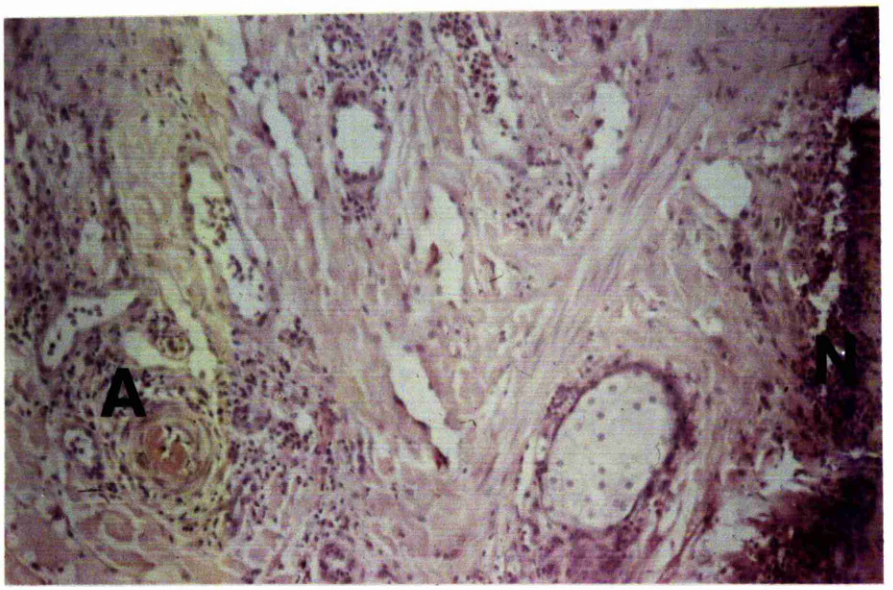


FIGURE 17 Skin biopsy from case C3 taken 24 hours after the intradermal injection of antigens derived from Micropolyspora faeni. A small thrombosed arteriole (A) can be seen as well as a dense accumulation of neutrophils (N) separating normal dermis from an area of dermal necrosis (H & E x 100).

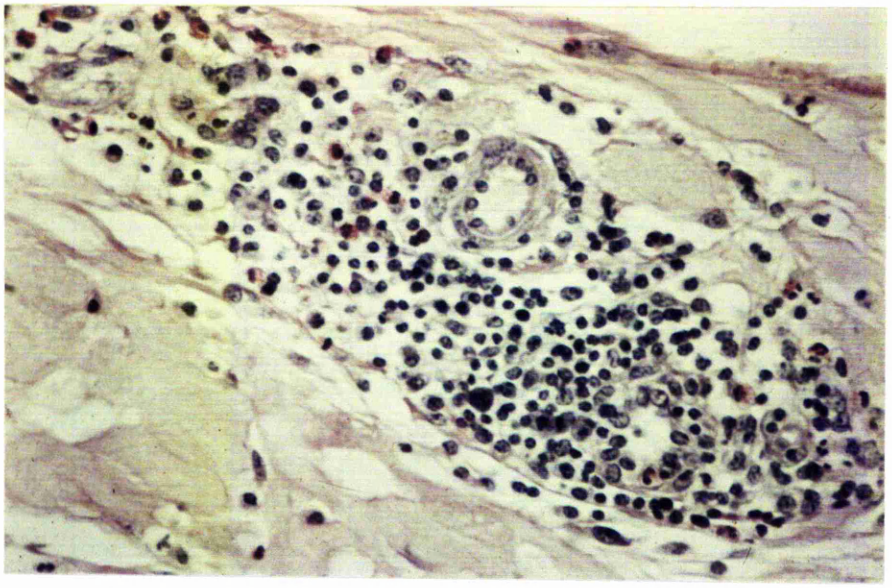


FIGURE 18 Skin biopsy from case A1 taken 72 hours after the intradermal injection of antigens derived from Micropolyspora faeni. There is a marked infiltration around the blood vessels of lymphocytes, plasma cells and eosinophils (H & E x 250).

FIGURE 19 A close-up view of a lung illustrating the pale areas of mild over-inflation at the periphery of the lobules.

DISCUSSION

The intra-dermal injection of M. faeni antigens produced detectable skin reactions in every cow with precipitins to M. faeni. The raised, plaque-like swellings which were usually visible after one hour, reached maximum size from three to five hours post-injection and then became less prominent. The reactions were not usually visible after 24 hours although firm pea-sized thickenings were often palpated in the skin up to 72 hours post-injection. The temporal development of the skin reactions is similar to an Arthus-type reaction (196).

From experimental studies with animals, various authors have concluded that the severity of an Arthus-type reaction is closely related to the titre of circulating precipitating antibody (25, 43, 80, 189). When there is a high titre of precipitating antibody a severe Arthus reaction develops with thrombosis of the dermal blood vessels and skin necrosis (8). In this investigation, skin necrosis was observed on only one (C3) of the nine cattle with precipitins to M. faeni. On the actual day that the skin tests were undertaken, the precipitin titres were estimated only in C3 (1/64), C4 (1/32) and C5 (1/4), all of whom came from the same farm. That skin necrosis only developed on the animal with a relatively very high antibody titre was in agreement with the views of the workers cited above. On the other hand, skin necrosis was not observed macroscopically on A1 which had a precipitin titre of 1/64 one week prior to her being skin tested. This may have been the result of differences in the reactivity of the M. faeni antigen preparations used, Ag 117 for C3 and Ag 42 for A1, because it has already been found that individual preparations of M. faeni vary greatly in their ability to produce precipitation reactions with cattle sera in agar gel (59). The optimum antigen to antibody ratio may not have been achieved at the injection sites on A1 since a gross excess of antibody is required for the maximum expression of a localised Arthus-type response (49). The difference in the maximum size of the reactions between the standard and the 1/10 dilutions of both Ag 42 and Ag 117 is most likely to have been the result of differing antigen/antibody ratios at the injection sites.

Although there may have been a relationship between the precipitin titre and the severity of the skin reactions, there was definitely no positive correlation between the precipitin titre and the

maximum diameter of the skin reactions on C3, C4 and C5. Indeed, the two largest reactions were on C5 which had the lowest titre (1/4).

The skin reactions were much larger on cows with precipitins to M. faeni than on the control animals with every antigenic preparation except the 1/10 dilution of Ag 42. With the standard concentration of antigen, the reactions on cows with precipitins were almost invariably in excess of 20 mm in diameter whereas on the control cows they never exceeded 20 mm in size. This is in agreement with the findings in milk allergy in which wheals of more than 20 mm in diameter were considered to indicate a positive skin test (41). PNC5 was the only control animal on which a measurable skin reaction did not develop following the injection of M. faeni antigens and it is important to note that she was only two years old. The mature control cows would almost certainly have been exposed to M. faeni previously and so they could have been sensitised even although precipitins were not detected before the skin tests were undertaken. Hence, the development of the small positive reactions in the older, precipitin-negative but nevertheless sensitised animals.

It is conceivable that some of the reaction on the control animals may have been induced by a non-specific irritant effect of the antigenic preparations. The large reactions produced by Ag 41 are likely to have been almost wholly non-specific since their maximum size and time of development were not dependent upon the presence of precipitins to M. faeni. Antigen 41 was prepared from the agar and contained the metabolic products from the growth of M. faeni and many of these are known to have enzymatic activity (29, 184, 273). The other three antigenic preparations were derived from the mycelium and spores only and so their enzymatic content was likely to have been very much smaller.

Several weeks after their experience with Ag 41, reactions developed on A2 and A3 to both saline and M. faeni antigens (Ag 113 and Ag 117) within 15 minutes of their being injected. Although these were not the only experimental animals, they were the only ones that reacted to saline. It was virtually impossible for the saline to have become contaminated with M. faeni antigens and the skin reactions did not look like typical wheal and flare reactions. Consequently, this peculiar finding would appear to have been an idiosyncrasy of the individual animals rather than the property of the saline.

Although these reactions to saline did not look like type I hypersensitivity reactions they could still have been histamine-mediated. Therefore, it was decided to administer mepyramine maleate, which has an antihistaminic action, and study the subsequent development of saline and M. faeni antigen reactions. After mepyramine maleate had been given to A2, the saline reactions were not abolished although their maximum size was markedly reduced and they persisted for a much shorter time. The reactions to Ag 117 developed more slowly but there was very little reduction in their maximum size. This was not entirely unexpected since it has been shown that, in experimental animals, anti-histaminic drugs do not inhibit the development of an Arthus-type reaction (190, 296). An unexpected finding after the administration of mepyramine maleate was the development of typical wheal and flare responses 15 minutes after the injection of Ag 117. These reactions had disappeared after two hours and it was the only time that such a response was detected in any of these experiments.

On microscopic examination of the skin biopsies taken from four to six hours post-injection, the most striking observation was the accumulation of neutrophils both within and surrounding small blood vessels which, in some cases, were thrombosed. The numbers of neutrophils had decreased within 24 hours and by 72 hours post-injection, mononuclear cells were the dominant type. Gell and Hinde (1954) produced Arthus reactions in the skin of rabbits and concluded that "where the necrosis is minimal the mononuclear response is more obvious". This was also found to be so in this study when the 72 hour biopsies from animals A1 and C3 were compared; there were greater numbers of mononuclear cells in the biopsy from A1 than from C3 in which there was thrombosis of the blood vessels and obvious skin necrosis. Since the microscopic findings in the skin biopsies from these cattle were similar to those of an Arthus-type reaction in the skin of rabbits (93), it can be deduced that these reactions were the result of an Arthus-type response. The presence of palpable thickenings at many of the injection sites after 72 hours provides some evidence that there could also have been a type IV hypersensitivity component involved.

Following the intra-dermal injection of M. faeni antigens, reactions developed after four to six hours only in animals with precipitins to M. faeni in their sera. However, if the ability to mount this Arthus-type skin response is dependent upon the presence of circulating antibody then, for routine diagnostic purposes, precipitins

can be detected more easily, although less quickly, by immunodiffusion than by skin testing.

SECTION V

THE USE OF PATHOLOGY IN THE DIAGNOSIS OF FARMER'S LUNG IN CATTLE

INTRODUCTION

The descriptions of the pathological lesions of farmer's lung in man have been based almost wholly on the examination of lung biopsy material (60, 71, 86, 90, 234, 250, 259). This method of obtaining pathological material for comprehensive investigation is unsatisfactory because the portion removed may not be representative of either the range or the severity of the lesions in other parts of the lungs. This difficulty need not arise in cattle because affected animals can be bought and, after slaughter, both lungs can be thoroughly examined.

The pathological lesions found after post-mortem examination in this series of 45 clinical cases of farmer's lung are discussed in the first and major part of this section. Following this, the differentiation of farmer's lung from other common respiratory diseases of adult cattle in Britain is presented.

MATERIALS AND METHODS

All the animals were slaughtered humanely and exsanguinated. The diagnosis of farmer's lung was confirmed in each case by macroscopic and microscopic examination of the lungs. Several portions of tissue representative of all lobes of the lungs and bronchial tree at various levels were collected from each animal together with routine samples of tissue from other organs. The tissues were fixed in corrosive formol or 10 per cent formalin, dehydrated and double embedded in celloidin and in paraffin wax in a vacuum. Sections were cut at 8 microns and stained with haematoxylin and eosin. When specific features were to be demonstrated, the following stains were also used: Prussian blue for haemosiderin, carbol chromotrope for eosinophils, astra blue saffronin for mast cells, Weigert-van Gieson for elastic and fibrous tissue and Rhinehart-Abu'l Haj for mucus and connective tissue.

RESULTS

Macroscopic pathology

Although the lungs from all cases looked relatively normal on superficial examination there was over-inflation on the peripheral acini of many lung lobules (Figure 19). Characteristically, this appeared as a pale pink raised edge around a red central portion in which a number of small grey spots (1-2 mm in diameter) could usually be seen (Figure 20). These lesions tended to be more frequent in the anterior parts of the lungs. In some animals, there were a few lobules which were pale white or yellow and firmer than normal as a result of fibrosis; these lobules were also found most often in the anterior parts of the lungs and about the carina in some long-standing cases. In several of the most severe cases, a few greyish-white "asteroid" bodies were present beneath the visceral pleura; they were 2-4 mm in diameter and projected above the surface of the surrounding lung parenchyma. These "asteroid" bodies were particularly obvious in A15 (Figure 21).

Microscopic pathology

Trachea and bronchi Many globule leukocytes and a small number of neutrophils were seen in the tracheo-bronchial epithelium of all cases and there was infiltration of the lamina propria by lymphocytes, plasma cells and other mononuclear cells. In some of the cases in which signs of respiratory disease had been noticed for a considerable time, there was a moderate degree of mucous gland hypertrophy. This was associated with the presence of excess volumes of mucus in the lumina of lungs in which fibrosed lobules were numerous.

Bronchioles Bronchiolar lesions were present in all cases although there was great variation in both their prevalence and severity. In some, bronchiolitis obliterans (Figure 22) was widespread being found in all lobes of both lungs at all levels. In the early stages, the obstructive lesion had the features of a granuloma and multinucleated giant cells were present. Macrophages, multinucleated giant cells, a few neutrophils, eosinophils and mucous plugs were to be found in the bronchiolar lumina. There were varying sized diffuse peribronchiolar aggregates of lymphocytes with some plasma cells and a few macrophages.

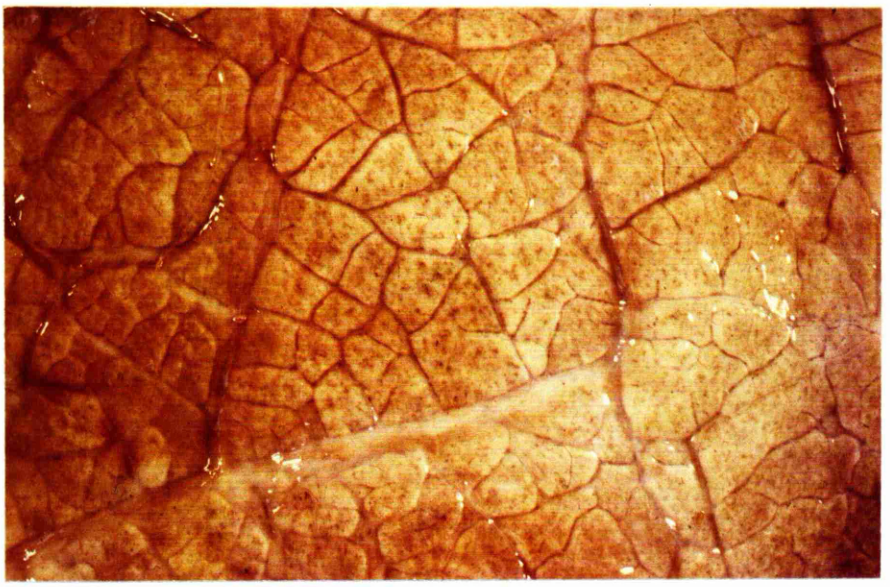


FIGURE 20 A close-up view of a lung illustrating many small grey spots within the lobules.

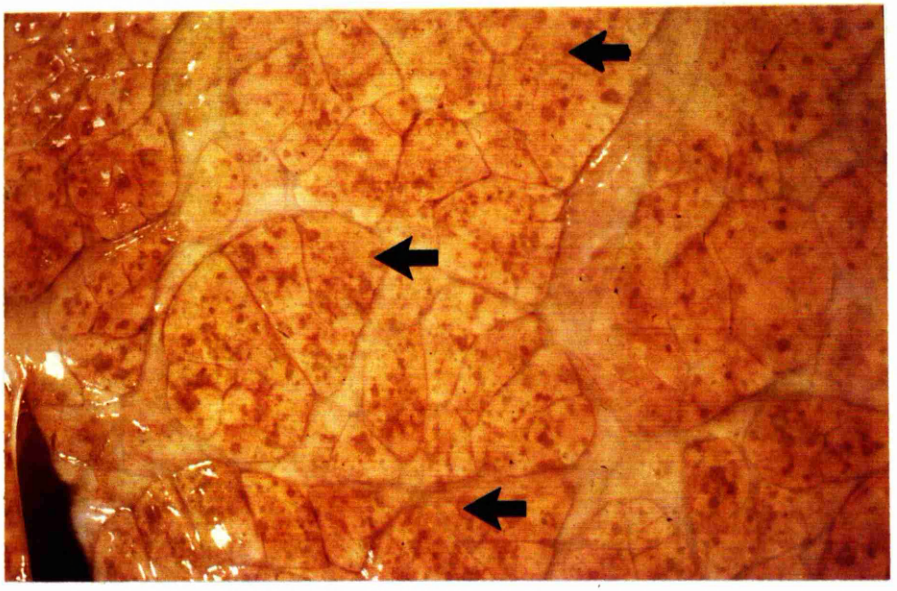


FIGURE 21 A close-up view of a lung illustrating larger greyish-white spots (arrowed), so-called "asteroid bodies".

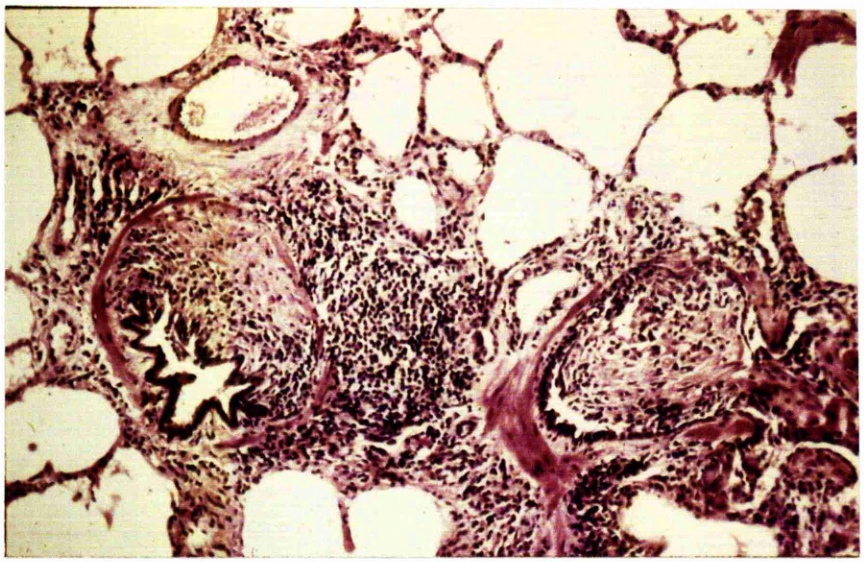


FIGURE 22 Foci of bronchiolitis obliterans which have almost completely obliterated the lumena of the affected bronchioles can be observed. A large aggregate of lymphocytes is present between the two bronchioles (H & E x 120).

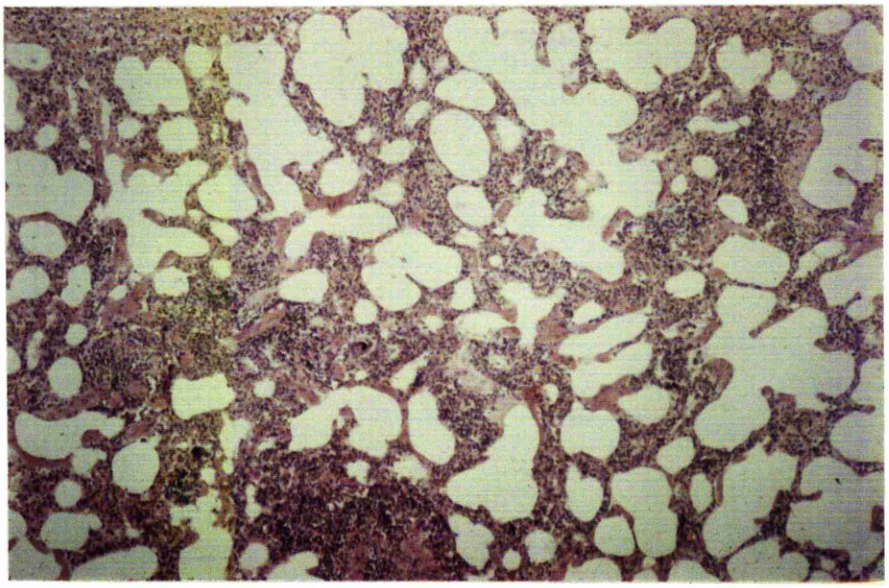


FIGURE 23 Diffuse cellular infiltration of alveolar septa and part of an interlobular septum can be observed (H & E x 100).

Alveolar ducts Obliterative lesions were sometimes seen blocking the ducts and extending into the bronchiolar lumen (Figure 22).

Alveolar spaces Free cells were not numerous in the alveolar spaces although the septa were markedly thickened. When present, they were usually lymphocytes and macrophages although plasma cells were also identified occasionally.

Inter-alveolar septa and alveolar walls In all the acute cases and in many of the chronic ones, the inter-alveolar septa and alveolar walls were thickened as a result of cellular infiltration mainly by lymphocytes, plasma cells and macrophages with a lesser number of multinucleated giant cells and eosinophils (Figure 23). In some lobules, there was also fibrosis of the inter-alveolar septa with alveolar epithelial hyperplasia (Figure 24) and even apparent focal metaplasia, where the alveoli were lined by cells resembling those of the bronchiolar epithelium.

Granulomata (Figure 25) were present in almost every case but their numbers decreased as the extent of the septal fibrosis increased. Most granulomata could be classified as epithelioid because they had a central core of neutrophils surrounded by epithelioid cells and an outer ring of lymphocytes, plasma cells and a few multinucleated giant cells (Figure 26). Fibroblasts were also seen to be intermingled with the latter cell types and there was obvious fibrosis around many granulomata. These epithelioid granulomata did not contain any demonstrable organisms, unlike the "asteroid" bodies in the centre of which fungal elements were observed ringed by amorphous eosinophilic material arranged in clubs and surrounded by multinucleated giant cells (Figure 27).

The small grey spots which were one of the characteristic features on macroscopic examination of the lungs were the sites of either bronchiolitis, bronchiolitis obliterans, granulomata or mononuclear cell aggregates.

Cardiovascular system In the three cows with definite clinical signs of cor pulmonale there was right ventricular hypertrophy (Figure 28) and dilatation of the pulmonary arterial trunk.

Interstitial emphysema This was not present in any of the 45 cases.

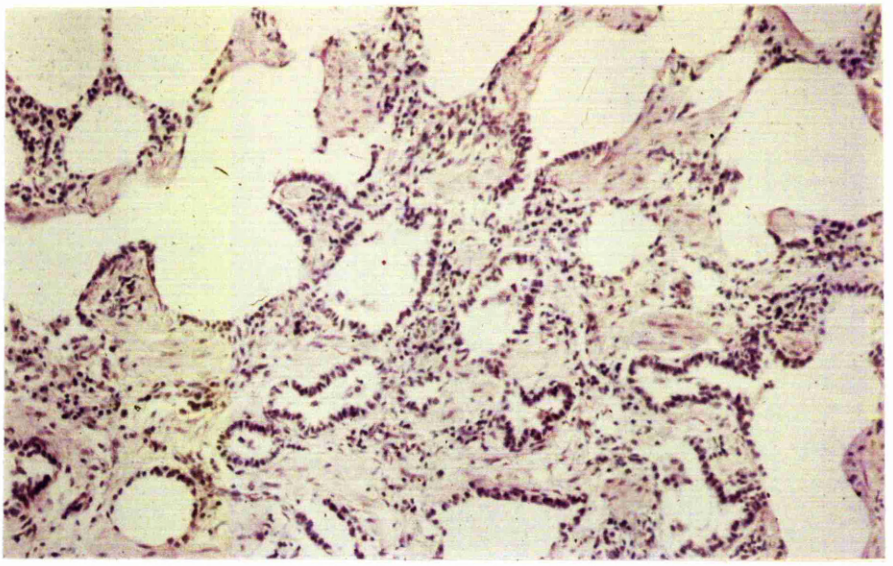


FIGURE 24 A focus of inter-alveolar fibrosis and hyperplasia of the alveolar epithelium can be seen (H & E x 100).

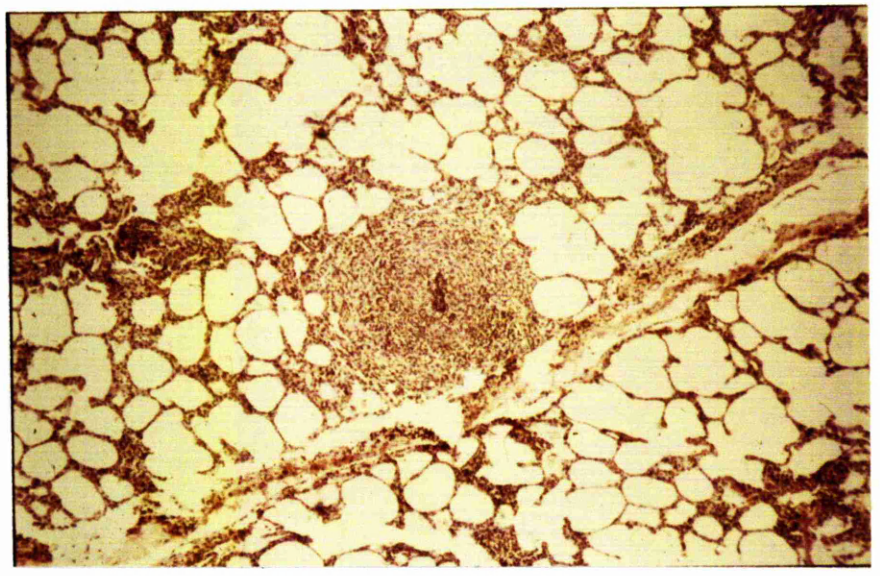


FIGURE 25 An epithelioid granulomata can be seen adjacent to an inter-lobular septum; there is also a mild cellular infiltration of the alveolar septa (H & E x 30).

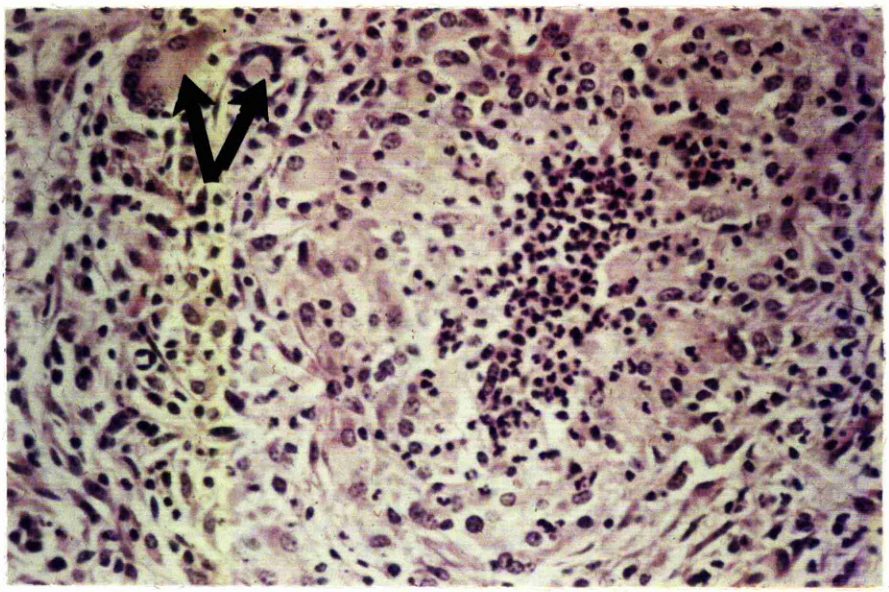


FIGURE 26 This is an epithelioid granulomata in which the central core of neutrophils is surrounded by epithelioid cells around which there are lymphocytes and plasma cells. Two multinucleated giant cells are also present (arrowed) (H & E x 250).

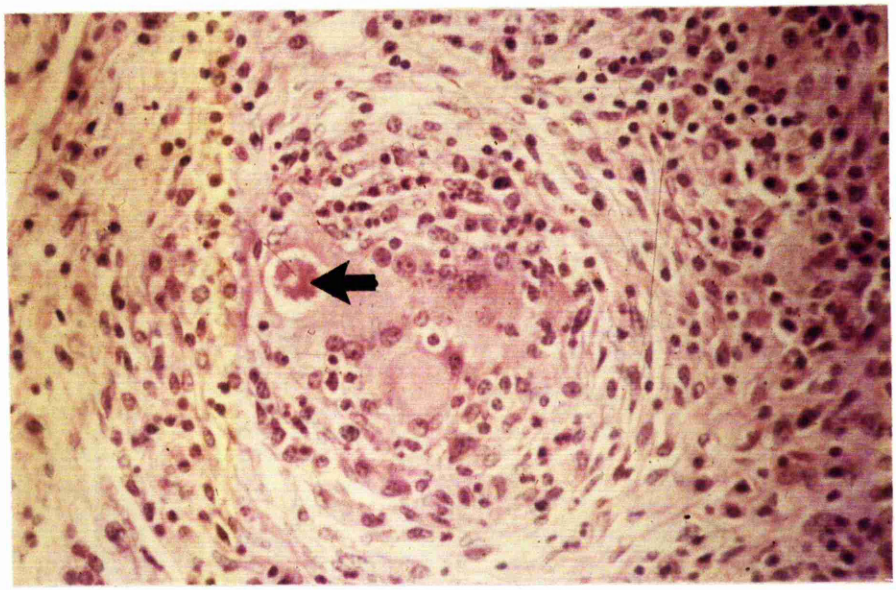


FIGURE 27 An "asteroid body" in the centre of which fungal elements can be seen surrounded by amorphous eosinophilic (arrowed) material and multinucleated giant cells (H & E x 250).

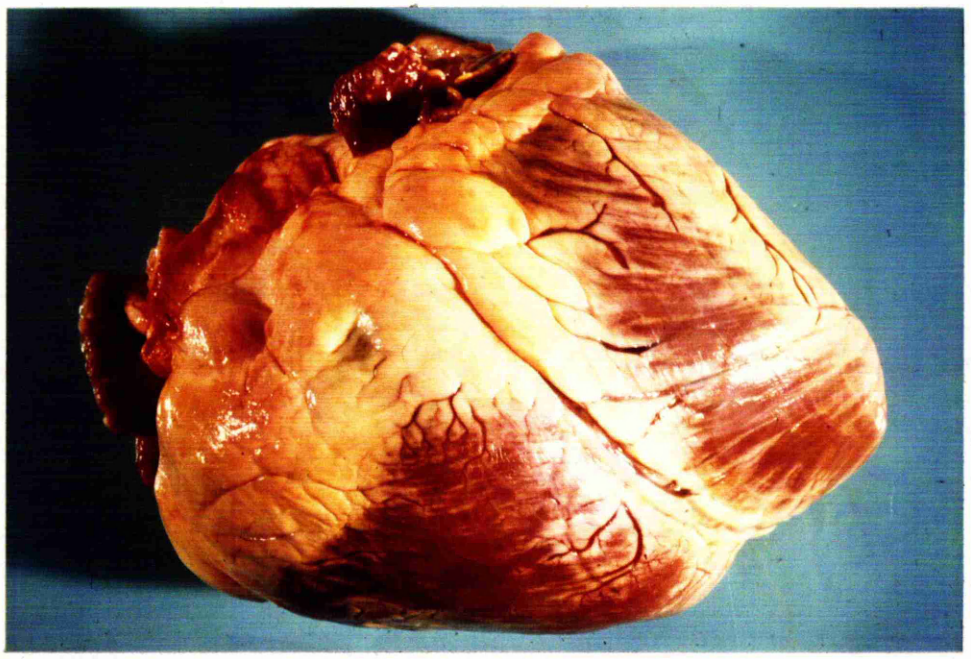


FIGURE 28 The heart from case C21 is showing obvious right ventricular hypertrophy indicative of cor pulmonale.

In the cases which had just experienced an acute episode, there was evidence of recent intra-alveolar haemorrhage with oedema fluid, neutrophils and macrophages in the alveolar spaces as well as neutrophils, macrophages and smaller numbers of plasma cells and lymphocytes in the inter-alveolar septa (Figure 29). Characteristic epithelioid granulomata with multinucleated giant cells were also prevalent. Mucus, free red blood corpuscles and neutrophils were present in the lumina of some bronchi and bronchioles. In the lamina propria there were numerous plasma cells and some foci of haemorrhage, oedema and infiltration of neutrophils and eosinophils. Bronchiolitis obliterans was widespread in all lobes and a diffuse infiltrate of lymphocytes and haemosiderin-containing macrophages was present in the peri-bronchiolar connective tissue.

Widespread pulmonary fibrosis was the most obvious lesion in cases in which respiratory signs had persisted for a considerable time. Because of the fibrosis, the lungs were up to twice as heavy as normal and also paler in colour (Figure 30) than lungs from a healthy ex-sanguinated bovine (Figure 31). Lesions of bronchitis, bronchiolitis, bronchiolitis obliterans, cellular infiltration of the inter-alveolar septa and epithelioid granulomata were found also. The infiltration of the inter-alveolar septa was mostly by lymphocytes and plasma cells and was invariably multi-focal. The granulomata consisted of aggregates of mononuclear cells without an obvious central core of neutrophils. In the lobules that were severely fibrotic, the alveolar epithelium of many acini was often replaced by tall columnar, ciliated or mucous-secreting cells resembling those of the bronchiolar epithelium. In some alveolar spaces, many alveolar macrophages or foamy desquamated type II pneumonocytes were seen. Areas of cystic change were also identified in some of the more fibrosed lobules. The small cystic spaces (3-5 mm in diameter) were visible usually at the edge of the lobules. No particular distribution pattern for the fibrosis or the cystic changes was recognised.

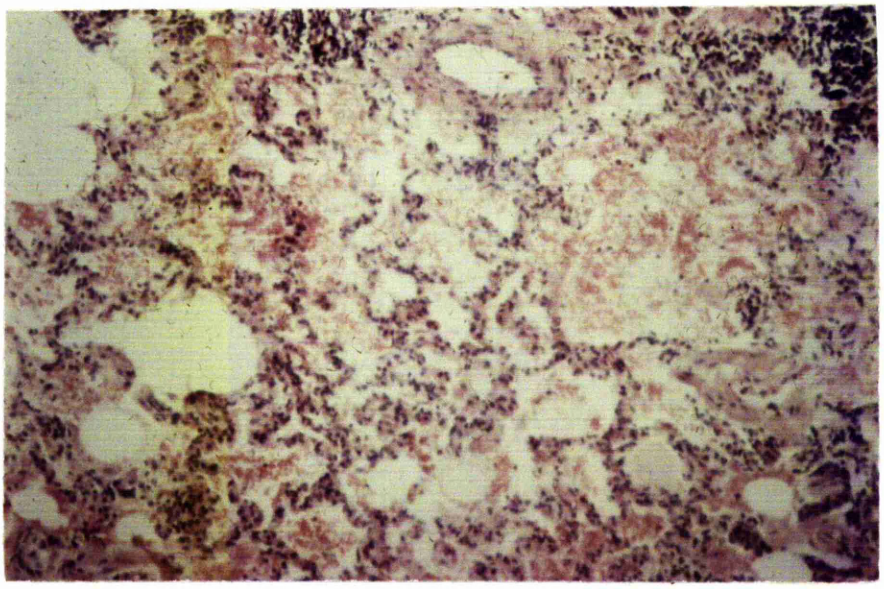


FIGURE 29 There is extensive intra-alveolar haemorrhage and cellular infiltration of the alveolar septa (H & E x 100).

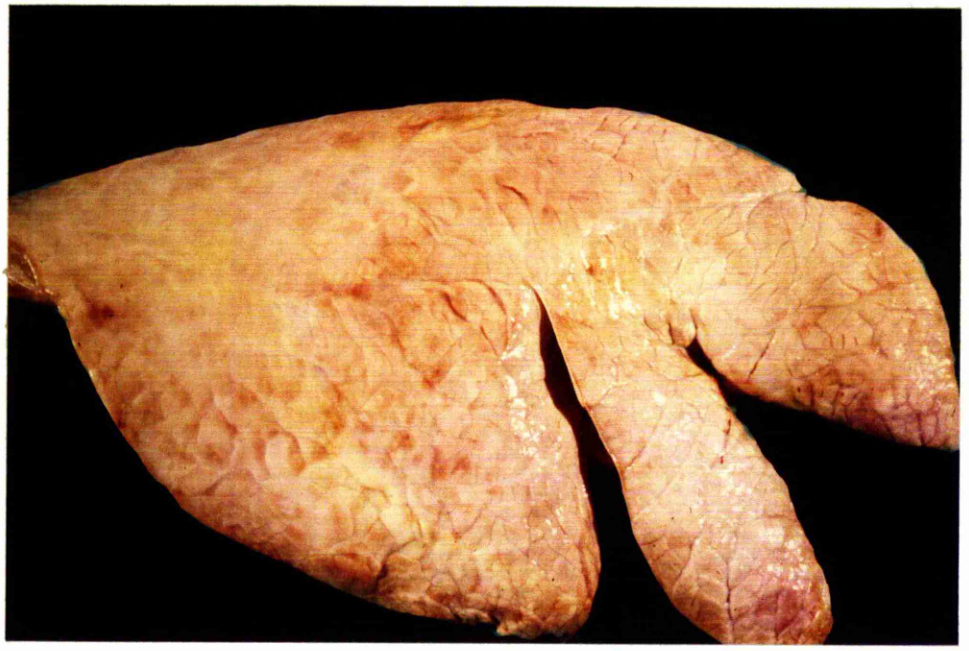


FIGURE 30 This lung from a long-standing case of chronic farmer's lung is pale in colour.

FIGURE 31 This set of healthy lungs from a calf show the typical pink colour in an animal that has been exsanguinated.

DISCUSSION

The most significant finding on macroscopic examination of the lungs of the 45 animals in this series was the apparent lack of dramatic pulmonary lesions even in those most severely affected. However, to the discerning pathologist, typical and often widespread abnormalities could be observed on close examination. The most obvious lesions were the small grey spots which were almost always situated in the middle of a lung lobule around the edge of which there was a pale zone. There are few descriptions of the macroscopic appearance of lungs from human patients with acute farmer's lung since virtually all the material has been obtained from lung biopsies (60, 71, 234). Nevertheless, in one case (259) the surgeon stated that there were numerous sub-pleural nodules and, in another, nodules were seen on the cut surface of every lung lobe (22).

The various lesions recognised on microscopic examination of the cattle lungs were identical to those which had already been described in man (14, 60, 71, 86, 234, 259). An intense mononuclear cellular infiltration of the inter-alveolar septa was widespread in all the acute and in many of the chronic bovine cases. Where there was extensive fibrosis, there were only scattered foci of mononuclear cells. This may have indicated that a considerable period of time had elapsed since the animal had last been exposed to mouldy hay or perhaps that there had been an alteration in the ability of the fibrosed lung to respond fully to further immunological assault.

Bronchiolitis obliterans was found in 25 per cent of the biopsies in one large series of acute human cases (71). In contrast, this lesion was seen in the airways in every one of the bovine cases probably because more sections were available for examination. The obliterative lesions, almost polyp-like in some areas, were most extensive and dramatic in the acute form of the disease. In the more long-standing cases, the airways were distorted as a result of permanent damage. This had probably resulted from local hypersensitivity episodes because it has been noticed in man that interstitial fibrosis developed in the same areas that parenchymal infiltration occurred (71).

Well-defined granulomata were present in every acute bovine case and also in many of the chronic cases. In the latter group in which the interstitial fibrosis was more widespread, aggregates of mononuclear cells were observed in the inter-alveolar septa. The

multinucleated giant cells commonly seen towards the periphery of these granulomatous lesions, were morphologically similar to those of the Langhans-type although others similar to the "foreign body" type were also seen. Seal and others (1968) found epithelioid granulomata only in the acute form of the human disease whereas in these cattle, granulomata were present in both acute and chronic forms. Consequently, their presence is more likely to be confirmation of relatively recent exposure to mouldy hay rather than microscopic evidence of a recent clinical acute episode of farmer's lung. Granulomata are said to take up to three weeks to develop in man and up to 12 months to resolve (234).

Although foreign material, probably of plant origin, was identified in several of these cases, it was not a common finding and tended to be associated with known recent exposure to very mouldy hay. Other lesions which were seen in cases examined within a few days of an acute episode included intra-alveolar haemorrhage, pulmonary oedema, a predominately mononuclear cellular infiltration of the inter-alveolar septa and similar cell types within the alveolar spaces. In the pulmonary blood vessels of acute human cases, Seal and others (1968) observed swelling of the muscle fibres and vacuolation of the endothelial cells. That this was a true "vasculitis" (233) was questioned by Emanuel (1974) who considered that these changes were simply the result of pulmonary hypertension. The vascular lesions described above (233, 234) have not been observed so far in acute bovine cases although hypertrophy of the media of the blood vessel walls and right ventricular hypertrophy indicating pulmonary hypertension was seen in the three cases with obvious clinical evidence of cor pulmonale.

The cystic changes which are so often found in the upper lung lobes of chronic farmer's lung patients (234) were rarely detected in cattle. This form of change is found most often in terminal cases and so the duration of exposure required for their development is likely to be several times greater than the life expectancy of the average dairy cow. On the other hand, the lack of cystic change could be a manifestation of the differences in the pulmonary anatomy between man and cattle or even the result of differences in their response to inhaled allergens.

In the cases with widespread pulmonary fibrosis, the lungs were up to twice as heavy as normal and this occurred in the absence of

pulmonary oedema. There was no obvious difference in the degree of fibrosis between the upper and lower areas of the lungs in cattle whereas in man fibrosis associated with farmer's lung is said to be more severe in the upper lobes (89, 234).

The characteristic pathological features of the common respiratory diseases of adult cattle (older than two years) in Britain that are of use in differential diagnosis have been described in detail and illustrated by Breeze and others (1975). The salient features have been summarised in Table 75. In farmer's lung, there are no dramatic macroscopic lesions compared with acute bacterial pneumonia. The mononuclear cellular infiltration of the alveolar septa and walls is typical only of a farmer's lung-type disease (extrinsic allergic alveolitis). Although bronchiolitis obliterans can be found in the diaphragmatic lobes in some cases of parasitic bronchitis (34) and also in the apical lobes in some forms of calf pneumonia (2), the accompanying lesions enable a diagnosis to be made without any difficulty.

Diffuse pulmonary fibrosis is not uncommon in adult cattle in Britain but as yet, farmer's lung is the only specific disease with which this type of change has been definitely associated (34, 209).

In the "asteroid" bodies which develop following the inhalation of Aspergillus spores (9), fungal elements can usually be distinguished in the centre of the lesion. The nodules associated with re-infection parasitic bronchitis are much larger than the farmer's lung granulomata and they are obviously dissimilar on microscopic examination (207).

Farmer's lung is a respiratory disease of adult cattle which can be differentiated relatively easily from other respiratory conditions because of the presence of the following characteristic lesions: mononuclear cellular infiltration of the alveolar septa and walls, bronchiolitis obliterans, epithelioid granulomata and a variable degree of interstitial fibrosis (35).

TABLE 75 The major pathological features of the common respiratory diseases of adult cattle.

Respiratory Disease	Macroscopic Features	Microcopic Features
Farmer's lung	Many centri-lobular, small grey spots. Overinfiltration of peripheral acini of lobule.	Diffuse mononuclear cellular infiltration of alveolar septa. Bronchiolitis obliterans. Epithelioid granulomata. Alveolar septal fibrosis.
Diffuse fibrosing alveolitis	Pale, heavy lungs. Some yellow-grey oedematous lobules. Excess mucus in bronchi and bronchioles.	Diffuse alveolar septal fibrosis. Diffuse alveolar epithelial hyperplasia. Focal replacement of alveolar epithelium by ciliated and mucous secreting cells.
Fog fever	Large voluminous lungs. Severe oedema, congestion and interstitial emphysema. Haemorrhages in trachea and bronchi.	Massive oedema and hyaline membranes. Alveolar epithelial hyperplasia of type 2 pneumonocytes.
Milk allergy	Large voluminous lungs. Severe oedema, congestion and interstitial emphysema.	Severe oedema and hyaline membranes. Intra-alveolar haemorrhage.
Acute bacterial pneumonia	Severe consolidation of anterior lobes. Pus in bronchioles and alveoli. Fibrinous pleurisy.	Massive accumulations of neutrophils and macrophages in alveoli. Local congestion and oedema.

TABLE 75 (Cont'd.)

Respiratory Disease	Macroscopic Features	Microscopic Features
Chronic suppurative pneumonia	Consolidation of anterior lobes with areas of suppurative and inter-lobular fibrosis. Bronchiectasis. Pulmonary abscesses.	
Embolic pneumonia (P.V.C. Thrombosis)	Areas of suppurative pneumonia and intra-pulmonary haemorrhage leading to clotted blood in airways and globular masses within the substance of the lung. Thrombosis of posterior vena cava.	
Patent parasitic bronchitis	Adult D. viviparus worms in airways. Areas of collapse and consolidation in diaphragmatic lobes. Interstitial emphysema.	Eosinophilic infiltration of bronchi. Aspirated, larvated eggs in alveoli surrounded by eosinophils and macrophages.
Reinfection parasitic bronchitis	Many sub-pleural raised, grey-green nodules (3-4 mm diameter).	Larval debris in bronchioles surrounded by eosinophils and lympho-reticular cells.

A BOVINE RESPIRATORY DISEASE SIMILAR TO FARMER'S LUNG IN MAN

TWO VOLUMES

VOLUME 2

by

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THE EXPERIMENTAL PRODUCTION OF FARMER'S LUNG IN CATTLE

GENERAL INTRODUCTION

The inhalation of organic dust can result in the development of two major forms of hypersensitivity respiratory disease in man (52). In the first which affects only the small proportion of people who are atopic, the bronchi are mainly affected and respiratory signs develop less than 30 minutes after exposure to the relevant antigens. This is a type I hypersensitivity reaction mediated by non-precipitating reaginic antibody (IgE). The second type affects non-atopic individuals and is due to the repeated inhalation of organic dust usually over a prolonged period. The respiratory symptoms which develop four to six hours after exposure are considered to be mainly the result of a precipitating antibody-mediated type III or Arthus-type reaction in the peripheral gas-exchanging parts of the lungs. Extrinsic allergic alveolitis is the name given to this latter form of respiratory disease (196) and, since farmer's lung was first reported in 1932 (40), many similar conditions have been described (48, 111, 181).

Hypersensitivity pneumonias have been produced experimentally in several species of laboratory animals in an attempt to understand the pathogenesis of extrinsic allergic alveolitis (Table 76). In many of these studies the animals were sensitised with soluble antigens, often in complete Freund's adjuvant, given intra-muscularly and then sacrificed after a single aerosol challenge. This type of experimental approach fails to take into account possible differences in the pulmonary anatomy and immune responsiveness of the experimental animals compared with man and also the cumulative effects of frequent and varied exposures to particulate antigens inhaled over a prolonged period. These objections might be overcome if it were possible to study a form of extrinsic allergic alveolitis that occurred naturally in an animal species. Farmer's lung has been shown to be a naturally-occurring respiratory disease of cattle (207, 291) and so this species would appear to be an appropriate model with which to begin an experimental investigation of extrinsic allergic alveolitis.

The following experiments were undertaken in order to find out whether clinical signs and pulmonary lesions similar to those occurring in the bovine form of farmer's lung could be produced under controlled conditions. The experimental details were as follows:

TABLE 76 A summary of the main details in experimental studies of extrinsic allergic alveolitis.

Authors	Experimental Animals	Sensitisation and Challenge Procedure	Clinical Response Post-Challenge	Major Pathological Findings
Zettergren (1950)	Rabbits	(i) Daily inhalation of threshing dust.	Dyspnoea	Bronchitis Alveolar emphysema
		(ii) Daily inhalation of threshing dust and *C. albicans*.	Stertorous respiration.	Granulomata
Parish (1961)	Guinea pigs Rabbits	(i) Inhalation of mouldy hay dust.	No response	Tuberculoid granulomata
		(ii) Prolonged inhalation of mouldy hay dust.	Dyspnoea	-
Tewkesbury and others (1968)	Guinea pigs	(i) Repeated intra-dermal injection of *C. corticale* spores.	Not mentioned	-
		(ii) As (i) followed by repeated daily inhalations of *C. corticale* spores.	Not mentioned	Granulomata. Infiltration of alveolar walls.
		(iii) Daily inhalation of *C. corticale* spores for 4 weekly periods.	Not mentioned	Granulomata. Infiltration of alveolar walls.
Fink and others (1970)	Rats	Prolonged daily inhalation of pigeon droppings extract.	Not mentioned	Mononuclear cellular infiltration of alveolar septa. "Foamy" cells. Granulomata.
Jones (1970)	Rabbits	Preparation of *M. faeni* given intra-tracheally.	Not mentioned	Many epithelioid tubercules. Features of type III and type IV reactions.

TABLE 76 (Continued)

Authors	Experimental Animals	Sensitisation and Challenge Procedure	Clinical Response Post-Challenge	Major Pathological Findings
Eskenasy (1971)	Rabbits	Several injections of bovine serum in C.F.A. Challenge - bovine serum given intra-tracheally.	Not mentioned	Macrophages and granulocytes in alveolar spaces. Granulomata in alveolar walls.
Richerson and others (1971)	Rabbits	Injection of ovalbumin in C.F.A. Challenge - ovalbumin aerosol.	None observed	Alveolitis Peribronchiolitis
Zaidi and others (1971)	Guinea pigs	(i) Saline solutions of M. faeni.	Not mentioned	Granulomata
		(ii) Saline solutions of sterile dust.	Not mentioned	Bronchitis
		(iii) Solutions of M. faeni and sterile dust.	Not mentioned	Inter-alveolar fibrosis
Kawai and others (1972)	Rabbits	(i) M. faeni antigens given by various routes.	Not mentioned	Minimal lung changes.
	Rats	(ii) Daily inhalation of bagasse extract for a variable period.	Not mentioned	Intense interstitial pneumonitis. Lymphocytic infiltration of alveolar septa. Peri-bronchial lymphoid hyperplasia.
Kochman and others (1972)	Rabbits	M. faeni antigens in C.F.A. Challenge - aerosol of M. faeni.	Death in 5-35 minutes.	Allergic alveolitis. Intra-vascular coagulation.

TABLE 76 (Continued)

Authors	Experimental Animals	Sensitisation and Challenge Procedure	Clinical Response Post-Challenge	Major Pathological Findings
Wilkie and others (1973)	Guinea pigs	M. faeni antigens in C.F.A. Challenge - weekly aerosol with M. faeni.	Tachypnoea	Acute vasculitis and thrombosis. Alveolar epithelial hyperplasia. Diffuse infiltration with eosinophils and neutrophils. Obstructive bronchiolitis.
Hensley and others (1974)	Monkeys	Injection of pigeon serum in C.F.A. Challenge - aerosol of pigeon serum.	Pyrexia Tachypnoea.	Haemorrhagic alveolitis. Granulocytic cuffing around blood vessels. Granulomata.
Wilkie (1976)	Calves	(i) Injection of M. faeni antigens in C.F.A. Challenge - aerosol of M. faeni antigens. (ii) Weekly inhalation of M. faeni antigens.	Cough Tachypnoea Dyspnoea	Alveolar septal thickening. Macrophages, neutrophils and red blood cells in alveolar spaces. Vasculitis.

C.F.A. - complete Freund's adjuvant.

Experiment 1 - Four calves were continually exposed to mouldy hay for ten weeks and then slaughtered.

Experiment 2 - Four calves were exposed to an aerosol of M. faeni antigens for a period of 30 minutes every week for 11 successive weeks.

Experiment 3 - Four calves were exposed to mouldy hay dust for a period of 30 minutes every week for 11 successive weeks.

Experiment 4 - At the end of Experiments 2 and 3 two calves were selected from each group and then exposed continually to mouldy hay for a total of 18 weeks before being slaughtered.

EXPERIMENT 1

MATERIALS AND METHODS

Experimental animals (EA)

The experimental animals (EA73, EA74, EA75, EA76) were four month old, parasite-free, castrated Friesian calves none of which had been treated for respiratory disease. In addition to the mouldy hay (see below) which was their only source of roughage, 5 lb per head per day of commercial calf-rearing pencils (BOCM-Silcocks, Basingstoke, England) were fed.

Method and duration of exposure

The four calves were kept in a loose-box (13.5 x 13.5 x 9 = 1640 cu. ft.) with the door and window permanently shut. Every morning and evening for ten weeks about 30 lb of mouldy baled hay was thoroughly shaken out and left on the floor. The hay been purchased from the owner of herd FL3 (Chapter 3, Section II).

Clinical examination

These calves were looked at daily for signs of respiratory disease and a full clinical examination was carried out at the end of the experiment.

Blood samples

Blood was taken from the jugular vein before the experiment began and at four, seven and ten weeks post-exposure. After the samples had been spun at 1300 g for 30 minutes, the serum was removed and stored at -20°C until required.

Preparation of Micropolyspora faeni antigens

The methods of preparing the M. faeni antigens for use in the double diffusion test were identical to those already described in Chapter 3, Section II.

Double diffusion test

The procedure for the double diffusion test was identical to that already described in Chapter 3, Section II.

Pathological examination

At the end of the experiment, the calves were slaughtered humanely and exsanguinated. Several portions of tissue representative of all lobes of the lungs and bronchial tree at various levels were collected from each animal. The tissues were fixed in corrosive formol or 10 per cent formalin, dehydrated and double embedded in celloidin and in paraffin wax in a vacuum. The sections were cut at 8 microns and stained with haematoxylin and eosin.

RESULTS

Serology

After four weeks exposure to mouldy hay, precipitating antibodies to M. faeni were detected in three calves (Table 77) and after seven weeks, they were present in the sera of all four animals. But when slaughtered, EA73 was precipitin-negative.

Clinical signs

During the ten week period that the four calves were in the loose-box and bedded with mouldy hay, no change in their respiratory disease status was observed. Every calf was seen to cough occasionally particularly during the time that the hay was actually being shaken out. The calves were never anorexic or dull and their resting respiratory rates remained at 30-40 per minute during the whole of the experiment. Adventitious lung sounds were not detected on auscultation just prior to necropsy.

Macroscopic pathology

A few small grey spots less than 1 mm in size were seen scattered in some lobules in cranial parts of the lungs of EA73 and EA76. There were no obvious lesions in the lungs of EA74 and EA75.

Microscopic pathology

Essentially similar lesions were present in all four animals; they were most pronounced in EA76, were slightly less severe in EA73 and were least extensive in EA74 and EA75.

There was a mild bronchitis in EA75 and EA76 with a slight increase in the numbers of lymphocytes and plasma cells in the lamina

TABLE 77

The temporal development of precipitating antibodies to Micropolyspora faeni, the clinical signs and comparative severity of the pathological lesions.

Calf No.	Precipitins to M. faeni				Clinical Signs	Comparative Pathological Score
	Pre-exposure	Week 4	Week 7	Week 10		
EA73	-	+	+	-	-	**
EA74	-	+	+	+	-	*
EA75	-	+	+	+	-	*
EA76	-	-	+	+	-	***

propria of the small bronchi. Some neutrophils were seen migrating through the bronchial epithelium. No bronchiolitis obliterans or well-developed epithelioid granulomata were found although several sections were examined from each block. Considerable accumulations of lymphocytes and macrophages, almost forming small nodules, were seen in the connective tissue around the bronchioles, particularly the terminal bronchioles, and infiltration from these sites extended into the adjacent alveolar walls. A few of the aggregates in the peri-bronchiolar tissue of EA76 had central haemorrhage.

There were focal infiltrations of the alveolar septa by macrophages and lymphocytes with some plasma cells and occasionally eosinophils. Small accumulations of cells, which were mostly macrophages, were also seen. Multinucleated giant cells were discovered in EA75 and EA76 and in one cell, brownish refractile material, possibly of plant origin, was seen. The multinucleated giant cells were present in alveolar air spaces adjacent to thickened septa. However, the air spaces were usually clear and the cellular infiltration was generally interstitial in the alveolar septa and walls.

Lymphocytes and plasma cells were seen in moderate numbers in some inter-lobular septa around infiltrated lobules. The inter-lobular septa were not significantly thickened.

EXPERIMENT 2

MATERIALS AND METHODS

Experimental animals (EA)

The four animals (EA6, EA7, EA17, EA20) were five to six month old, parasite-free, castrated Friesian calves none of which had been treated for respiratory disease. They were given good quality hay ad libitum and 7 to 8 lb of a commercial calf rearing concentrate (BOCM-Silcocks, Basingstoke, England). These four calves were housed together with the four calves on Experiment 3 and four environmental control animals in two pens in a large airy building.

Method and duration of exposure

The four calves were exposed for 30 minutes to an aerosol of *M. faeni* antigens generated by a Wright nebuliser (Aerosol Products (Colchester) Ltd., London). The nebuliser was connected to a small funnel inserted through a hole in the bottom of a plastic bucket. A firm cardboard cover was placed over the top of the bucket and in the centre of this, there was a hole into which the anterior part of the calf's head was inserted. The pail was then kept in place by being tied to the calf's halter. The calves were exposed once per week for 11 successive weeks and, during the 30 minute aerosolisation period, from 1.5 to 2.0 ml of antigen solution was aerosolised.

The *M. faeni* antigen preparation for aerosolisation was derived from strain IMI 134062 which had been grown on half-nutrient agar slopes in universal bottles for six days. The culture growth was then scraped off, mixed with 10-12 ml of sterile water and made into a uniform solution by mixing in a tissue-grinder for five minutes. This solution was used to inoculate 7 litres of half-nutrient broth in a bulk fermentor which had been developed jointly in the Mycology laboratories of the Departments of Botany and Chemistry in the University of Glasgow. After three days incubation, the culture was harvested and stored in 10 ml aliquots at -20°C until required for aerosolisation.

Clinical examination

The calves were looked at regularly for several hours after exposure to the *M. faeni* aerosol.

Blood samples

Blood was removed from the jugular vein before the start of the experiment and then at weeks 1, 3, 7 and 10 post-exposure. After the samples had been spun at 1300 g for 30 minutes, the serum was taken off and stored at -20°C until required.

Preparation of Micropolyspora faeni antigens

The methods of preparing M. faeni antigens for use in the double diffusion test were identical to those already described in Chapter 3, Section II.

Double diffusion test

The procedure for the double diffusion test was identical to that already described in Chapter 3, Section II.

RESULTS

Serology

Precipitating antibodies to M. faeni were not detected in any of the samples taken before the experiment began or after one, three, seven and ten periods of exposure to the aerosol. Precipitins were not detected in any of the four control calves.

Clinical signs

Apart from occasional coughing, detectable signs of respiratory disease were absent when these calves were looked at regularly up to six hours post-exposure. Six hours after the 11 successive weekly exposures, none of the calves was tachypnoeic or hyperpnoeic, their rectal temperatures were within the normal range and adventitious lung sounds were not heard on auscultation.

Pathology

As neither precipitating antibodies to M. faeni had developed nor clinical signs of respiratory disease had become obvious, none of the calves was slaughtered.

EXPERIMENT 3

MATERIALS AND METHODS

Experimental animals

The four animals (EA4, EA8, EA16, EA37) were five to six month old, parasite-free, castrated Friesian calves none of which had been treated for respiratory disease. They were given good quality hay ad libitum and 7 to 8 lb of a commercial calf-rearing concentrate (BOCM-Silcocks, Basingstoke, England). These four experimental calves were housed together with the four calves on Experiment 2 and four environmental control animals in two pens in a large airy building.

Method and duration of exposure

The calves were put into individual calf boxes (4 x 8 x 8 = 256 cu. ft.) and exposed to mouldy hay dust. This was achieved by vigorously shaking out 15-20 lb very mouldy hay in the box and then leaving the calf for 10 minutes. This procedure was carried out three times during the 30 minute exposure period. The calves were exposed to mouldy hay dust once per week for 11 successive weeks. The hay used in this experiment came from farm FL3 (Chapter 3, Section II) and was part of the same consignment as that used in Experiment 1.

Clinical examination

The calves were looked at regularly for several hours after exposure to the mouldy hay dust.

Blood samples

Blood was removed from the jugular vein before the start of the experiment and then at weeks 1, 3, 7 and 10 post-exposure. After these samples had been spun at 1300 g for 30 minutes, the serum was taken off and stored at -20^{o}C until required.

Preparation of Micropolyspora faeni antigens

The methods of preparing the M. faeni antigens for use in the double diffusion test were identical to those already described in Chapter 3, Section II.

Double diffusion test

The procedure for the double diffusion test was identical to that already described in Chapter 3, Section II.

RESULTS

Serology

Precipitating antibodies to M. faeni were not detected in any of the samples taken before the experiment began or following one, three, seven or ten periods of exposure.

Clinical signs

While they were in the calf boxes and inhaling the mouldy hay dust, the calves coughed frequently, they became tachypnoeic (Resp. Rate = 40-50 per minute) and moderately hyperpnoeic. Within 15 minutes of their coming out of the boxes, their frequency of coughing decreased markedly and they reverted to their previous rate and depth of respiration. Apart from occasional coughing, no obvious signs of respiratory disease were detected when these calves were looked at regularly for up to six hours post-exposure. None of the calves was hyperpnoeic or tachypnoeic six hours after the 11 successive weekly exposures; their rectal temperatures were within the normal range and adventitious lung sounds were not heard on auscultation.

Pathology

As neither precipitating antibodies to M. faeni had developed nor clinical signs of respiratory signs had become obvious, none of the calves was slaughtered.

EXPERIMENT 4

MATERIALS AND METHODS

Experimental animals (EA)

Four weeks after the end of Experiments 2 and 3, two animals were selected from Experiment 2 (EA17, EA20) and two from Experiment 3 (EA4, EA16). At this time the calves were approximately eight months of age. When they were not being exposed to mouldy hay, these four animals were housed in a big airy court along with four environmental control calves of the same age from the same farm. During the course of the experiment, the experimental and the control calves were given 8-10 lb of low protein dairy cattle nuts (BOCM-Silcocks, Basingstoke, England) and the control calves were always given good hay which was not dusty. During their periods of exposure, the mouldy hay provided the experimental animals with their only source of roughage. Between these periods of exposure, they were given good hay which was not dusty.

Method and duration of exposure

While they were being exposed to mouldy hay dust, the four experimental animals were kept in the same loose-box and under the same conditions as had been used in Experiment 1. Two bales of hay (about 80 lb) were vigorously shaken out on to the floor every morning and evening. During the course of the experiment which lasted for almost 12 months, the animals had four periods of exposure of varying length (Table 77).

After two weeks (January 7th) and one week (March 3rd) of freedom from exposure to mouldy hay, the stirks were exposed constantly to mouldy hay dust for one hour; these periods are referred to hereafter as the first and second massive exposures.

The hay used in this experiment was not purchased from a farmer known to be suffering from farmer's lung, but it was so mouldy that it had been considered unfit to feed even to store cattle.

Clinical examination

During their periods of exposure to mouldy hay, the experimental animals were examined one day per week about seven to eight hours after their morning's exposure. At this time, the

resting respiratory rates, rectal temperature and the findings of thoracic auscultation were recorded.

Following the first and second massive exposures to mouldy hay dust, the calves were examined at hourly intervals for 12 hours and again at 24 hours post-exposure.

Blood samples

Blood samples were examined for the presence of precipitating antibodies to M. faeni before exposure to the mouldy hay began and, during the first period of exposure, after two and five weeks. During the second and third periods of exposure, blood samples were taken and examined every week.

Blood samples were taken for haematological examination just before the first and second massive exposures and then subsequently as follows: first exposure at four, eight, 12 and 24 hours post-exposure and second exposure at two, four, six, eight, ten, 12 and 24 hours post-exposure.

Preparation of Micropolyspora faeni antigens

The methods of preparing the M. faeni antigens for use in the double diffusion test were identical to those already described in Chapter 3, Section II.

Double diffusion test

The procedure for the double diffusion test was identical to that already described in Chapter 3, Section II. The titres of precipitating antibody to M. faeni were estimated in the same manner as described in Chapter 4, Section IV.

Pathological examination

Following their second massive exposure to mouldy hay dust, EA16 and EA20 were slaughtered humanely and exsanguinated six hours post-exposure and EA4 and EA17 24 hours post-exposure. Several portions of tissue representative of all lobes of the lungs and bronchial tree at various levels were collected from each animal. The tissues were fixed in corrosive formol or 10 per cent formalin, dehydrated and double embedded in celloidin and in paraffin wax in a vacuum. The sections were cut at 8 microns and stained with haematoxylin and eosin.

RESULTS

Serology

Detectable levels of precipitating antibody to *M. faeni* had developed in all four animals after five weeks during the first period of constant exposure to the mouldy hay (Table 78). When the animals were blood sampled again 22 weeks later, no precipitins were detected. However, serum samples had not been examined during the 22 week period in which the animals had not been exposed to mouldy hay.

At the end of the first week of the second period of constant exposure, precipitating antibodies were detected in EA16 and, by the end of the second week, EA4 and EA20 were also precipitin-positive. It was only after four weeks exposure that precipitins were detected in EA17. Precipitins were subsequently detected in every sample taken from every calf until the end of the experiment on the 3rd/4th March.

The titres of precipitating antibody to *M. faeni*, which were estimated immediately prior to the first and second massive exposure to mouldy hay dust, are also given in Table 77. EA20 had the highest titre (1/16) on both occasions.

Precipitins to *M. faeni* were not detected in any of the samples from the four control calves.

Clinical examination

Constant exposure The results of the weekly examinations during the three periods of constant exposure to mouldy hay dust are given in Appendix 3, Table 1. During these three periods of constant exposure, the four experimental animals were never noticed to be either dull or anorexic. From the start of the second period of exposure on 10th November until the experiment ended on 3rd/4th March, the calves had only three weeks in which they were not eating very mouldy hay and yet their weights increased by about 0.75 lb per day (Table 79).

A significantly elevated rectal temperature was never recorded in any of these calves.

The resting respiratory rates were usually within the range from 30 to 40 per minute. The highest rate recorded

TABLE 78 The results of the examination of sera from the calves in Experiment 4 for precipitating antibodies to Micropolyspora faeni.

	Temporal Sequence of Exposure to Mouldy Hay Dust																					
	Period 1 (week)				Period 2 (week)								Period 3 (week)									Time of Necropsy
Calf No.	0	2	5		0	1	2	3	4	5	6		0*	1	2	3	4	5	7		0**	Post-exposure
EA4	-	-	+	CALVES	-	-	+	+	+	+	+	CALVES	+	+	+	+	+	+	+	CALVES	+	24 hours
EA16	-	-	+	NOT EXPOSED	-	+	+	+	+	+	+	NOT EXPOSED	+	+	+	+	+	+	+	NOT EXPOSED	+	6 hours
EA17	-	-	+	FOR	-	-	-	-	+	+	+	FOR	+	+	+	+	+	+	+	FOR	+	24 hours
EA20	-	-	+	22 WEEKS	-	-	+	+	+	+	+	2 WEEKS	+	+	+	+	+	+	+	1 WEEK	+	6 hours
EA5	-	-			-		-		-				-				-				-	-
EA33	-	-			-		-		-				-				-				-	-
EA34	-	-			-		-		-				-				-				-	-
EA35	-	-			-		-		-				-				-				-	-

* = time of first massive exposure to mouldy hay dust.

** = time of second massive exposure to mouldy hay dust.

EA4, EA16, EA17, EA20 - calves exposed to mouldy hay dust.

EA5, EA33, EA34, EA35 - control calves.

TABLE 79

The weights of the four calves at the beginning and end of Experiment 4 during which time they were exposed to mouldy hay dust for a total of 18 weeks.

Calf No.	Weight of Calves (lb)				
	10 November	3/4 March	Weight Gain	No. of Days	Liveweight Gain/Day
EA4	540	625	85	116	0.73
EA16	590	680	90	115	0.78
EA17	560	650	90	116	0.78
EA20	675	770	95	115	0.83

was 50 per minute during week 1 in the second constant exposure period with EA16 and in week 5 with EA4.

Only EA4 and EA16 were seen to be coughing during the examination periods. Although EA16 was seen to cough on fewer occasions than EA4, it did so more frequently. The production of mucus was not observed.

During the second constant period of exposure, EA17 and EA4 were considered to be hyperpnoeic on weeks 1 and 6 respectively. In week 4 of the third constant exposure period, EA4 and EA20 were hyperpnoeic and the following week, every calf was hyperpnoeic.

Unilateral crackles were heard antero-ventrally in EA4 at every weekly examination during the second constant exposure period but only in weeks 1 and 2 during the third period. During the second period, crackles and rhonchi were heard antero-ventrally on the left side in EA17 in week 3 and in week 5, occasional crackles were heard antero-ventrally in EA20.

First massive exposure The clinical details are given in Appendix 3, Table 2. EA4 was thought to be slightly dull five hours post-exposure, otherwise the animals were bright and alert throughout the examination period.

The rectal temperatures of all the calves were equal to or greater than 102.5°F at seven hours post-exposure. At this time, EA20 had a temperature of 103°F and it remained consistently higher than those of the other animals at each of the remaining six examination periods, reaching 103°F again nine hours post-exposure.

EA20 was slightly tachypnoeic from 8-10 hours post-exposure.

Crackles, which were usually unilateral, were heard antero-ventrally in EA4 at three, seven, eight and ten hours post-exposure.

Second massive exposure The clinical details are given in in Appendix 3, Table 3. EA20 was thought to be slightly dull two hours post-exposure, otherwise the animals were bright and alert throughout the examination period.

A significantly elevated rectal temperature was not recorded in any of these animals; EA16 had the highest temperature (102.5°F)

one hour post-exposure.

The resting respiratory rates stayed at 30 per minute throughout the experiment.

EA16 was slightly hyperpnoeic four hours post-exposure. Rhonchi were heard antero-ventrally on the right side of EA4 one hour and eight hours post-exposure.

Haematology

First massive exposure The details from the individual animals are given in Appendix 3, Table 4. Following exposure, the mean total white cell count increased to reach a maximum after eight hours (Table 80) and then decreased towards the pre-exposure value. The number of neutrophils decreased in three animals during the first four hours post-exposure (EA4 - 302 cells, EA16 - 546 cells, EA20 - 1401 cells). During the same period, the mean number of neutrophils decreased but then it rose from four to eight hours to reach a value that was greater than the pre-exposure one (Figure 32); this increase was statistically significant. The mean increased slightly from eight to 12 hours post-exposure but decreased again during the next 12 hours.

Second massive exposure The details from the individual animals are given in Appendix 3, Table 5. Following exposure, the mean total white cell count decreased during the first two hours (Table 80) and, after it had risen to reach the pre-exposure value by eight hours, it decreased slightly. The number of neutrophils decreased in every animal within the first two hours after exposure (EA4 - 672 cells, EA16 - 1004 cells, EA17 - 502 cells, EA20 - 1020 cells). The mean remained low from two to four hours post-exposure, then increased to reach a maximum by eight hours after which time it gradually decreased.

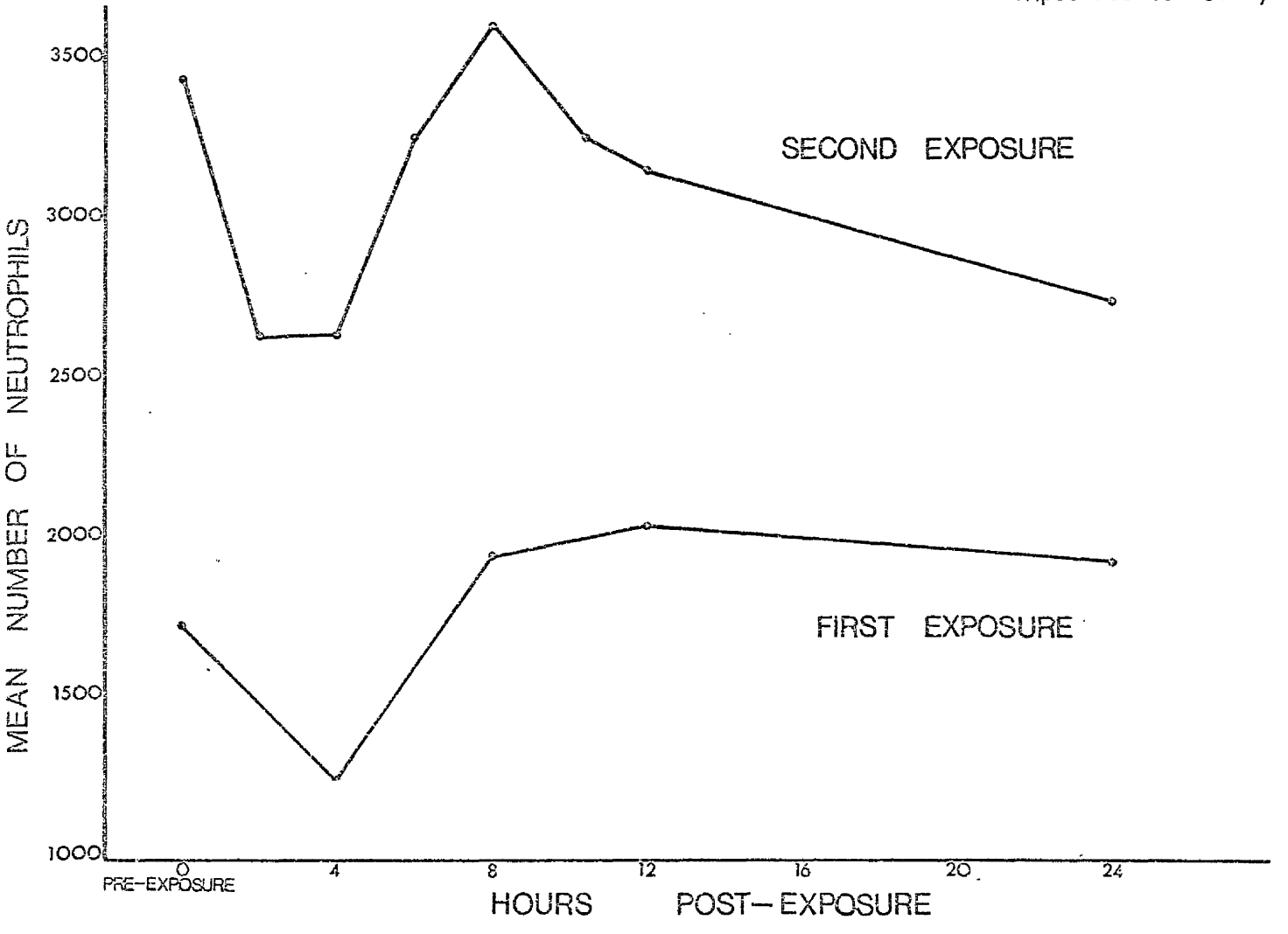
When the results from the two massive exposures were combined, there was a slight peak in the mean total white cell count at eight hours post-exposure (Table 80). As before, the mean number of neutrophils fell during the first four hours post-exposure, rose during the next four hours almost to the pre-exposure level and was then declining gradually at 12 and 24 hours post-exposure.

TABLE 80 The mean total white blood cell and neutrophil counts at specific times after the first and second massive exposures to mouldy hay dust.

Total Cells	Pre-exposure	Hours Post-exposure 2	4	6	8	10	12	24	Exposure
W.B.C.	5975 ± 670*	-	7100 ± 596	-	7850 ± 698	-	7550 ± 1053	6500 ± 434	FIRST
Neutrophils	1736 ± 354*	-	1251 ± 101	-	1951 ± 211	-	2054 ± 290	1946 ± 207	
W.B.C.	8125 ± 1083	7175 ± 527	7000 ± 1067	7900 ± 727	8100 ± 1300	7250 ± 850	6950 ± 1350	7050 ± 950	SECOND
Neutrophils	3442 ± 409	2643 ± 324	2649 ± 341	3263 ± 436	3632 ± 504	3262 ± 383	3126 ± 775	2751 ± 129	
W.B.C.	7050 ± 716	-	7050 ± 566	-	7933 ± 557	-	7350 ± 762	6683 ± 386	COMBINED FIRST AND SECOND
Neutrophils	2589 ± 408	-	1950 ± 311	-	2511 ± 400	-	2411 ± 353	2214 ± 217	

* = Mean and standard deviation.

FIGURE 32 The change in the mean number of neutrophils following the first and second massive exposures to mouldy hay dust.



Macroscopic pathology

EA16 A moderate number of small grey spots less than 1 mm in diameter were seen in the anterior and dorsal parts of both lungs. There was also an adhesive pleurisy of the diaphragmatic lobes particularly on the dorsal surface.

EA20 Similar but slightly less severe changes were observed in this animal as were seen in EA16. Fewer small grey spots were seen in the anterior parts of the lungs.

EA4 There was a considerable number of small grey spots in the lobules in the apical lobes, cardiac lobes and the anterior parts of the diaphragmatic lobes, dorsally as well as ventrally. Some spots were also present on the dorsal border of the diaphragmatic lobes. A slight adhesive pleurisy was present dorsally in both diaphragmatic lobes and a small focus of cuffing pneumonia was seen in the ventral tip of the right apical lobe.

EA17 A moderate number of small grey spots was seen in the anterior parts of both lungs and a smaller number was also observed in the dorsal parts of the diaphragmatic lobes.

Microscopic pathology

EA16 There was a mild bronchitis with neutrophils in the lamina propria and a few were seen migrating through the epithelium. Several globule leukocytes and eosinophils were also seen in the bronchial epithelium. Several focal single lymphoid peribronchiolar follicles, similar to those which have been described in Experiment 1, were also observed. There was thickening of the alveolar septa and walls by plasma cells, macrophages and neutrophils. Within the alveolar walls and, occasionally in the air spaces, there were focal accumulations of neutrophils and also some binucleate macrophages. An early granuloma in the form of a collection of macrophages was identified.

The air spaces were usually clear and there seemed to be many more neutrophils than were seen in the four animals in Experiment 1.

EA20 There was a mild bronchitis with some neutrophils in the lamina propria. The number of bronchiolar lymphocytic foci and the extent of the alveolar wall thickening were similar to EA16.

In the alveolar septa, two well-formed granulomata with epithelioid-like macrophages were seen and, in one, a central collection of neutrophils was identified.

EA4 The changes were similar to those in the previous two cases but it was thought that there were fewer neutrophils in this animal although it would have been difficult to quantify this accurately. One definite epithelioid granulomata with a central core of neutrophils was seen.

EA17 Fewer neutrophils were seen than in EA16 but, in general, the same changes were observed. A granulomata was not found in the sections examined from this animal.

Changes in the various parameters as a result of the first and second massive exposures are given in Table 81. After the first exposure EA20, which had the highest titre also had the most severe clinical response and the greatest fall in the number of neutrophils during the first four hours post-exposure. In EA17, which stayed clinically normal, the number of neutrophils actually increased during the first four hours post-exposure. There appeared to be an association between the precipitating antibody titres, the clinical responses and the haematological changes. However, following the second massive exposure, no relationship was apparent between the precipitin titres, the clinical responses and the haematological changes. On this occasion, the smallest decrease in the number of neutrophils occurred in EA20. The extent of the macroscopic pathological changes did not appear to be related to any of the other parameters. The microscopic changes did appear to have some relationship with precipitin titre, perhaps with clinical response also but not to haematological changes.

DISCUSSION

In order to study the development of farmer's lung, calves were exposed for varying periods of time to either mouldy hay dust or an aerosol of soluble *M. faeni* antigens. Precipitating antibodies to *M. faeni* were detected after four weeks (Experiment 1) and five weeks (Experiment 4) but only in calves that had been continually exposed to mouldy hay dust. These were both primary serological

TABLE 81 The relationships between the titre of precipitating antibody to *Micropolyspora faeni*, the clinical response after the first and second massive exposures to mouldy hay dust and the comparative severity of the pathological lesions after the second massive exposure to mouldy hay dust.

	Calf No.	Precipitin Titre (Reciprocal)	Comparative Severity of Clinical Response	Change in total Neutrophils from 0-4 hours Post-exposure	Comparative Severity of Pathological Lesions			
					Macroscopic		Microscopic	
					6 hours	24 hours	6 hours	24 hours
FIRST MASSIVE EXPOSURE	EA4	2	++	- 17%	-	-	-	-
	EA16	2	++	- 36%	-	-	-	-
	EA17	2	-	+ 31%	-	-	-	-
	EA20	16	+++	- 52%	-	-	-	-
SECOND MASSIVE EXPOSURE	EA4	8	+	- 17%		+++		+++
	EA16	8	+	- 37%	++		+++	
	EA17	2	-	- 34%		++		+
	EA20	16	-	- 2%	+		++	

responses. In contrast, the development of precipitins within two weeks of the calves being re-exposed to mouldy hay in Experiment 4 must have been a secondary response. Therefore, it can be deduced that the 11 weekly 30 minute periods of exposure to soluble M. faeni antigens (Experiment 2) or to mouldy hay dust (Experiment 3) had been insufficient to sensitise the calves to M. faeni. This confirms that a minimum threshold of antigenic exposure is necessary for animals to become sensitised to M. faeni and to develop precipitating antibodies.

Precipitating antibodies developed after about 14 days in rats aerosolised daily with an extract of pigeon droppings (79). That it took up to five weeks for precipitins to M. faeni to develop in calves exposed daily to mouldy hay could be the result of cattle being less efficient than rats in producing precipitating antibodies or, more likely, that the amount of M. faeni antigen inhaled varied markedly from day to day. Under laboratory conditions, a constant amount of antigen is available for inhalation during the whole of the exposure period, whereas under natural conditions of exposure to mouldy hay dust, the amount of M. faeni antigen in the air can vary enormously over a short period of time. When mouldy hay is shaken up vast numbers of spores are released into the atmosphere but after approximately 20 minutes only about 10 per cent of the maximum number will probably still be airborne (147). In addition, it has already been shown that mouldy hays do vary in their M. faeni antigen content (109, 199).

It has been stated that the severity of an Arthus-type response is proportional to the titre of precipitating antibody (43, 189) and, assuming that acute farmer's lung is the result mainly of this type of hypersensitivity reaction, then the lack of a severe clinical response following both massive challenges with mouldy hay dust can be attributed to the relatively low precipitin titres at the time of exposure. However, a mild clinical response (pyrexia, tachypnoea) did develop on one occasion with EA20 which had the highest titre (1/16). Although the duration of exposure to mouldy hay may not have been optimal with a view to maximising the precipitin titre, it is also likely that the periods of one and two weeks freedom from exposure to mouldy hay dust were not sufficiently long to allow a build-up of the precipitin titres and any other mediators that may be required for the pathogenesis of acute farmer's lung.

During the periods of constant exposure both tachypnoea and coughing were noticed. The tachypnoea was considered to have been more physiological than pathological since the atmosphere in the box was stuffy most of the time. The sporadic coughing could have been due to the direct irritant effect of the dust on the airways or perhaps, the result of cuffing pneumonia which is an endemic chronic respiratory disease of housed calves in Britain (129). Lesions of cuffing pneumonia were confirmed in EA4 at necropsy.

The calves given an aerosol of M. faeni antigens for 30 minutes for 11 successive weeks (Experiment 2) did not even develop detectable levels of precipitating antibody let alone a clinical response. These findings are in sharp contrast to those of Wilkie (1976a) who claimed that hyperpnoea and a significantly elevated respiratory rate developed from three hours up to 48 hours in both sensitised and non-sensitised calves which had inhaled M. faeni antigens for only 15 minutes once per week on six successive occasions. However, these animals did not become pyrexic although the clinical signs became more severe and the M. faeni haemagglutinating antibody titre increased with the number of exposures.

The lack of obvious signs of respiratory disease in many of the laboratory animal model systems for producing extrinsic allergic alveolitis (Table 75) is probably why clinical observations are absent from a number of reports (79, 133, 136, 219, 256, 295). A dramatic clinical response was produced by Kochman and others (1972) but it did not resemble in any way farmer's lung as described in either man or cattle because the sensitised rabbits were all dead within 35 minutes of their being challenged with an aerosol of M. faeni. On the other hand, when sensitised guinea pigs were exposed by aerosol to M. faeni antigens, they became tachypnoeic four to eight hours post-exposure (285) and monkeys sensitised to pigeon serum developed tachypnoea and pyrexia six hours after challenge by aerosol (115).

Following the two massive exposures to mouldy hay dust, a marked decrease in the total numbers of neutrophils occurred during the first four hours post-exposure but, after a further four hours, the total numbers in the individual calves had returned to their pre-exposure values. The decrease in the numbers of circulating neutrophils coincided with the appearance of large numbers of neutrophils in the lungs of calves killed six hours post-exposure (EA16,

EA20). Considerably fewer neutrophils were seen in those animals killed 24 hours post-exposure (EA4, EA17). Since neutrophils are necessary for the expression of a type III hypersensitivity reaction, these findings support the thesis that this type of hypersensitivity response does play a significant role in the pathogenesis of farmer's lung in cattle.

The range of pathological lesions in the lungs of the experimental calves were similar to that in the field cases of farmer's lung. The changes were less severe in the younger animals which had only been exposed continually to mouldy hay for ten weeks compared with the older group which had been exposed continually for a total of 18 weeks.

The small grey spots seen on macroscopic examination of the lungs in six of the eight calves, were most likely to have been foci of intense peri-bronchiolar reaction because it was around the bronchioles that the most severe cellular reactions were found on microscopic examination. In lung biopsies from human cases, the cellular reactions are frequently severe within the walls of the bronchioles and in the adjacent parenchyma (22, 71, 234, 259). Almost certainly this is because the bronchioles and the alveolar ducts are the sites of maximum deposition of particles 1-2 microns in diameter that are responsible for the production of farmer's lung (104, 114). The peri-bronchiolar lymphocytic and macrophage aggregations were smaller, less cellular and not so well organised as those seen in cuffing pneumonia (129, 203). There is an increasing amount of evidence to suggest that cuffing pneumonia is the result of infection with one or more mycoplasmas(100, 101, 203). However, the only species isolated from these experimental calves at necropsy was Acholeplasma laidlawii (2) and it is universally accepted that this species is non-pathogenic (55).

A proportion of the small grey spots were epithelioid granulomata that had developed in the alveolar septa. Typical granulomata with a central core of neutrophils surrounded by epithelioid cells and then by mononuclear cells were identified in two calves, both of which had been exposed to mouldy hay dust for 18 weeks. An early granuloma was present in a third calf in the same group. In a series of biopsies from acute farmer's lung cases in man, definite epithelioid granulomata were seen in only about one-third of

the cases, mononuclear cellular aggregates were present in another third while no cellular accumulations were identified in the remaining cases (71).

Seal and others (1968) suggested that the presence of epithelioid granulomata was associated with a recent acute episode of farmer's lung. Since there was no clinical evidence of acute farmer's lung in any of these calves, the presence of epithelioid granulomata is likely to indicate only that the animal had recently been exposed to the relevant antigens. Nevertheless, it is worth recording that two well-formed granulomata were seen in the alveolar septa in EA20 which, following a massive exposure to mouldy hay dust, was the only animal to develop clinical signs suggestive of farmer's lung.

In his experimental studies of thresher's lung, Zettergren (1950) identified two types of granuloma; a foreign body granuloma associated with the inhalation of sterile dust alone and an allergic granuloma that only developed in rabbits exposed to both dust and Candida albicans. Foreign body material, probably of plant origin, was identified in one of the mononuclear cellular aggregates in EA75. There was also evidence of haemorrhage in the centre of several of the peri-bronchiolar cellular aggregates in EA76 and these could have indicated that an Arthus-type reaction had occurred.

The most striking microscopic change associated with the naturally occurring cases of bovine farmer's lung is the cellular infiltration and thickening of the alveolar septa. Both the degree of thickening and the mononuclear cellular infiltration in the experimental calves seemed to be directly related to their duration of exposure to mouldy hay dust. The infiltration was only focal in Experiment 1 (exposure time of ten weeks) whereas in Experiment 4 (exposure time of 18 weeks) the mononuclear cellular infiltration was much more widespread and the thickening of the alveolar septa more obvious.

Bronchiolitis obliterans was not seen in any of the sections from these experimental calves although a mild bronchitis was invariably present. The finding of globule leukocytes, which are discharged mast cells (176), in the bronchial epithelium of EA16 was of particular interest since it has always been assumed that this

type of cell was associated with exposure to the cattle lungworm, D. viviparus (34). As none of these calves had ever eaten grass, their presence cannot readily be explained unless perhaps they were indicative of a type I hypersensitivity reaction to antigens, other than those of M. faeni, in mouldy hay.

At the end of Experiment 4, the pathological lesions were judged to be more severe and more widespread in EA4 and EA16 than they were in EA17 and EA20. It may have been coincidence but EA4 and EA16 were the two animals which had been exposed on 11 occasions to mouldy hay during Experiment 3.

After six weekly exposures of only 15 minutes each to an aerosol of M. faeni antigens, Wilkie (1976b) reported severe lung changes including cellular infiltration and thickening of the alveolar septa in sensitised and non-sensitised calves. The changes were much more severe in the group that had been sensitised with M. faeni antigens in Freund's complete adjuvant. Several areas of severe vasculitis and adjacent focal haemorrhage were found in two sensitised calves. Neither bronchiolitis obliterans nor epithelioid granulomata were observed. The changes cited above are not directly comparable with any of those reported here since none of the eight calves were examined at necropsy following the experimental aerosolisation of M. faeni antigens (Experiment 2) or mouldy hay dust (Experiment 3).

From this limited experimental study, it would appear that a type III hypersensitivity reaction is involved in the pathogenesis of farmer's lung in cattle since the number of circulating neutrophils decreased markedly during the first four hours post-exposure to mouldy hay and clinical signs of respiratory disease developed a few hours later. The population of neutrophils in the lungs of two calves examined at necropsy six hours post-exposure was considerably greater than that normally seen and it was also greater than the number present in the calves killed after 24 hours. An investigation of the sequential haematological changes does not appear to have been undertaken in any of the experiments concerning laboratory animals.

The characteristic clinical and pathological features of a type III reaction were produced in the lungs of a group of monkeys which had been given only serum from sensitised donors, but not in another group which had been given only leukocytes (115). A similar

experimental procedure had been used earlier with guinea pigs when tachypnoea developed and lung lesions were found in both serum and leukocyte recipient animals (285). Nonetheless, the clinical response and the pathological lesions were more severe in the serum recipients.

One interpretation of a mononuclear cellular infiltration of the alveolar septa and the presence of epithelioid granulomata is that both type III and type IV hypersensitivity reactions are taking place in the lungs of cattle with farmer's lung (115). Emanuel and others (1964) had already concluded that cellular immune processes were involved in farmer's lung in man because of the clinical, radiological and histopathological similarities between farmer's lung and maple bark disease. This latter condition (261) was considered to result from a type IV hypersensitivity reaction, despite the presence of precipitins to Cryptostroma corticale in patients' sera, because an interstitial pneumonia with granuloma formation was present at necropsy (72). In addition, when guinea pigs were frequently exposed to an aerosol of C. corticale spores, the skin reactions were maximal at 24 hours and could be transferred to recipient pigs by buffy coat cells but not by serum alone (256). Fink and others (1970) identified pulmonary lesions in guinea pigs sensitised to extracts of pigeon droppings before they were able to detect precipitating antibodies. Consequently, they also concluded that a non-precipitating antibody dependent hypersensitivity reaction (type IV) was involved in the pathogenesis of extrinsic allergic alveolitis.

In order to clarify the relative importance of the different types of hypersensitivity reaction in the pathogenesis of farmer's lung, Jones (1970) compared experimentally-produced type III and type IV reactions in the lungs of rabbits with the changes that developed following pulmonary sensitisation to M. faeni. With the type III reaction, which was induced by the repeated introduction of heterologous serum intra-tracheally, lymphoid hyperplasia was produced initially. This was followed, after continued administration, by diffuse interstitial alveolitis with vasculitis, thrombosis and infarction and, after many weeks exposure, interstitial fibrosis developed. However, "tubercules" were not produced. In the type IV pulmonary reaction which was produced by giving live Mycobacterium tuberculosum (BCG strain) to rabbits subcutaneously and then introducing purified M. tuberculosum protein derivative endotracheally, occasional "tubercules" were seen as well as focal areas of necrosis and alveolar

cellular hyperplasia. Numerous epithelioid granulomata were seen in addition to "many of the features of both type III and type IV mechanisms" in the rabbits that were sensitised with various antigenic preparations of M. faeni. Jones (1970) concluded that farmer's lung was a complex hypersensitivity reaction and not a simple type III response as had originally been suggested (196).

The role of type IV hypersensitivity in experimentally produced acute hypersensitivity pneumonitis is difficult to assess when Freund's complete adjuvant has been used in the sensitisation protocol (73, 115, 136, 143, 219, 283, 285) because this material preferentially induces a type IV hypersensitivity response (218). Despite producing a hypersensitivity pneumonitis in rabbits that resembled acute farmer's lung in man, Richerson and his colleagues (1971) concluded that "further speculation on the pathogenetic correlation with human disease is, however, premature at this time". It was demonstrated later that the type of pulmonary hypersensitivity reaction which develops in guinea pigs at any rate is dependent upon the specific antigen used, the method of sensitisation and the route of challenge (218).

In the laboratory animal model systems that have been used to study extrinsic allergic alveolitis (Table 75), the sensitised animals have usually been challenged with an aerosol of soluble antigenic material whereas in the natural disease, particulate material of variable size and antigenicity is generally inhaled. In farmer's lung the use of antigenic preparations derived from M. faeni alone ignores the effect that the dust particles themselves may have together with any possible effect which other inhaled micro-organisms might exert. The inhalation of sterile dust can induce the development of granulomata in the lungs (297) and several workers have commented on the presence of foreign body material in biopsies taken after an acute episode of farmer's lung (71, 90, 234). That this material has not been observed in many cases is likely to have been a function of the time interval between the patient's last exposure to mouldy hay and the taking of the lung biopsy. Indeed, it has even been suggested that M. faeni plays a part only in the early stages of farmer's lung and that the dust itself is a more important pathogenic factor (295). This almost heretical statement has achieved a degree of credability following recent work (68) in

which it was demonstrated that the complement system can be activated by dust particles via the alternative pathway (98) as well as by antigen-antibody complexes via the classical pathway. Therefore, it is likely that both pathways of complement activation are involved in the pathogenesis of farmer's lung.

Almost all the animal model systems used so far have been examples of an acute, self-limiting hypersensitivity reaction and consequently, are unlikely to be fully representative of the whole spectrum of changes that can take place in naturally-produced cases of extrinsic allergic alveolitis. Under field conditions, there is prolonged and variable exposure to a whole multitude of antigens, some of which may be soluble and others particulate, and this results in the development of chronic inflammatory and degenerative lung changes. The use of this model which involves the exposure of cattle to mouldy hay enables many of these difficulties to be overcome.

CHAPTER 6

GENERAL DISCUSSION AND CONCLUSIONS

GENERAL DISCUSSION AND CONCLUSIONS

The extrinsic allergic alveolitis of cattle described by Pirie and others (1971) has been called "bovine farmer's lung" because of its clinical, epidemiological and pathological similarity to the human respiratory disease, farmer's lung (109, 198, 234). It has been established that farmer's lung in cattle is a respiratory disorder of adult beef and dairy animals in the wet hilly areas of western Britain. The clinical signs usually developed during the winter housing period as a result of the animals having been regularly exposed to the dust of mouldy hay. It is interesting that bovine farmer's lung was first confirmed in a cow from Kirkby Stephen as a few of Campbell's original farmer's lung patients had worked in the same area (40, 75).

Each case of farmer's lung in cattle was classified as acute (sudden onset) or chronic (insidious onset) according to the mode of onset of the disease. The presenting signs of acute farmer's lung included evidence of constitutional involvement (agalactia, anorexia, pyrexia) in addition to a variable degree of respiratory distress. In contrast, the major presenting signs of chronic farmer's lung were wholly referable to the respiratory system (coughing, hyperpnoea, tachypnoea) although weight loss and a decreased milk yield had also been noticed during one or more winter housing periods. Dullness was not a common presenting sign with either form of the disease.

That the clinical differences between the two forms of farmer's lung in cattle were not marked on admission to the Veterinary School can be attributed largely to the time interval which elapsed from the animals first being seen to be ill to their being examined on admission. This delay was particularly marked with the chronic cases many of which were admitted during, or at the end of, the summer grazing season when several months freedom from exposure to mouldy hay had minimised the clinical signs of respiratory disease which had been obvious before they had been put out to grass. In general, cows affected with chronic farmer's lung were in poorer bodily condition, coughed more frequently, were more hyperpnoeic and more tachypnoeic than animals with the acute form of the disease. The adventitious lung sounds which were detected in just over half of both acute and chronic cases were crackles or rhonchi or a combination of both. They were almost invariably heard antero-ventrally except

in the more severe cases when occasionally they were detected over the whole lung field.

The classification of farmer's lung as acute or chronic according to the mode of onset of the clinical signs did not correspond in every case to the classification as judged by the pathological findings. Again the time interval between the onset of illness and the post-mortem examination must undoubtedly have contributed to this lack of correlation. On microscopic examination, widespread inter-alveolar haemorrhage and oedema were present in acute cases examined within one day of exposure to mouldy hay. However, the most obvious feature in every case was thickening of the alveolar septa due to mononuclear cellular infiltration; this was much more obvious and widespread in the acute than in the chronic cases. Bronchiolitis obliterans and epithelioid granulomata were also more common in acute than in chronic cases. Nonetheless, it cannot be inferred that bronchiolitis obliterans and epithelioid granulomata are characteristic of acute farmer's lung, rather that they confirmed recent exposure to the allergens of farmer's lung. Areas of fibrosis with alveolar epithelial hyperplasia were more prevalent in the chronic than in the acute form of the disease and there was diffuse pulmonary fibrosis in every case admitted with cor pulmonale. Several chronic cases should perhaps have been classified as sub-acute since the clinical signs were becoming more severe as the winter progressed and the pathological findings were more typical of the acute than of the chronic disease. In addition, dyspnoea was found to be precipitated by exercise in some chronic cases with widespread pulmonary fibrosis. Since coughing had been observed in a few cases prior to their first acute respiratory episode it could be argued that they should have been included in the insidious onset group. Nevertheless, when thinking about clinical differential diagnosis, farmer's lung in cattle must be considered as presenting as both a sudden onset and an insidious onset respiratory disease.

It is not possible to differentiate between severe cases of chronic farmer's lung and diffuse fibrosing alveolitis of cattle on clinical grounds alone and so the final diagnosis must be made after histopathological examination of the lungs (35). It has not been possible to state that animals with diffuse fibrosing alveolitis had never been exposed to mouldy hay dust although precipitins to M. faeni were not detected in their sera. It may be that some of these cases with diffuse

fibrosing alveolitis were M. faeni precipitin-negative terminal chronic farmer's lung cases or, on the other hand, the allergens responsible may not have been derived from M. faeni.

Farmer's lung has been found to be the most common respiratory disease of housed adult cattle in Britain but it is probably even more widespread than this investigation has shown since 12 cows culled as a result of poor performance, weight loss or allegedly old age from three herds in which farmer's lung has been confirmed had mild clinical respiratory disease on admission to Glasgow Veterinary School (292). At necropsy, significant pathological lesions, other than those of farmer's lung, were not detected.

Each of the 45 clinical cases of bovine farmer's lung had been fed hay which in virtually every case the farmer admitted was mouldy. Regular feeding with mouldy hay during the winter housing period has been shown to result in a significant proportion of the cattle developing precipitating antibodies to M. faeni. The prevalence of precipitins in a herd at the end of the winter and the number of cows that had developed precipitins during the winter, was found to be closely related to the mouldiness of the hay as judged by the farmer. While a high prevalence of precipitins at the end of winter confirmed that mouldy hay had been fed, it did not confirm the presence of clinical farmer's lung since many cattle that were precipitin-positive did not have detectable clinical respiratory disease.

Regular exposure to mouldy hay during successive winter housing periods had a cumulative effect because the prevalence of precipitins in individual animals followed serologically over several years was positive correlated with the age of cattle sampled and the titres of precipitating antibody were generally higher in cattle more than six years of age (57). The additive effect of repeated insults to the lungs obviously had increased the probability of clinical respiratory disease because the number of clinical cases was also positively correlated with age. The prevalence of precipitins to M. faeni was significantly higher in the herds in which bovine farmer's lung had been confirmed. The prevalence of precipitins was also significantly greater in herds owned by farmers who had farmer's lung than in other herds selected because precipitins had been detected in sera from cows that had developed signs of

respiratory disease during the winter or in herds selected at random. The chronic cases of farmer's lung from farms where the farmer developed an adverse clinical reaction after exposure to mouldy hay dust were significantly younger than those admitted from the farms where the farmer experienced no adverse reaction. These findings confirmed the hypothesis that farmer's lung had developed in specific herds because of their greater exposure to mouldy hay dust.

During the summer grazing period when exposure to mouldy hay dust ceased, the prevalence of precipitins fell markedly in every herd. Not unexpectedly those animals with the lowest antibody titre in the spring were precipitin-negative at the beginning of the following winter while those with the highest titre were still precipitin-positive. This difference in precipitin titre might explain why older cattle were usually found to have developed obvious signs of respiratory disease within a short period of their having been re-exposed to mouldy hay dust, while clinical disease was not usually observed in the younger animals until after several months exposure. The association between age (titre) and the onset of clinical signs was noticed in both acute and chronic forms of the disease.

The response of an individual animal following the inhalation of mouldy hay dust containing farmer's lung allergens will depend upon its immunological reactivity and the pattern of exposure. Although two farmers commented that one family in each of their herds appeared to be particularly susceptible to farmer's lung, it was not possible either to confirm or to refute their impressions. Probably these two families were easily identified because they were particularly high yielding cows and so had been kept longer in the herd than other cows. As they were older, it follows that they had been exposed to mouldy hay dust for a longer period than other cows and it has already been proved that there is a positive correlation between age, the prevalence of precipitins to M. faeni and the incidence of farmer's lung disease. Therefore, a number of closely related cattle that had developed farmer's lung had given the impression that there was a genetic susceptibility to disease when, in reality, it was more likely to be an age-related, accumulative environmental effect. Within a group of cattle, the genetic susceptibility of related and unrelated individuals to the effects

of mouldy hay dust cannot be realistically compared when the exposure to which the individuals have been subjected is unknown. For the same reason, the report of familial farmer's lung in man (255) must also be viewed with some doubt.

Nonetheless, it must still be borne in mind that acute farmer's lung invariably presented as a single animal condition and that these cases were significantly younger than those which presented with the chronic form of the disease. This apparent individual susceptibility to the effects of mouldy hay dust may have been related to recent parturition since around this time the precipitating antibody titre and the amount of inhaled antigens change dramatically. The precipitin titre falls before parturition and rises again during the first few weeks post-partum. At the same time, the amount of dust inhaled will decrease as cows are moved from the "dry" cow accommodation in which they will have been fed the mouldiest hay to the milking cow accommodation in which they will be fed the least mouldy hay.

Retrospectively, gross differences in the pattern of exposure to mouldy hay dust between the acute and chronic forms of farmer's lung in cattle were not apparent. The amount and duration of exposure were apparently determined largely by husbandry and by housing factors. That dairy cows were exposed for longer periods and probably to greater amounts of mouldy hay dust than beef cows is possibly the major reason why the acute dairy cases were significantly younger than the acute beef cases. However, dairy cows are supervised more closely than are beef cows and this might not only explain the greater incidence of farmer's lung in dairy cattle but also why farmer's lung was only confirmed as a group disease under dairy conditions.

In the county of Westmorland farmer's lung was proportionately more common in beef than in dairy cattle. This was undoubtedly due to the type of housing in which most of these animals had been kept during the winter: many beef cows in Westmorland were over-wintered in field-houses, as were the two youngest cases which were both dairy heifers, and since there is no ventilation in field-houses, the amount of exposure to mouldy hay dust is particularly intense. All cattle in Westmorland were likely to have been subjected to comparatively large amounts of mouldy hay dust because the prevalence of farmer's lung in cattle was higher and the chronic cases signifi-

cantly younger than those from the other areas.

Farmer's lung has only been confirmed in cattle from the mainly upland areas of north-west Britain where there is regular rainfall at hay-making time. During the two years of the serological survey, most of the hay in these areas had been made in July and it was found that the mouldiness of the hay was closely associated with the number of raindays, but not the monthly rainfall, during July. In the herds sampled for the serological survey, the prevalence of precipitins to M. faeni at the end of winter and the number of cows which developed precipitins during the winter, were found to be closely associated with the mouldiness of the hay. However, no relationship was found between the prevalence of precipitins at the end of winter or the number of cows that developed precipitins during the winter and the amount of hay that had been fed. This confirmed the view that it was the mouldiness of the hay that was of paramount importance in the development of clinical farmer's lung disease in cattle.

The clinical and epidemiological features of bovine farmer's lung in Britain are very similar to those of urner pneumonia in southern Switzerland where cattle are over-wintered in small buildings identical to Westmorland field-houses (74, 118, 154, 185). In the Canton Uri it has been found that a wet hay-making season results in a large proportion of the hay becoming mouldy and this in turn results in a particularly high incidence of urner pneumonia the following winter. Under Swiss conditions, exposure to mouldy hay must be especially intense because urner pneumonia is common in cattle during their second winter housing period while farmer's lung has been shown to be mainly a disease of old cows in Britain.

In this study, the keeping of dairy cows in byres has been found to be closely associated with the development of farmer's lung in the dairyman. Of the 29 herds from which these bovine cases were admitted, farmer's lung had been confirmed on medical grounds in five dairy farmers but only one beef farmer. This is neither a reflection of the relative numbers of beef and dairy units which we have studied nor of the relative numbers of units in the north-west of Britain. It can be inferred, therefore, that exposure to farmer's lung antigens had been high on these farms since the prevalence of farmer's lung in the farming population in north-west Britain is less than 20 per cent (102, 250). Although farmer's lung had only been firmly diagnosed in

six farmers, another seven suffered an adverse clinical reaction during or soon after working with mouldy hay. This confirms that exposure to mouldy hay dust over a prolonged period results in the development of respiratory symptoms in a large proportion of the human population at risk.

Since farmer's lung developed in cattle regularly exposed to mouldy hay dust for several months in poorly ventilated accommodation, it was logical to produce the disease experimentally under similar conditions. In two groups of four experimental calves that were fed mouldy hay twice daily, precipitating antibodies to M. faeni were detected in every calf within seven weeks. However, clinical signs of respiratory disease had not become apparent even after the second group had been exposed for a total of 18 weeks. The duration of exposure must have been insufficient for the development of clinical disease since the youngest field case, a two year old heifer, had been exposed to mouldy hay for at least one winter housing period (24 weeks). However, pyrexia and tachypnoea did develop in one of the four calves in the second group several hours after they had been given the first of two massive exposures to mouldy hay dust. The first and second massive exposures had occurred after two weeks and after one week of freedom from exposure to mouldy hay dust respectively.

The first group of calves were subjected to post-mortem examination after ten weeks exposure to mouldy hay while the second group, which had been exposed for a total of 18 weeks, were examined six hours (two calves) and 24 hours (two calves) after their second massive exposure to mouldy hay dust. The microscopic lung changes were similar in both groups although the degree of lung involvement was greater in the second group than in the first. Bronchitis and bronchiolitis were present in every calf although bronchiolitis obliterans was never seen. This may have resulted from an insufficient duration and intensity of exposure since the bronchioles are the site of maximum deposition of M. faeni spores and similar sized particles in mouldy hay dust (104, 114). While aggregates of macrophages and epithelioid granulomata were seen in the alveolar septa and walls of both groups, the mononuclear cellular infiltration and alveolar septal thickening were more diffuse in the calves that had been exposed for the longer period. Since every calf developed precipitins to M. faeni and was shown to have pulmonary lesions characteristic of farmer's lung at necropsy, it can be deduced that

precipitins not only confirm exposure to M. faeni but also the presence of lung damage.

The number of circulating neutrophils was monitored in the second group of calves after both massive exposures to mouldy hay dust and it was found that the mean number in the group decreased during the first four hours post-exposure only to return to the pre-exposure level during the next four hours. On histopathological examination, not only was there a greater number of neutrophils in the lungs of all four calves than is seen in healthy bovine lungs but there were also appreciably more neutrophils in the lungs of the two calves killed six hours after their second exposure than in those killed after 24 hours.

Neutrophils are necessary for the full expression of a type III hypersensitivity reaction (49) and they are the dominant type of cell from four to eight hours after the initiation of this reaction. Vasculitis and thrombosis are usually seen at the site of a type III hypersensitivity reaction and their presence together with large numbers of neutrophils is highly suggestive that this type of reaction has taken place. Vasculitis and thrombosis were not observed in the pulmonary blood vessels but they were present in skin biopsies from clinical cases taken six hours post-injection at which time neutrophils were the dominant type of cell. Since the following responses all occurred four to eight hours after challenge with M. faeni antigens viz. a detectable clinical response, a decrease in the circulating number of neutrophils, a marked increase in the number of pulmonary neutrophils and the presence of vasculitis and thrombosis in biopsies of skin tests, it is evident that a type III hypersensitivity reaction is involved in the pathogenesis of acute farmer's lung in cattle.

The importance of the type IV hypersensitivity reaction in the pathogenesis of farmer's lung has not been established although the cellular reactions in the skin 72 hours after challenge by injection of M. faeni antigens were microscopically similar to those of a tuberculin reaction. Also, the large numbers of mononuclear cells found in the alveolar septa and walls of clinical cases could have been indicative of a type IV hypersensitivity reaction. Mononuclear cellular infiltration, however, is present 24 hours after the initiation of type III as well as type IV hypersensitivity reactions (93) and, unfortunately, in every case examined at necropsy, the time which had elapsed between the animal's last exposure to farmer's lung

antigens was well in excess of 24 hours. The pathogenesis of farmer's lung almost certainly depends upon the interaction of two major components; firstly there is the immunological component made up of a type III hypersensitivity reaction with possibly type IV and perhaps even type II reaction, and secondly there is a non-immunological component. Mouldy hay dust particles by themselves have been shown to induce clinical signs of farmer's lung in man probably because they had stimulated the alternative pathway of complement activation (68).

By far the most important factor common to the development of farmer's lung in cattle and in man is the inhalation of dust from mouldy hay. Therefore, the obvious way to prevent the development of this disease is to minimise the amount of mouldy hay dust inhaled or, ideally, to avoid feeding mouldy hay to cattle.

Once hay has been made, methods of reducing the amount of exposure of cattle to mouldy hay dust are limited (Table 82). Hay may be fed outside, shaken up outside before being fed inside and even dampened with water, but these procedures are labour intensive. After extractor fans had been installed in the dry cow byre which had a very low roof, farmer six considered that the incidence of coughing had decreased noticeably. Consequently, it can be stated that fans, provided they are sited in the proper place, can reduce the amount of exposure to mouldy hay dust. The most obvious method of preventing exposure to mouldy hay dust is to make silage instead of hay (Table 82). This had been done on farm FL7 and the serological results over two winter housing periods confirmed that the amount of M. faeni antigens inhaled had not been sufficient to sensitise any of the cows. In addition, a farmer who has farmer's lung is probably the most sensitive system for detecting the presence of M. faeni antigens and the fact that clinical symptoms did not develop after this farmer had fed silage was additional confirmation that his silage did not contain M. faeni antigens. It has been reported from the United States of America that exposure to mouldy silage can produce a farmer's lung-like respiratory disease in cattle (139), but from the results quoted here and from other studies, there is no evidence to suggest that the same is true in this country. The major disadvantage of changing over completely and suddenly from making hay to making silage is the large capital expenditure required for new machinery and new buildings. Investment on such a scale is not economically feasible at present in the areas

TABLE 82 Possible methods of reducing the amount of exposure to *Micropolyspora faeni* in mouldy hay dust.

Aim	Possible Methods of Reducing Exposure		Advantage	Disadvantage
Prevention of Heating and Moulding	Change of enterprise	Silage	No *M. faeni*.	Capital cost - buildings. - equipment.
		Dried grass	No *M. faeni*.	Cost - bought in.
	Treatment of hay	Hot air drying	High quality product	Cost - equipment. - housing. - labour.
		Cold air drying	No special buildings	Cost - equipment. - labour.
		Mould inhibitors	Ease of application	Acids - effect on workers. Not shown to be effective.
Reduction of Exposure	Feeding routine	Feed hay outside	-	Cost - labour.
		Shake-up hay outside	-	Risk to workers.
	Alteration of ventilation	Extractor fans	Ease of installation	Cost - alterations to buildings. - equipment.

where farmer's lung is common.

Of the conserved grass in Britain, 80 per cent is made into hay (32, 238) and since in the western parts of the country this is likely to be mouldy three years out of every four (215), a cheap and practical method of inhibiting mould growth on baled hay is required. Capital expenditure is the main disadvantage of all the methods of artificially drying grass (Table 82) although the blowing of air at ambient temperature through newly baled hay is the cheapest and most practical method at present to minimise heating and moulding (292).

It has been shown that heating and moulding in wet-stored barley (178) and in baled bagasse (293) can be prevented by spraying with propionic acid before storage. Many organic chemicals with bacteriostatic and mycostatic properties have been sprayed onto hay in an attempt to prevent heating and moulding (124). A commercial hay additive, (Hay Savor; Agil Ltd., Maidenhead, Berkshire) which was claimed to inhibit heating and moulding on baled hay, had been used on two farms (FL3, FL5) in the serological survey. The proportion of precipitin-negative cattle that developed precipitins when fed Hay Savor treated hay during the first winter was similar to the proportion in the other herds which develop precipitins when given untreated hay (219). Consequently, no obvious benefit had been gained from using that particular additive to reduce the amount of exposure to M. faeni. The results of field trials carried out by the National Agricultural Advisory Service (now the Agricultural Development and Advisory Service) confirmed that the commercial hay additives on the market at that time did not reduce significantly the amount of exposure to M. faeni (13). The efficiency of chemical mould inhibitors is considerably reduced when an effective uniform concentration cannot be achieved throughout the bale since there is very little lateral movement of additive (146). This is probably the major reason for the failure of these proprietary additives under field conditions because, unlike barley and bagasse, hay is not a uniform crop.

This study has confirmed that cattle and their attendants can develop farmer's lung disease under similar conditions of exposure and so the development of a cheap, simple and safe method of preventing heating and moulding in hay baled at between 35 and 45 per cent moisture is one of the major areas in which progress is required in

the future. The best method of achieving this still appears to be further development of chemical sprays with bacteriostatic and mycostatic properties. Unlike a number of sprays on the market at present, new chemical mould inhibitors will not have to present a health hazard to farm workers. In addition, methods will have to be developed that will ensure the uniform application of an effective concentration of these chemicals on to hay as it is being baled. Once such a system has been successfully developed, the major health hazard to the continued and widespread use of hay will have been overcome.

Although the importance of M. faeni in the pathogenesis of farmer's lung in cattle has been confirmed by these investigations, it is likely that allergens derived from other thermophilic actinomycetes may be involved in some cases of the bovine disease as they are known to be in man. Extrinsic allergic alveolitis has been diagnosed clinically and confirmed pathologically in several cows in one herd although exhaustive serological testing with a multitude of environmentally derived antigens failed to identify the precise cause of the syndrome (292). Further work is therefore necessary to identify other respiratory allergenic antigens.

The alternative pathway of complement activation requires to be assessed in cattle so that the role dust particles play in the pathogenesis of bovine farmer's lung can be ascertained. Only then will the relative importance of the non-immunological and the immunological components involved in the pathogenesis of this condition be fully elucidated. The production of farmer's lung in cattle under controlled conditions of exposure would enable the precise pathogenesis of the disease to be determined. It might then prove possible to develop more sensitive diagnostic techniques involving serology to enable the degree of lung damage to be assessed even in the absence of detectable respiratory disease.

Soluble circulating antigen-antibody complexes are considered to be produced when a sensitised animal (type III hypersensitivity) is subjected to a massive challenge with inhaled antigens. A particularly interesting line of investigation would be to confirm the production of such immune complexes and to study their effect on bovine kidneys as four of the clinical farmer's lung cases had a significant proteinuria. Although renal amyloidosis was

diagnosed in two animals, no specific reasons were found for the protein leak in the other two cases.

Farmer's lung and the other samples of extrinsic allergic alveolitis represent a type of hypersensitivity pulmonary disease in man that is of increasing importance. Consequently, it is imperative that a better understanding of the basic disease processes be obtained so that the diagnosis and assessment of lung damage can be made at the earliest possible stage to enable therapeutic and preventive measures to be implemented. Once the model of farmer's lung has been established in cattle, further studies utilising methods and techniques not possible for use in the human can add to the knowledge and understanding of this interesting and complex respiratory disorder.

APPENDIX 1

CASE NO. A1

WHEN SEEN ILL — May, 1970.

CLINICAL SIGNS — Sudden onset respiratory distress. Tachypnoea. Dull. Reduced milk yield. Temperature - 102°F.

V.S. DIAGNOSIS — Indoors fog fever.

TREATMENT — Antibiotics. Tripelenamine. Poor clinical response.

OTHER INFORMATION

THIS COW — No history of any previous disease. Retrospectively, poor milk yield during spring, 1970.

OTHER COWS — Total = 34. Occasional coughing. No recent cases of pneumonia in housed adults.

HAY — Very dusty.

FARMER — Unaffected by mouldy hay dust.

CLINICAL EXAMINATION ON ADMISSION - 18 MAY, 1970.

Age - 6 years. Breed - Friesian cross. Condition - fair.

Demeanour - bright.

Heart Rate - 70/minute. Pulse - good. Temperature - 101°F.

Resp. Rate - 30/minute. Slight hyperpnoea.

Coughing - occasional, harsh, non-productive.

Auscultation - no adventitious sounds.

Other findings - nil.

Time in hospital - 11 days.

CLINICAL DIAGNOSIS - Acute Farmer's Lung.

CASE NO. A2

WHEN SEEN ILL — May, 1970

CLINICAL SIGNS — Sudden onset respiratory distress. Dull. Anorexia. Was mouth-breathing and grunting. Reduced milk yield. Temperature - 103°F. Auscultation - bilateral crackles A/V.

V.S. DIAGNOSIS — Peculiar pneumonia.

TREATMENT — Antibiotics. Betamethasone. Good clinical response.

OTHER INFORMATION

THIS COW — No history of any previous disease.

OTHER COWS — Total = 42. Coughing present but not marked. No recent cases of pneumonia in housed adults.

HAY — Dusty. Fed before milking.

FARMER — Unaffected by mouldy hay dust although he and his wife have precipitins to *M. faeni*.

CLINICAL EXAMINATION ON ADMISSION - 23 SEPTEMBER, 1970.

Age - 6 years. Breed - Ayrshire. Condition - good.

Demeanour - bright.

Heart Rate - 70/minute. Pulse - good. Temperature - 101.4°F.

Resp. Rate - 30/minute. Slight hyperpnoea.

Coughing - occasional, harsh, non-productive.

Auscultation - Left, intermittent rhonchus A/V.

Other findings - nil.

Time in hospital - 1 year.

CLINICAL DIAGNOSIS - Farmer's Lung.

CASE NO. A3

WHEN SEEN ILL	February, 1967.
CLINICAL SIGNS	Anorexia. Dyspnoea. Tachypnoea. Frequent, productive coughing. Clinical relapses every subsequent winter and spring. Poor milk yield. Weight loss. Occurred soon after calving.
V.S. DIAGNOSIS	None made.
TREATMENT	Antibiotics. Poor clinical response.

OTHER INFORMATION

THIS COW	No history of any previous disease.
OTHER COWS	Total = 90. Frequent coughing. In previous years, several cows have developed acute pneumonia whilst indoors.
HAY	Very dusty.
FARMER	Farmer's lung diagnosed in early 1969.

CLINICAL EXAMINATION ON ADMISSION - 21 OCTOBER, 1970

Age - 13 years. Breed - Friesian X. Condition - poor.

Demeanour - bright.

Heart Rate - 70/minute. Pulse - good. Temperature - 101.6°F,

Resp. Rate - 40/minute. Moderate hyperpnoea.

Coughing - occasional, harsh, non-productive.

Auscultation - no adventitious sounds.

Other findings - nil.

Time in hospital - 11 months.

CLINICAL DIAGNOSIS - Farmer's Lung.

CASE NO. A4

WHEN SEEN ILL	November, 1970.
CLINICAL SIGNS	Anorexia. Hyperpnoea. Tachypnoea. Occasional coughing. Temperature - 103°F. Reduced milk yield. Respiratory disease 2 weeks after calving.
V.S. DIAGNOSIS	Farmer's lung ?
TREATMENT	Antibiotics. Poor clinical response.

OTHER INFORMATION

THIS COW	No history of any previous disease.
OTHER COWS	Total = 60. Occasional coughing. In previous years has had one or two cases of pneumonia in housed adults.
HAY	Mixed quality.
FARMER	Unaffected by mouldy hay dust.

CLINICAL EXAMINATION ON ADMISSION - 7 DECEMBER, 1970.

Age - 6 years. Breed - Friesian. Condition - good.

Demeanour - bright.

Heart Rate - 70/minute. Pulse - good. Temperature - 102.2°F.

Resp. Rate - 30/minute. Slight hyperpnoea.

Coughing - occasional, non-productive.

Auscultation - no adventitious sounds.

Other findings - nil.

Time in hospital - 9 months.

CLINICAL DIAGNOSIS - Farmer's Lung.

CASE NO. A5

WHEN SEEN ILL	February, 1971.
CLINICAL SIGNS	Sudden onset respiratory distress. Dull. Anorexia. Standing with its tongue out. Farmer diagnosed "choke". Temperature $< 103^{\circ}F$. Crackling heard high up over left lung.
V.S. DIAGNOSIS	Fog fever.
TREATMENT	Antibiotics. Poor clinical response.

OTHER INFORMATION

THIS COW	No history of any previous disease.
OTHER COWS	Total = 40. Occasional coughing. No recent cases of pneumonia in housed adults.
HAY	Very dusty.
FARMER	Long standing bronchitis. Possibility of farmer's lung not investigated.

CLINICAL EXAMINATION ON ADMISSION - 6 FEBRUARY, 1971.

Age - 5 years. Breed - Galloway. Condition - poor.

Demeanour - bright.

Heart Rate - 80/minute. Pulse - good. Temperature - $101.7^{\circ}F$.

Resp. Rate - 40/minute. Moderate hyperpnoea.

Coughing - occasional, non-productive, not harsh.

Auscultation - no adventitious sounds.

Other findings - exercise intolerance. Resented percussion.

Aborted 7 FEB. Not Brucellosis. Not mycotic abortion.

Time in hospital - 2 days.

CLINICAL DIAGNOSIS - Atypical Interstitial Pneumonia.

CASE NO. A6

WHEN SEEN ILL	February, 1972.
CLINICAL SIGNS	Coughing. Hyperpnoea. Tachypnoea. Dull. Temperature - 104°F. Reduced milk yield. Respiratory disease within 2 weeks of calving. Retained placenta.
V.S. DIAGNOSIS	None made.
TREATMENT	Antibiotics. Poor clinical response.

OTHER INFORMATION

THIS COW	No history of any previous disease.
OTHER COWS	Total = 55. Occasional coughing. Over last 8 years, several cows have developed acute pneumonia just after calving whilst housed. Retained placenta is common also.
HAY	Very dusty.
FARMER	Gets "choked up" with mouldy hay dust.

CLINICAL EXAMINATION ON ADMISSION - 29 FEBRUARY, 1972.

Age - 4 years. Breed - Friesian. Condition - good.

Demeanour - bright.

Heart Rate - 80/minute. Pulse - good. Temperature - 102.1°F.

Resp. Rate - 30/minute. Slight hyperpnoea.

Coughing - occasional, non-productive.

Auscultation - harsh. No adventitious sounds.

Other findings - nil.

Time in hospital - 1 day.

CLINICAL DIAGNOSIS - Farmer's Lung.

CASE NO. A7

WHEN SEEN ILL September, 1973.

CLINICAL SIGNS Anorexia. Dyspnoea. Reduced milk yield. Coughing. Respiratory disease within 4 weeks of calving and 2 weeks after being housed. Left on farm until June, 1974. No further acute episodes.

V.S. DIAGNOSIS Indoor fog fever.

TREATMENT Antibiotics. Betamethasone. Good clinical response.

OTHER INFORMATION

THIS COW No history of any previous disease.

OTHER COWS Total = 60. Occasional coughing. In previous years, a few cases of acute pneumonia in housed adults.

HAY Mixed quality.

FARMER Unaffected by mouldy hay dust.

CLINICAL EXAMINATION ON ADMISSION - 4 JUNE, 1974.

Age - 10 years. Breed - Friesian. Condition - poor.

Demeanour - bright.

Heart Rate - 60/minute. Pulse - good. Temperature - 101.9°F.

Resp. Rate - 40/minute. Moderate hyperpnoea.

Coughing - occasional, non-productive, harsh.

Auscultation - Left, crackles A/V, rhonchi widespread.

Right, crackles A/V, rhonchi widespread.

Other findings - slight mucoid nasal discharge.

Time in hospital - 3 weeks.

CLINICAL DIAGNOSIS - Farmer's Lung.

CASE NO. A8

WHEN SEEN ILL	May, 1974.
CLINICAL SIGNS	Dyspnoea. Frequent productive coughing. Reduced milk yield. Temperature - 105°F. Put out to grass on 14 May. Respiratory signs noticed after walking in to be milked.
V.S. DIAGNOSIS	Farmer's lung ?
TREATMENT	Antibiotics. Betamethasone. Poor clinical response.

OTHER INFORMATION

THIS COW	No history of any previous disease. Productive coughing had been noticed during the winter.
OTHER COWS	Total = 32. Frequent coughing in spring. No recent cases of pneumonia in housed adults.
HAY	Mixed quality.
FARMER	Wife feeds cows: farmer's lung diagnosed in 1971.

CLINICAL EXAMINATION ON ADMISSION - 10 SEPTEMBER, 1974.

Age - 8 years. Breed - Friesian. Condition - poor.

Demeanour - slightly dull.

Heart Rate - 90/minute. Pulse - poor. Temperature - 101.8°F.

Resp. Rate - 50/minute. Gross hyperpnoea - rocking.

Coughing - frequent, paroxysmal, productive - thick mucus.

Auscultation - Left, crackles A/V, rhonchi widespread.

Right, crackles A/V, rhonchi A/V.

Other findings - enlarged, non-pulsating, jugular veins.

Time in hospital - 4 weeks.

CLINICAL DIAGNOSIS - Farmer's Lung - early cor pulmonale.

CASE NO. A9

WHEN SEEN ILL	January, 1974.
CLINICAL SIGNS	Anorexia. Dull. Hyperpnoea. Tachypnoea. Reduced milk yield. Respiratory disease 3 weeks after being housed, 2 weeks after calving.
V.S. DIAGNOSIS	Farmer's lung.
TREATMENT	Antibiotics. Betamethasone. Poor clinical response.

OTHER INFORMATION

THIS COW	No history of any previous disease.
OTHER COWS	Total = 40. Occasional coughing. No recent cases of pneumonia in adults. One cow "wheezes" during the winter but doesn't while at grass.
HAY	Dusty.
FARMER	Farmer's lung diagnosed in 1970.

CLINICAL EXAMINATION ON ADMISSION - 18 NOVEMBER, 1974.

Age - 8 years. Breed - Friesian. Condition - poor.

Demeanour - bright.

Heart Rate - 70/minute. Pulse - good. Temperature - 101.8°F.

Resp. Rate - 50/minute. Moderate hyperpnoea.

Coughing - occasional, non-productive.

Auscultation - no adventitious sounds.

Other findings - nil.

Time in hospital - 8 days.

CLINICAL DIAGNOSIS - Farmer's Lung.

CASE NO. A10

WHEN SEEN ILL	November, 1974.
CLINICAL SIGNS	Dyspnoea following exercise. Coughing. Nasal discharge. Respiratory disease 2 weeks after being housed. Crackles and squeaks heard A/V in lungs.
V.S. DIAGNOSIS	Farmer's lung.
TREATMENT	None given.

OTHER INFORMATION

THIS COW	No history of any previous disease.
OTHER COWS	Total = 25. No coughing. Several cases of acute pneumonia in housed adults in recent years.
HAY	Mixed, the worst is fed just after the cows are housed.
FARMER	Unaffected by mouldy hay dust.

CLINICAL EXAMINATION ON ADMISSION - 30 NOVEMBER, 1974.

Age - 8 years. Breed - Aberdeen Angus cross. Condition - poor. Demeanour - bright.

Heart Rate - 60/minute. Pulse - good. Temperature - 101.6°F.

Resp. Rate - 30/minute. Moderate hyperpnoea.

Coughing - occasional non-productive.

Auscultation - Left, crackles A/V.

Other findings - nil.

Time in hospital - 17 days.

CLINICAL DIAGNOSIS - Farmer's Lung.

CASE NO. A11

WHEN SEEN ILL December, 1974.

CLINICAL SIGNS Developed peculiar "fit" and became recumbent. Tachypnoea. Squeaks heard on auscultation.

V.S. DIAGNOSIS Farmer's lung.

TREATMENT None given.

OTHER INFORMATION

THIS COW No history of any previous disease. On arrival, she was hyperaesthetic, probably hypomagnesaemia.

OTHER COWS Total = 30. Occasional coughing. Two oldest cows are also hyperpnoeic. (See case A15)

HAY Very dusty.

FARMER Farmer's lung diagnosed in 1972.

CLINICAL EXAMINATION ON ADMISSION - 12 DECEMBER, 1974.

Age - 9 years. Breed - Aberdeen Angus cross. Condition - poor.

Demeanour - bright.

Heart Rate - 60/minute. Irregularly irregular. Heart sounds difficult to hear because of adventitious lung sounds. Pulse - good. Temperature - 102.4°F.

Resp. Rate - 30/minute. Slight hyperpnoea.

Coughing - not heard.

Auscultation - Left, crackles and rhonchi A/V.
Right, crackles and rhonchi A/V.

Other findings - papilloma on hard palate. Teeth very worn.

Time in hospital - 3 weeks.

CLINICAL DIAGNOSIS - Farmer's Lung.

CASE NO. A12

WHEN SEEN ILL January, 1975.

CLINICAL SIGNS Anorexia. Sudden onset dyspnoea (mouth breathing). Coughing heard before this. Temperature - 105°F. Reduced milk yield.

V.S. DIAGNOSIS Allergic pneumonia.

TREATMENT Antibiotics. Betamethasone. Good clinical response.

OTHER INFORMATION

THIS COW No history of any previous disease.

OTHER COWS Total = 20. Occasional coughing. No previous cases of pneumonia in housed adults.

HAY Not considered dusty.

FARMER Unaffected by dust.

CLINICAL EXAMINATION ON ADMISSION - 22 JANUARY, 1975.

Age - 6 years. Breed - Friesian cross. Condition - fair.

Demeanour - bright.

Heart Rate - 90/minute. Pulse - good. Temperature - 101.9°F.

Resp. Rate - 40/minute. Moderate hyperpnoea.

Coughing - occasional paroxysms, non-productive.

Auscultation - Left, loud crackles A/V.
Right, crackles A/V, rhonchi widespread.

Other findings - nil.

Time in hospital - 2 weeks.

CLINICAL DIAGNOSIS - Farmer's Lung.

CASE NO. A13

WHEN SEEN ILL	April, 1971.
CLINICAL SIGNS	Hyperpnoea. Coughing. Tachypnoea. Appeared to recover during the summer while at grass. Ten days after being housed in September she had a second acute episode followed by a third in February.
V.S. DIAGNOSIS	Farmer's lung.
TREATMENT	Antibiotics. Betamethasone. Good clinical response.

OTHER INFORMATION

THIS COW	No history of any previous disease.
OTHER COWS	Total = 20 cows. Occasional coughing. No recent cases of pneumonia in housed adults.
HAY	Mixed quality.
FARMER	He feels "seedy" a few hours after working with mouldy hay.

CLINICAL EXAMINATION ON ADMISSION - 18 FEBRUARY, 1972.

Age - 5 years. Breed - Friesian. Condition - poor.

Demeanour - bright.

Heart Rate - 80/minute. Pulse - good. Temperature - 101.7°F.

Resp. Rate - 70/minute. Slight hyperpnoea.

Coughing - occasional, non-productive.

Auscultation - Left, rhonchi widespread.

Right, crackles A/V, rhonchi widespread.

Other findings - resented thoracic percussion.

Time in hospital - 10 days.

CLINICAL DIAGNOSIS - Farmer's Lung.

CASE NO. A13

WHEN SEEN ILL	April, 1971.
CLINICAL SIGNS	Hyperpnoea. Coughing. Tachypnoea. Appeared to recover during the summer while at grass. Ten days after being housed in September she had a second acute episode followed by a third in February.
V.S. DIAGNOSIS	Farmer's lung.
TREATMENT	Antibiotics. Betamethasone. Good clinical response.

OTHER INFORMATION

THIS COW	No history of any previous disease.
OTHER COWS	Total = 20 cows. Occasional coughing. No recent cases of pneumonia in housed adults.
HAY	Mixed quality.
FARMER	He feels "seedy" a few hours after working with mouldy hay.

CLINICAL EXAMINATION ON ADMISSION - 18 FEBRUARY, 1972.

Age - 5 years. Breed - Friesian. Condition - poor.

Demeanour - bright.

Heart Rate - 80/minute. Pulse - good. Temperature - 101.7°F.

Resp. Rate - 70/minute. Slight hyperpnoea.

Coughing - occasional, non-productive.

Auscultation - Left, rhonchi widespread.

Right, crackles A/V, rhonchi widespread.

Other findings - resented thoracic percussion.

Time in hospital - 10 days.

CLINICAL DIAGNOSIS - Farmer's Lung.

CASE NO. A14

WHEN SEEN ILL January, 1975.

CLINICAL SIGNS Anorexia. Dyspnoea (mouth-breathing). Tachypnoea. Reduced milk yield. Coughing not heard. Temperature $\leq 103^{\circ}F$. Two acute episodes - Jan. 25 and Jan. 29.

V.S. DIAGNOSIS Allergic Pneumonia.

TREATMENT Antibiotics. Betamethasone. Good clinical response.

OTHER INFORMATION

THIS COW No history of any previous disease.

OTHER COWS Total = 42. Frequent coughing. Occasional cases of pneumonia in housed adults.

HAY Mixed quality.

FARMER Develops hay fever on exposure to dust.

CLINICAL EXAMINATION ON ADMISSION - 21 FEBRUARY, 1975.

Age - 6 years. Breed - Friesian. Condition - poor.

Demeanour - bright.

Heart Rate - 70/minute. Pulse - good. Temperature - $102.2^{\circ}F$.

Resp. Rate - 30/minute. Slight hyperpnoea.

Coughing - occasional, non-productive.

Auscultation - no adventitious sounds.

Other findings - nil.

Time in hospital - 7 days.

CLINICAL DIAGNOSIS - Farmer's Lung.

CASE NO. A15

WHEN SEEN ILL March, 1975.

CLINICAL SIGNS Anorexia. Hyperpnoea. Frequent coughing. Temperature $< 103^{\circ}F$.

V.S. DIAGNOSIS Farmer's lung.

TREATMENT Antibiotics. Betamethasone. Good clinical response.

OTHER INFORMATION

THIS COW No history of any previous disease. Hyperpnoea and coughing seen on Jan. 21 (A.W.).

OTHER COWS Total = 30. Occasional coughing. One previous case of pneumonia in a housed adult (case A11).

HAY Very dusty.

FARMER Farmer's lung diagnosed in 1972.

CLINICAL EXAMINATION ON ADMISSION - 19 MARCH, 1975.

Age - 11 years. Breed - Shorthorn. Condition - very poor.

Demeanour - bright.

Heart Rate - 90/minute. Pulse - good. Temperature - $101.7^{\circ}F$.

Resp. Rate - 40/minute. Moderate hyperpnoea.

Coughing - occasional, harsh, non-productive.

Auscultation - no adventitious sounds.

Other findings - nil.

Time in hospital - 2 days.

CLINICAL DIAGNOSIS - Farmer's Lung.

CASE NO. A16

WHEN SEEN ILL April, 1975.

CLINICAL SIGNS Anorexia. Dyspnoea (mouth-breathing). Seen to be coughing and losing weight for several weeks before acute episode. Temperature $< 103^{\circ}F$.

V.S. DIAGNOSIS Farmer's lung ?

TREATMENT Antibiotics. Betamethasone. Poor clinical response.

OTHER INFORMATION

THIS COW Bought in October, 1974.

OTHER COWS Total = 34. No coughing but now going outside. No previous cases of pneumonia in housed adults.

HAY Very dusty.

FARMER Cattleman is unaffected by mouldy hay dust.

CLINICAL EXAMINATION ON ADMISSION - 15 APRIL, 1975.

Age - 5 years. Breed - Aberdeen Angus cross. Condition - poor.

Demeanour - slightly dull.

Heart rate - 100/minute. Pan-systolic murmur loudest on right side. Enlarged, pulsating jugular and mammary veins. Palpable liver. Brisket oedema. Pulse - poor. Temperature - $101.2^{\circ}F$.

Resp. Rate - 30/minute. Gross hyperpnoea - rocking.

Coughing - frequent, non-productive, harsh.

Auscultation - Left, crackles widespread, rhonchi occasional A/V. Right, crackles A/V, rhonchi occasional A/V.

Other findings - resented percussion. Diarrhoea.

Time in hospital - 2 days.

CLINICAL DIAGNOSIS - Congestive Cardiac Failure from Endocarditis with pulmonary thrombo-embolism.

CASE NO. A17

WHEN SEEN ILL March, 1975.

CLINICAL SIGNS Anorexia. Dyspnoea. Coughing. Temperature - 104°F. Had a more severe acute episode 3 weeks prior to this one. Aborted after treatment.

V.S. DIAGNOSIS Farmer's lung.

TREATMENT Antibiotics. Betamethasone. Good clinical response.

OTHER INFORMATION

THIS COW No history of any previous disease.

OTHER COWS TOTAL = 50. Frequent coughing. Has had several cases of pneumonia in housed adults. One or two cows calve "early" each year.

HAY Very dusty. Worst fed to the heifers.

FARMER Unaffected by mouldy hay dust but mother who helps in byre has had a "bad chest" for years.

CLINICAL EXAMINATION ON ADMISSION - 15 APRIL, 1975.

Age - 2 years. Breed - Friesian. Condition - fair.

Demeanour - bright.

Heart Rate - 70/minute. Pulse - good. Temperature - 102°F.

Resp. Rate - 30/minute. Slight hyperpnoea.

Coughing - occasional, harsh, non-productive.

Auscultation - Left, crackles A/V, rhonchi A/V.
Right, rhonchi A/V.

Other findings - nil.

Time in hospital - 2 days.

CLINICAL DIAGNOSIS - Bacterial Pneumonia.

CASE NO. A18

WHEN SEEN ILL April, 1975.

CLINICAL SIGNS Anorexia. Coughing. Hyperpnoea.

V.S. DIAGNOSIS Farmer's lung.

TREATMENT Antibiotics. Betamethasone. Good clinical response.

OTHER INFORMATION

THIS COW No history of any previous disease.

OTHER COWS Total = 40. Not coughing. First case of pneumonia in housed adult for many years.

HAY Dusty.

FARMER He wheezes when works with mouldy hay.

CLINICAL EXAMINATION ON ADMISSION - 8 MAY, 1975.

Age - 3 years. Breed - Friesian. Condition - fair.

Demeanour - bright.

Heart Rate - 70/minute. Pulse - good. Temperature - 102°F.

Resp. Rate - 50/minute. Moderate hyperpnoea.

Coughing - occasional, short paroxysms, non-productive.

Auscultation - Left, loud crackles A/V.

Right, loud crackles A/V, rhonchi occasional A/V.

Other findings - nil.

Time in hospital - 7 days.

CLINICAL DIAGNOSIS - Farmer's Lung/Bacterial Pneumonia?

CASE NO. C1

WHEN SEEN ILL March, 1969.

CLINICAL SIGNS Coughing. Hyperpnoea. Tachypnoea. Weight loss. Slightly dull. Poor milk yield.

V.S. DIAGNOSIS None made.

TREATMENT None given.

OTHER INFORMATION

THIS COW No history of any previous disease. One of first cows to develop respiratory signs.

OTHER COWS Total = 90. Frequent coughing. In previous years several cows have developed acute pneumonia whilst indoors (Chapter 2, Section 1, Herd 1).

HAY Very dusty for several years.

FARMER Farmer's lung diagnosed in early 1969.

CLINICAL EXAMINATION ON ADMISSION - 15 DECEMBER, 1969.

Age - 11 years. Breed - Ayrshire. Condition - fair.

Demeanour - bright.

Heart rate - 70/minute. Pulse - good. Temperature - 102.1°F.

Resp. rate - 20/minute. Slight hyperpnoea.

Coughing - occasional, non-productive, harsh.

Auscultation - right, crackles A/V.

Other findings - nil.

Time in hospital - 7 months.

CLINICAL DIAGNOSIS - Overeating. Chronic farmer's lung.

CASE NO. C2

WHEN SEEN ILL April, 1971.

CLINICAL SIGNS Coughing. Hyperpnoea. Tachypnoea. Frequent coughing and exercise intolerance during the summer. Brisket oedema seen in October.

V.S. DIAGNOSIS Cor pulmonale.

TREATMENT None given.

OTHER INFORMATION

THIS COW No history of any previous disease.

OTHER COWS Total = 100. Occasional coughing. No recent cases of pneumonia in housed adults.

HAY Mouldy for last few years.

FARMER Suffers from hay fever.

CLINICAL EXAMINATION ON ADMISSION - 1 NOVEMBER, 1971.

Age - 10 years. Breed - Friesian. Condition - poor.

Demeanour - slightly dull.

Heart rate - 90/minute. Pulse - poor volume. Distended and pulsating jugular and mammary veins. Palpable liver. Marked brisket oedema. Diarrhoea. Temperature - 102.1°F.

Resp. rate - 40/minute. Moderate hyperpnoea.

Coughing - occasional, harsh.

Auscultation - left, crackles A/V, rhonchi widespread.

- right, rhonchi A/V, no respiratory sounds at all over diaphragmatic area.

Other findings - enlarged left kidney.

Time in hospital - 8 days.

CLINICAL DIAGNOSIS - Cor pulmonale due to Chronic Farmer's Lung.

CASE NO. C3

WHEN SEEN ILL — January, 1971.

CLINICAL SIGNS — Coughing. Hyperpnoea. Reduced appetite. Poor milk yield. Dull. Weight loss. Temperature - 103°F.

V.S. DIAGNOSIS — None made.

TREATMENT — Antibiotics. Poor clinical response.

OTHER INFORMATION

THIS COW — No history of any previous disease. One of most severely affected cows.

OTHER COWS — Total = 54. Herd respiratory problem - Chapter 2, Section 1, Herd 2.

HAY — Very mouldy for last few years.

FARMER — Farmer's lung confirmed in early summer of 1971 at Glasgow Royal Infirmary.

CLINICAL EXAMINATION ON ADMISSION - 27 APRIL, 1971.

Age - 6 years. Breed - Friesian. Condition - poor.

Demeanour - bright.

Heart rate - 80/minute. Pulse - good. Temperature - 102°F.

Resp. rate - 40/minute. Gross hyperpnoea.

Coughing - frequent, productive - moderate amount of greenish mucus.

Auscultation - no adventitious sounds.

Other findings - nil.

Time in hospital - 13 days.

CLINICAL DIAGNOSIS - Chronic Farmer's Lung.

CASE NO. C4

WHEN SEEN ILL — January, 1971.

CLINICAL SIGNS — Coughing. Hyperpnoea. Reduced appetite. Poor milk yield. Dull. Weight loss. Temperature - 103°F.

V.S. DIAGNOSIS — None made.

TREATMENT — Antibiotics. Poor clinical response.

OTHER INFORMATION

THIS COW — No history of any previous disease. One of most severely affected cows.

OTHER COWS — Total = 54. Herd respiratory problem - Chapter 2, Section 1, Herd 2.

HAY — Very mouldy for last few years.

FARMER — Farmer's lung confirmed in early summer of 1971 at Glasgow Royal Infirmary.

CLINICAL EXAMINATION ON ADMISSION - 27 APRIL, 1971.

Age - 6 years. Breed - Friesian. Condition - very poor.

Demeanour - bright.

Heart rate - 60/minute. Pulse - good. Temperature - 101.9°F.

Resp. rate - 50/minute. Gross hyperpnoea.

Coughing - frequent, productive - small amount of greenish mucus.

Auscultation - no adventitious sounds.

Other findings - nil.

Time in hospital - 20 days.

CLINICAL DIAGNOSIS - Chronic Farmer's Lung.

CASE NO. C5

WHEN SEEN ILL — January, 1971.

CLINICAL SIGNS — Coughing. Tachypnoea. Reduced appetite. Poor milk yield. Dull. Weight loss. Temperature - 103°F.

V.S. DIAGNOSIS — None made.

TREATMENT — Antibiotics. Poor clinical response.

OTHER INFORMATION

THIS COW — No history of any previous disease. One of most severely affected cows.

OTHER COWS — Total = 54. Herd respiratory problem - Chapter 2, Section 1, Herd 2.

HAY — Very mouldy for last few years.

FARMER — Farmer's lung confirmed in early summer of 1971 at Glasgow Royal Infirmary.

CLINICAL EXAMINATION ON ADMISSION - 17 JUNE, 1971.

Age - 6 years. Breed - Friesian. Condition - poor.

Demeanour - bright.

Heart rate - 70/minute. Pulse - good. Temperature - 101.2°F.

Resp. rate - 30/minute. Gross hyperpnoea.

Coughing - occasional, productive - small amount of greenish mucus.

Auscultation - left, crackles A/V.

- right, crackles A/V.

Other findings - nil.

Time in hospital - 3 weeks.

CLINICAL DIAGNOSIS - Chronic Farmer's Lung.

CASE NO. C6

WHEN SEEN ILL — February, 1974.

CLINICAL SIGNS — Coughing. Hyperpnoea. Reduced milk yield. Had several "hyperpnoeic" episodes around Xmas, 1974, but not ill enough for V.S. to be called.

V.S. DIAGNOSIS — Farmer's lung ?

TREATMENT — None given.

OTHER INFORMATION

THIS COW — Aborted in early December, 1974.

OTHER COWS — Total = 110. Frequent coughing. Occasional cases of pneumonia in housed adults. In Nov./Dec. 1974 6 cows aborted, probably mycotic abortion. Not brucellosis.

HAY — Very mouldy.

FARMER — He has a "weak" chest and avoids dust.

CLINICAL EXAMINATION ON ADMISSION - 18 FEBRUARY, 1974.

Age - 6 years. Breed - Friesian. Condition - fair.

Demeanour - bright.

Heart rate - 100/minute. Irregularly irregular. Pulse deficit.
Systolic murmur on left. Temperature - 100.5°F.

Resp. rate - 40/minute. Slight hyperpnoea.

Coughing - frequent, short paroxysms, non-productive.

Auscultation - left, crackles A/V.
- right, very harsh respirations.

Other findings - Nervous cow. Resented thoracic percussion.

Time in hospital - 10 days.

CLINICAL DIAGNOSIS - Endocarditis? Farmer's Lung?

CASE NO. C7

WHEN SEEN ILL November, 1971.

CLINICAL SIGNS Hyperpnoea.

V.S. DIAGNOSIS No consultation.

TREATMENT None given.

OTHER INFORMATION

THIS COW No history of any previous disease. Seen to be abnormal during serological survey. Bought when culled.

OTHER COWS Total = 90. Frequent coughing. Several were hyperpnoeic. No recent cases of pneumonia in housed adults.

HAY Very dusty.

FARMER Farmer's lung confirmed about 1965.

CLINICAL EXAMINATION ON ADMISSION - 31 DECEMBER, 1971.

Age - 7 years. Breed - Ayrshire. Condition - good.

Demeanour - Bright.

Heart rate - 80/minute. Pulse - Good. Temperature - 101.1°F.

Resp. rate - 40/minute. Moderate hyperpnoea.

Coughing - occasional, non-productive.

Auscultation - no adventitious sounds.

Time in hospital - 3 months.

CLINICAL DIAGNOSIS - Chronic Farmer's Lung.

CASE NO. C8

WHEN SEEN ILL December, 1972.

CLINICAL SIGNS Coughing. Hyperpnoea. Tachypnoea. Respiratory signs became worse during the following month.

V.S. DIAGNOSIS Farmer's lung?

TREATMENT None given.

OTHER INFORMATION

THIS COW No history of any previous disease.

OTHER COWS Total = 35. Occasional coughing. No recent cases of pneumonia in housed adults.

HAY Very dusty.

FARMER Unaffected by mouldy hay dust.

CLINICAL EXAMINATION ON ADMISSION - 11 JANUARY, 1972.

Age - 8 years. Breed - Galloway. Condition - fair.

Demeanour - bright.

Heart rate - 90/minute. Pulse - good. Temperature - 102.2°F.

Resp. rate - 50/minute. Gross hyperpnoea - occasionally dyspnoeic.

Coughing - frequent, harsh, non-productive.

Auscultation - left, widespread rhonchi especially A/V.

- right, widespread rhonchi especially A/V.

Other findings - nil.

Time in hospital - 17 days.

CLINICAL DIAGNOSIS - Chronic Farmer's Lung.

CASE NO. C9

WHEN SEEN ILL May, 1972.

CLINICAL SIGNS Coughing. Hyperpnoea. Tachypnoea.

V.S. DIAGNOSIS No consultation.

TREATMENT None given.

OTHER INFORMATION

THIS COW No history of any previous disease. Seen to be abnormal during serological survey. Bought when culled. During the summer, she lay down as soon as she entered the byre to be milked.

OTHER COWS Total = 90. Frequent coughing. Several were hyperpnoeic. No recent cases of pneumonia in housed adults.

HAY Very dusty.

FARMER Farmer's lung confirmed about 1965.

CLINICAL EXAMINATION ON ADMISSION - 16 OCTOBER, 1972.

Age - 6 years. Breed - Ayrshire. Condition - poor.

Demeanour - bright.

Heart rate - 80/minute. Pulse - good. Temperature - 101.9°F.

Resp. rate - 40/minute. Slight hyperpnoea.

Coughing - occasional, non-productive.

Auscultation - left, crackles A/V, rhonchi widespread.

- right, crackles A/V, rhonchi widespread.

Other findings - nil.

Time in hospital - 6 weeks.

CLINICAL DIAGNOSIS - Chronic Farmer's Lung/D.F.A.

CASE NO. C10

WHEN SEEN ILL May, 1972.

CLINICAL SIGNS Coughing. Hyperpnoea.

V.S. DIAGNOSIS No consultation.

TREATMENT None given.

OTHER INFORMATION

THIS COW No history of any previous disease. Seen to be abnormal during serological survey. Bought when culled.

OTHER COWS Total = 90. Frequent coughing. Several were hyperpnoeic. No recent case of pneumonia in housed adults.

HAY Very dusty.

FARMER Farmer's lung confirmed about 1965.

CLINICAL EXAMINATION ON ADMISSION - 16 OCTOBER, 1972.

Age - 10 years. Breed - Ayrshire. Condition - poor.

Demeanour - bright.

Heart rate - 70/minute. Pulse - good. Temperature - 102.1°F.

Resp. rate - 25/minute. Slight hyperpnoea.

Coughing - occasional, non-productive.

Auscultation - no adventitious lung sounds.

Other findings - bilateral serous nasal discharge.

Time in hospital - 2 weeks.

CLINICAL DIAGNOSIS - Chronic Farmer's Lung.

CASE NO. C11

WHEN SEEN ILL May, 1972.

CLINICAL SIGNS Coughing. Hyperpnoea. Tachypnoea. Weight loss.

V.S. DIAGNOSIS No consultation.

TREATMENT None given.

OTHER INFORMATION

THIS COW Treated for mastitis in January, 1972. Seen to be abnormal during serological survey. Bought when culled.

OTHER COWS Total = 30. Frequent coughing. No recent cases of pneumonia in housed adults.

HAY Dusty.

FARMER Unaffected by mouldy hay dust.

CLINICAL EXAMINATION ON ADMISSON - 21 OCTOBER, 1972.

Age - 5 years. Breed - Friesian. Condition - good.

Demeanour - bright.

Heart rate - 80/minute. Pulse - good. Temperature - 101.1°F.

Resp. rate - 25/minute. Not hyperpnoeic.

Coughing - occasional, non-productive.

Auscultation - no adventitious sounds.

Other findings - nil.

Time in hospital - 12 days.

CLINICAL DIAGNOSIS - Chronic Farmer's Lung.

CASE NO. C12

WHEN SEEN ILL June, 1972.

CLINICAL SIGNS Coughing. Tachypnoea. Exercise intolerance.

V.S. DIAGNOSIS Farmer's lung?

TREATMENT None given.

OTHER INFORMATION

THIS COW No history of any previous disease. Farmer not worried by her becoming dyspnoeic and mouth-breathing on being moved because she always recovered.

OTHER COWS Total = 25. No coughing. No recent cases of pneumonia in housed adults.

HAY Dusty.

FARMER Unaffected by mouldy hay dust.

CLINICAL EXAMINATION ON ADMISSION - 2 NOVEMBER, 1972.

Age - 8 years. Breed - Aberdeen Angus cross. Condition - poor. Demeanour - bright.

Heart rate - 80/minute. Pulse - good. Temperature - 101.7°F.

Resp. rate - 50/minute. Moderate hyperpnoea.

Coughing - frequent paroxysms, non-productive, harsh.

Auscultation - left, crackles A/V, rhonchi widespread.

- right, crackles A/V, rhonchi A/V.

Other findings - nil.

Time in hospital - 4 weeks.

CLINICAL DIAGNOSIS - Chronic Farmer's Lung/D.F.A.

CASE NO. C13

WHEN SEEN ILL — February, 1971.

CLINICAL SIGNS — Coughing. Hyperpnoea. Reduced appetite. Poor milk yield. Dull. Weight loss. Temperature - 102°F.

V.S. DIAGNOSIS — None made.

TREATMENT — None given.

OTHER INFORMATION

THIS COW — No history of any previous disease. Bought when culled.

OTHER COWS — Total = 54. Herd respiratory problem - Chapter 2, Section 1, Herd 2.

HAY — Very mouldy for last few years.

FARMER — Farmer's lung confirmed in early summer of 1971 at Glasgow Royal Infirmary.

CLINICAL EXAMINATION ON ADMISSION - 27 NOVEMBER, 1972.

Age - 7 years. Breed - Friesian. Condition - very poor.

Demeanour - bright.

Heart rate - 70/minute. Pulse - good. Temperature - 101.9°F.

Resp. rate - 50/minute. Moderate hyperpnoea.

Coughing - frequent, non-productive, harsh.

Auscultation - left, crackles and rhonchi A/V.

- right, crackles and rhonchi A/V.

Other findings - bilateral serous nasal discharge.

Time in hospital - 3 weeks.

CLINICAL DIAGNOSIS - Chronic Farmer's Lung/D.F.A.

CASE NO. C14

WHEN SEEN ILL — February, 1971.

CLINICAL SIGNS — Coughing. Hyperpnoea. Reduced appetite. Poor milk yield. Dull. Weight loss. Temperature - 101°F.

V.S. DIAGNOSIS — None made.

TREATMENT — None given.

OTHER INFORMATION

THIS COW — No history of any previous disease. Bought when culled.

OTHER COWS — Total = 54. Herd respiratory problem - Chapter 2, Section 1, Herd 2.

HAY — Very mouldy for last few years.

FARMER — Farmer's lung confirmed in early summer of 1971 at Glasgow Royal Infirmary.

CLINICAL EXAMINATION ON ADMISSION - 27 NOVEMBER, 1972.

Age - 9 years. Breed - Friesian. Condition - very poor.

Demeanour - bright.

Heart rate - 60/minute. Pulse - good. Temperature - 101.9°F.

Resp. rate - 30/minute. Slight hyperpnoea.

Coughing - occasional, non-productive, harsh.

Auscultation - left, rhonchi A/V.

- right, rhonchi widespread.

Other findings - nil.

Time in hospital - 3 weeks.

CLINICAL DIAGNOSIS - Chronic Farmer's Lung/D.F.A.

CASE NO. C15

WHEN SEEN ILL April, 1971.

CLINICAL SIGNS Coughing. Hyperpnoea. Tachypnoea.

V.S. DIAGNOSIS No consultation.

TREATMENT None given.

OTHER INFORMATION

THIS COW Treated for pneumonia 6 years ago but has not suffered any relapse. Seen to be abnormal during serological survey. Bought when culled.

OTHER COWS Total = 60. Occasional coughing. No recent cases of pneumonia in housed adults.

HAY Very dusty.

FARMER Unaffected by mouldy hay dust.

CLINICAL EXAMINATION ON ADMISSION - 29 NOVEMBER, 1972.

Age - 8 years. Breed - Ayrshire. Condition - poor.

Demeanour - bright.

Heart rate - 70/minute. Pulse - good. Temperature - 101.3°F.

Resp. rate - 50/minute. Gross hyperpnoea.

Coughing - frequent, non-productive, harsh.

Auscultation - no adventitious sounds, harsh respirations.

Other findings - enlarged left kidney.

Time in hospital - 3 weeks.

CLINICAL DIAGNOSIS - Chronic Farmer's Lung.

CASE NO. C16

WHEN SEEN ILL — November, 1972.

CLINICAL SIGNS — Coughing. Hyperpnoea. Tachypnoea. These signs became worse after she was housed.

V.S. DIAGNOSIS — Pneumonia.

TREATMENT — Antibiotics. Poor clinical response.

OTHER INFORMATION

THIS COW — "Unwell" during 1970-71 winter, but not treated for any specific disease.

OTHER COWS — No information.

HAY — Dusty.

FARMER — Suffers from bronchitis.

CLINICAL EXAMINATION ON ADMISSION - 11 DECEMBER, 1972.

Age - 4 years. Breed - Galloway. Condition - fair.

Demeanour - slightly dull.

Heart rate - 70/minute. Pulse - good. Temperature - 102°F.

Resp. rate - 70/minute. Moderate hyperpnoea.

Coughing - frequent, non-productive, soft.

Auscultation - left, crackles and rhonchi A/V.

- right, crackles and rhonchi A/V.

Other findings - nil.

Time in hospital - 9 days.

CLINICAL DIAGNOSIS - Chronic Farmer's Lung/D.F.A.

CASE NO. C17

WHEN SEEN ILL May, 1973.

CLINICAL SIGNS Coughing. Hyperpnoea.

V.S. DIAGNOSIS Farmer's lung.

TREATMENT None given.

OTHER INFORMATION

THIS COW Treated several times for insidious onset respiratory disease during the previous winter.

OTHER COWS Not available.

HAY Very mouldy.

FARMER Unaffected by mouldy hay dust.

CLINICAL EXAMINATION ON ADMISSION - 30 MAY, 1973.

Age - 10 years. Breed - Shorthorn cross. Condition - poor.

Demeanour - bright.

Heart rate - 90/minute. Pulse - good. Temperature - 102.3°F.

Resp. rate - 50/minute. Gross hyperpnoea.

Coughing - frequent, non-productive, harsh.

Auscultation - left, crackles and rhonchi A/V.

- right, crackles and rhonchi A/V.

Other findings - nil.

Time in hospital - 5 months.

CLINICAL DIAGNOSIS - Chronic Farmer's Lung/D.F.A.

CASE NO. C18

WHEN SEEN ILL May, 1972.

CLINICAL SIGNS Coughing. Hyperpnoea.

V.S. DIAGNOSIS No consultation.

TREATMENT None given.

OTHER INFORMATION

THIS COW No history of any previous disease. Seen to be abnormal during serological survey. Bought when culled.

OTHER COWS Total = 54. Herd respiratory problem - Chapter 2, Section 1, Herd 2.

HAY Very mouldy for last few years.

FARMER Farmer's lung confirmed in early summer of 1971 at Glasgow Royal Infirmary.

CLINICAL EXAMINATION ON ADMISSION - 19 JANUARY, 1974.

Age - 7 years. Breed - Jersey. Condition - poor.

Demeanour - bright.

Heart rate - 80/minute. Pulse - good. Temperature - 102.4°F.

Resp. rate - 60/minute. Gross hyperpnoea - rocking.

Coughing - frequent paroxysms, non-productive, harsh.

Auscultation - left, crackles widespread.

- right, crackles widespread.

Other findings - mastitis.

Time in hospital - 4 weeks.

CLINICAL DIAGNOSIS - Chronic Farmer's Lung.

CASE NO. C19

WHEN SEEN ILL March, 1974.

CLINICAL SIGNS Coughing. Hyperpnoea. Tachypnoea. Slightly dull.

V.S. DIAGNOSIS Farmer's lung.

TREATMENT None given.

OTHER INFORMATION

THIS COW No history of any previous disease. Slight clinical improvement immediately she was put out to grass, then her condition deteriorated.

OTHER COWS Total = 33. Occasional coughing. Another cow was similarly affected and she died 5 July. At post-mortem she had patent husk and chronic farmer's lung. No other recent cases of pneumonia in housed adults.

HAY Very dusty.

FARMER Unaffected by mouldy hay dust.

CLINICAL EXAMINATION ON ADMISSION - 6 JULY, 1974.

Age - 8 years. Breed - Shorthorn cross. Condition - very poor. Demeanour - bright.

Heart rate - 70/minute. Pulse - good. Temperature - 101.7°F.

Resp. rate - 50/minute. Moderate hyperpnoea.

Coughing - frequent, paroxysms, non-productive, harsh.

Auscultation - left, crackles and rhonchi A/V.

- right, crackles A/V.

Other findings - nil.

Time in hospital - 1 week.

CLINICAL DIAGNOSIS - Chronic Farmer's Lung/D.F.A.

CASE NO. C20

WHEN SEEN ILL September, 1974.

CLINICAL SIGNS Frequent coughing. Hyperpnoea. Bilateral crackles and rhonchi.

V.S. DIAGNOSIS No consultation.

TREATMENT None given.

OTHER INFORMATION

THIS COW No history of any previous disease. Farmer thinks this cow "is going the same way as her stall-mate", Case A8.

OTHER COWS Total = 32. Frequent coughing in spring. No recent cases of pneumonia in housed adults.

HAY Mixed quality.

FARMER Wife feeds cows: farmer's lung diagnosed in 1971.

CLINICAL EXAMINATION ON ADMISSION - 30 OCTOBER, 1974.

Age - 7 years. Breed - Friesian. Condition - poor.

Demeanour - bright.

Heart rate - 80/minute. Pulse - good. Temperature - 102.1°F.

Resp. rate - 50/minute. Gross hyperpnoea - rocking.

Coughing - frequent, occasionally productive-thick mucus, harsh.

Auscultation - left, crackles A/V.

- right, crackles A/V, rhonchi widespread.

Other findings - fracture and ventral displacement of left tuber coxae.

Time in hospital - 4 weeks.

CLINICAL DIAGNOSIS - Chronic Farmer's Lung /D.F.A.

CASE NO. C21

WHEN SEEN ILL November, 1974.

CLINICAL SIGNS Exercise intolerance, e.g. dyspnoea, when being housed. Weight loss.

V.S. DIAGNOSIS Farmer's lung?

TREATMENT None given.

OTHER INFORMATION

THIS COW Not treated for any previous disease, but she had lost weight during 1973-74 winter and put it on again in the summer. By November she had begun to lose weight again.

OTHER COWS Total about 100. Others in same group (15) not coughing at present. Several of the older cows are thin.

HAY Mixed quality.

FARMER Unaffected by mouldy hay dust, but his brother has had farmer's lung for about 20 years.

CLINICAL EXAMINATION ON ADMISSION - 14 NOVEMBER, 1974.

Age - 10 years. Breed - Galloway. Condition - very poor.

Demeanour - dull.

Heart rate - 100/minute. Pulse - poor volume. Jugular and mammary veins distended but not pulsating. Brisket oedema, ascites and palpable liver. Heart sounds difficult to hear because of adventitious lung sounds. Temperature - 101.6°F.

Resp. rate - 40/minute. Moderate hyperpnoea.

CASE NO. C21 (Cont'd.)

Coughing - not heard.

Auscultation - left, crackles and rhonchi both widespread.

- right, crackles and rhonchi both widespread.

Other findings - profuse diarrhoea. Papilloma on hard palate.

CLINICAL DIAGNOSIS - Cor pulmonale resulting from Chronic Farmer's Lung.

CASE NO. C22

WHEN SEEN ILL	February, 1975.
CLINICAL SIGNS	Frequent coughing. Hyperpnoea. Weight loss since calving in February.
V.S. DIAGNOSIS	Farmer's lung.
TREATMENT	None given.

OTHER INFORMATION

THIS COW	No history of any previous disease.
OTHER COWS	Total = 70. Herd respiratory problem - Chapter 2, Section 1, Herd 4.
HAY	Usually dusty.
FARMER	Cattleman is unaffected by dust.

CLINICAL EXAMINATION ON ADMISSION - 1 MAY, 1975.

Age - 12 years. Breed - Jersey. Condition - poor.

Demeanour - bright.

Heart rate - 50/minute. Pulse - good. Temperature - 101.3°F.

Resp. rate - 25/minute. Gross hyperpnoea.

Coughing - frequent, non-productive, harsh.

Auscultation - left, crackles A/V, rhonchi A/V.
right, crackles A/V, rhonchi A/V.

Other findings - nil.

Time in hospital - 6 days.

CLINICAL DIAGNOSIS - Chronic Farmer's Lung/D.F.A.

CASE NO. C23

WHEN SEEN ILL October.

CLINICAL SIGNS Frequent coughing. Hyperpnoea. Widespread bilateral crackles and rhonchi.

V.S. DIAGNOSIS Parasitic bronchitis.

TREATMENT None given.

OTHER INFORMATION

THIS COW No history of any previous disease.

OTHER COWS Total = 70. Herd respiratory problem - Chapter 2, Section 1, Herd 4.

HAY Usually dusty.

FARMER Cattleman is unaffected by dust.

CLINICAL EXAMINATION ON ADMISSION - 5 DECEMBER, 1974.

Age - 10 years. Breed - Jersey. Condition - poor.

Demeanour - bright.

Heart rate - 65/minute. Pulse - good. Temperature - 101.3°F.

Resp. rate - 40/minute. Moderate hyperpnoea.

Coughing - frequent short paroxysms, non-productive.

Auscultation - left, crackles A/V, rhonchi A/V.

- right, crackles A/V, rhonchi dorsally.

Other findings - nil.

Time in hospital - 7 days.

CLINICAL DIAGNOSIS - Chronic Farmer's Lung.

CASE NO. C24

WHEN SEEN ILL October.

CLINICAL SIGNS Frequent coughing. Hyperpnoea.

V.S. DIAGNOSIS Parasitic bronchitis.

TREATMENT None given.

OTHER INFORMATION

THIS COW No history of any previous disease.

OTHER COWS Total = 70. Herd respiratory problem - Chapter 2, Section 1, Herd 4.

HAY Usually dusty.

FARMER Cattleman is unaffected by dust.

CLINICAL EXAMINATION ON ADMISSION - 5 DECEMBER, 1974.

Age - 10 years. Breed - Jersey. Condition - poor.

Demeanour - bright.

Heart rate - 80/minute. Pulse - good. Temperature - 107.4°F.

Resp. rate - 50/minute. Slight hyperpnoea.

Coughing - not heard.

Auscultation - No adventitious sounds heard. Harsh respirations.

Other findings - Bilateral arthritis of hip-joints.

Time in hospital - 7 days.

CLINICAL DIAGNOSIS - Chronic Farmer's Lung.

CASE NO. C25

WHEN SEEN ILL November, 1974.

CLINICAL SIGNS Frequent coughing.

V.S. DIAGNOSIS Parasitic Bronchitis.

TREATMENT None given.

OTHER INFORMATION

THIS COW No history of any previous disease.

OTHER COWS Total = 70. Herd respiratory problem - Chapter 2, Section 1, Herd 4.

HAY Usually dusty.

FARMER Cattleman is unaffected by dust.

CLINICAL EXAMINATION ON ADMISSION - 14 MARCH, 1975.

Age - 13 years. Breed - Jersey. Condition - poor.

Demeanour - bright.

Heart rate - 80/minute. Pulse - good. Temperature - 101.5°F.

Resp. rate - 40/minute. Moderate hyperpnoea.

Coughing - occasional, non-productive.

Auscultation - left, crackles widespread.

- right, crackles A/V, rhonchi widespread.

Other findings - unable to see properly.

Time in hospital - 4 days.

CLINICAL DIAGNOSIS - Chronic Farmer's Lung/D.F.A.

CASE NO. C26

WHEN SEEN ILL December, 1974.

CLINICAL SIGNS Frequent productive coughing. Hyperpnoea. Tachypnoea.

V.S. DIAGNOSIS Farmer's lung.

TREATMENT None given.

OTHER INFORMATION

THIS COW Treated for pneumonia within 2 weeks of being bought 3 years ago. Has coughed ever since. In summer, after milking, she lay down as soon as she went into the field. Frequent bouts of hyperpnoea during the winter.

OTHER COWS Total = 24. Eight are coughing and/or hyperpnoeic. No recent cases of pneumonia in housed adults.

HAY Not dusty for last 2 years.

FARMER Had "bad chest" for 5 years. Significant improvement since she began sleeping with her head towards the north!!

CLINICAL EXAMINATION ON ADMISSION - 15 APRIL, 1975.

Age - 7 years. Breed - Friesian. Condition - good.

Demeanour - bright.

Heart rate - 80/minute. Pulse - good. Temperature - 103.2°F.

Resp. rate - 30/minute. Moderate hyperpnoea.

Coughing - harsh, frequent, productive.

Auscultation - no adventitious sounds.

Other findings - nil.

Time in hospital - 2 days.

CLINICAL DIAGNOSIS - Chronic Farmer's Lung/D.F.A.

CASE NO. C27

WHEN SEEN ILL March, 1975.

CLINICAL SIGNS Frequent coughing. Hyperpnoea. Weight loss since calving in February.

V.S. DIAGNOSIS Farmer's lung.

TREATMENT None given.

OTHER INFORMATION

THIS COW No history of any previous disease.

OTHER COWS Total = 70. Herd respiratory problem - Chapter 2, Section 1, Herd 4.

HAY Usually dusty.

FARMER Cattleman is unaffected by dust.

CLINICAL EXAMINATION ON ADMISSION - 1 MAY, 1975.

Age - 10 years. Breed - Jersey. Condition - poor.

Demeanour - bright.

Heart rate - 80/minute. Pulse - good. Temperature - 102.1°F.

Resp. rate - 30/minute. Moderate hyperpnoea.

Coughing - frequent, harsh, non-productive.

Auscultation - no adventitious sounds.

Other findings - nil.

Time in hospital - 6 days.

CLINICAL DIAGNOSIS - Chronic Farmer's Lung.

PARAMETER	CASE NUMBER					NORMAL RANGE
	A1	A2	A3	A4	A5	
HAEMATOLOGY						
P.C.V. %	29.5	32	C	26.5	29	25-35
Hb.g./100 ml.	9.75	11.2	L	8.35	10.7	10-14
R.B.C. $10^6/mm^3$	6.09	6.95	O	4.06	5.16	6-8
W.B.C. mm^3	11,500	8,400	T	10,800	22,000	$7\text{-}10^4$
Neutrophils %	48.5	38.0	T	62	68.5	25-35
Lymphocytes %	48.5	61.0	E	37	31.5	60-70
Eosinophils %	3.0	1.0	D	1	0	0-5
BIOCHEMISTRY						
Urea m.mol/l	3.3	1.8	6.8	3.3	4.0	0-8.3
Sodium m.mol/l	140	142	-	-	-	136-151
Potassium m.mol/l	4.4	4.2	-	-	-	3.2-5.8
Chloride m.mol/l	110	101	-	-	-	96-111
Calcium m.mol/l	2.0	2.5	-	2.1	2.5	2.3-3.1
Magnesium m.mol/l	0.6	0.8	-	1.1	0.9	0.6-1.4
Inorg. PO_4 m.mol/l	1.9	2.1	1.2	1.5	1.7	1.1-2.8
Bilirubin u.mol/l	1.7	-	3.4	17.0	1.5	0-8.5
Alk. phosphatase I.U.	36	-	64	21	70	0-100
S.G.O.T. I.U.	65	-	74	113	198	0-100
S.G.P.T. I.U.	9	-	15	5	27	0-50
Total Protein g/l	92	83	92	102	81	50-90
Albumin g/l	28	38	24	48	22	25-40
Globulin g/l	64	45	68	54	59	25-50
OTHER TESTS						
Urine Protein g/l	-	-	-	-	-	0-0.5
D. viviparus larvae	0	0	0	0	0	Negative
Strongyle eggs	-	-	-	-	-	0-500
Ppt. to *M. faeni*	+	+	+	+	+	Negative
Plasma pepsinogen I.U.	-	-	-	-	-	0-1500
Acid-fast bacteria	-	-	-	-	-	Negative

PARAMETER	CASE NUMBER					NORMAL RANGE
	A6	A7	A8	A9	A10	
HAEMATOLOGY						
P.C.V. %	27.5	33	33	29.5	32	25-35
Hb.g./100 ml.	9.5	10.4	-	-	-	10-14
R.B.C. $10^6/mm^3$	4.80	6.54	-	-	-	6-8
W.B.C. mm^3	7,300	9,400	6,300	15,400	8,000	$7\text{-}10^4$
Neutrophils %	65.5	36.5	-	58	26	25-35
Lymphocytes %	32.5	62	-	38	41	60-70
Eosinophils %	2	1.5	-	4	33	0-5
BIOCHEMISTRY						
Urea m.mol/l	3.2	8.3	4.0	2.7	3.8	0-8.3
Sodium m.mol/l	139	143	140	148	152	136-151
Potassium m.mol/l	3.8	3.4	5.3	4.2	4.6	3.2-5.6
Chloride m.mol/l	104	105	103	105	104	96-111
Calcium m.mol/l	2.5	2.6	2.5	2.0	2.4	2.3-3.1
Magnesium m.mol/l	1.0	0.8	0.8	0.7	0.7	0.6-1.4
Inorg, PO_4 m.mol/l	1.3	1.6	1.3	0.9	2.7	1.1-2.8
Bilirubin u.mol/l	3.4	1.7	1.5	1.4	1.7	0-8.5
Alk. phosphatase I.U.	50	57	71	85	50	0-100
S.G.O.T. I.U.	43	103	114	32	90	0-100
S.G.P.T. I.U.	34	25	34	23	43	0-50
Total Protein g/l	87	100	69	88	86	50-90
Albumin g/l	27	29	31	29	21	25-40
Globulin g/l	60	71	38	59	65	25-50
OTHER TESTS						
Urine Protein g/l	0.06	0.21	0.06	0.03	0.13	0-0.5
D. viviparus larvae	0	0	0	0	0	Negative
Strongyle eggs	-	-	-	-	-	0-500
Ppt. to *M. faeni*	+	+	+	+	+	Negative
Plasma pepsinogen I.U.	-	-	-	-	-	0-1500
Acid-fast bacteria	-	-	-	-	-	Negative

PARAMETER	CASE NUMBER					NORMAL RANGE
	A11	A12	A13	A14	A15	
HAEMATOLOGY						
P.C.V. %	28	26.5	31.5	30.5	23	25-35
Hb.g./100 ml.	8.2	-	11.1	9.7	7.9	10-14
R.B.C. $10^6/mm^3$	4.74	-	6.69	5.95	4.14	6-8
W.B.C. mm^3	7,800	7,600	7,100	13,200	7,800	$7-10^4$
Neutrophils %	25	25	48	21	52	25-35
Lymphocytes %	71	75	44.5	48	40	60-70
Eosinophils %	4	0	7.5	31	8	0-5
BIOCHEMISTRY						
Urea m.mol/l	9.3	1.1	3.2	3.6	1.2	0-8.3
Sodium m.mol/l	144	136	140	137	140	136-151
Potassium m.mol/l	5.5	3.9	4.4	4.6	4.5	3.2-5.8
Chloride m.mol/l	105	100	92	100	94	96-111
Calcium m.mol/l	2.1	2.1	2.5	2.5	2.2	2.3-3.1
Magnesium m.mol/l	1.4	0.6	0.6	0.8	0.5	0.6-1.4
Inorg, PO_4 m.mol/l	2.3	1.3	1.8	1.0	2.5	1.1-2.8
Bilirubin u.mol/l	1.4	3.0	3.4	16.0	1.0	0-8.5
Alk. phosphatase I.U.	85	71	50	66	160	0-100
S.G.O.T. I.U.	211	74	58	81	66	0-100
S.G.P.T. I.U.	23	17	14	25	34	0-50
Total Protein g/l	68	95	98	84	83	50-90
Albumin g/l	20	17	26	24	21	25-40
Globulin g/l	48	78	72	60	62	25-50
OTHER TESTS						
Urine Protein g/l	-	0.03	3.75	0.06	-	0-0.5
D. viviparus larvae	0	0	0	0	0	Negative
Strongyle eggs	-	-	-	-	-	0-500
Ppt. to *M. faeni*	+	+	+	+	+	Negative
Plasma pepsinogen I.U.	-	-	-	-	-	0-1500
Acid-fast bacteria	-	-	-	-	-	Negative

PARAMETER	CASE NUMBER					NORMAL RANGE
	A16	A17	A18			
HAEMATOLOGY						
P.C.V. %	27	28	39.5			25-35
Hb.g./100 ml.	-	-	-			10-14
R.B.C. $10^6/mm^3$	-	-	-			6-8
W.B.C. mm^3	11,000	6,100	7,100			$7-10^4$
Neutrophils %	63	47	40			25-35
Lymphocytes %	37	46	55			60-70
Eosinophils %	0	7	5			0-5
BIOCHEMISTRY						
Urea m.mol/l	3.4	3.5	3.4			0-8.3
Sodium m.mol/l	142	147	142			136-151
Potassium m.mol/l	4.6	4.5	3.8			3.2-5.8
Chloride m.mol/l	103	93	87			96-111
Calcium m.mol/l	2.3	2.3	2.3			2.3-3.1
Magnesium m.mol/l	0.4	0.8	0.5			0.6-1.4
Inorg. PO_4 m.mol/l	1.3	2.6	1.8			1.1-2.8
Bilirubin u.mol/l	4.0	2.0	13.0			0-8.5
Alk. phosphatase I.U.	149	59	93			0-100
S.G.O.T. I.U.	188	68	251			0-100
S.G.P.T. I.U.	77	20	33			0-50
Total Protein g/l	82	89	84			50-90
Albumin g/l	17	22	22			25-40
Globulin g/l	65	67	62			25-50
OTHER TESTS						
Urine Protein g/l	0.29	0.07	0.20			0-0.5
D. viviparus larvae	0	0	0			Negative
Strongyle eggs	0	-	-			0-500
Ppt. to *M. faeni*	+	+	+			Negative
Plasma pepsinogen I.U.	654	-	-			0-1500
Acid-fast bacteria	0	-	-			Negative

PARAMETER	CASE NUMBER					NORMAL RANGE
	C1	C2	C3	C4	C5	
HAEMATOLOGY						
P.C.V. %	34	34.5	24	25.5	30.5	25-35
Hb.g./100 ml.	11.5	11.7	8.0	8.4	10.5	10-14
R.B.C. $10^6/mm^3$	5.65	6.94	5.02	4.87	6.73	6-8
W.B.C. mm^3	5,900	11,600	6,200	7,000	9,000	$7-10^4$
Neutrophils %	29.5	62.5	59	41.5	42.5	25-35
Lymphocytes %	55.5	37.5	33.5	47.5	51	60-70
Eosinophils %	15	-	7.5	11	6.5	0-5
BIOCHEMISTRY						
Urea m.mol/l	14.0	9.0	2.8	2.8	5.4	0-8.3
Sodium m.mol/l	133	142	148	148	142	136-151
Potassium m.mol/l	3.4	4.0	4.2	4.3	4.0	3.2-5.8
Chloride m.mol/l	98	100	101	99	101	96-111
Calcium m.mol/l	-	8.6	-	-	2.4	2.3-3.1
Magnesium m.mol/l	-	0.6	-	-	0.9	0.6-1.4
Inorg. PO_4 m.mol/l	-	2.2	2.1	2.0	1.5	1.1-2.8
Bilirubin u.mol/l	12	12	1.7	12	1.3	0-8.5
Alk. phosphatase I.U.	490	12	36	36	50	0-100
S.G.O.T. I.U.	125	121	99	96	147	0-100
S.G.P.T. I.U.	46	15	20	24	40	0-50
Total Protein g/l	89	8.0	102	91	84	50-90
Albumin g/l	30	32	31	31	27	25-40
Globulin g/l	59	48	72	60	57	25-50
OTHER TESTS						
Urine Protein g/l	-	7.0	-	-	0.2	0-0.5
D. viviparus larvae	0	0	0	0	0	Negative
Strongyle eggs	-	0	-	-	-	0-500
Ppt. to *M. faeni*	+	+	+	+	+	Negative
Plasma pepsinogen I.U.	-	1250	-	-	-	0-1500
Acid-fast bacteria	-	0	-	-	-	Negative

PARAMETER	CASE NUMBER					NORMAL RANGE
	C6	C7	C8	C9	C10	
HAEMATOLOGY						
P.C.V. %	29.5	32.5	25	34	26	25-35
Hb.g./100 ml.	-	12.5	8.2	-	-	10-14
R.B.C. $10^6/mm^3$	-	6.61	5.10	-	-	6-8
W.B.C. mm^3	10,400	9,900	7,400	8,300	8,900	$7-10^4$
Neutrophils %	-	44.5	57	43.5	60	25-35
Lymphocytes %	-	46.5	40	51.5	39.5	60-70
Eosinophils %	-	9	3	5	0.5	0-5
BIOCHEMISTRY						
Urea m.mol/l	5.8	1.7	1.8	6.3	6.6	0-8.3
Sodium m.mol/l	146	136	130	142	140	136-151
Potassium m.mol/l	3.6	4.0	4.4	3.8	3.6	3.2-5.8
Chloride m.mol/l	101	99	97	98	101	96-111
Calcium m.mol/l	3.1	2.8	2.3	2.5	2.5	2.3-3.1
Magnesium m.mol/l	0.5	0.8	0.4	0.9	0.9	0.6-1.4
Inorg. PO_4 m.mol/l	2.3	2.0	1.1	2.1	2.0	1.1-2.8
Bilirubin u.mol/l	18.0	5.1	5.1	3.4	3.4	0-8.5
Alk. phosphatase I.U.	253	28	36	57	50	0-100
S.G.O.T. I.U.	502	61	69	67	55	0-100
S.G.P.T. I.U.	17	29	14	31	32	0-50
Total Protein g/l	97	100	90	97	84	50-90
Albumin g/l	13	42	21	23	24	25-40
Globulin g/l	84	58	69	74	60	25-50
OTHER TESTS						
Urine Protein g/l	-	0.05	0.24	0.03	-	0-0.5
D. viviparus larvae	0	0	0	0	0	Negative
Strongyle eggs	-	-	-	-	-	0-500
Ppt. to *M. faeni*	+	+	+	+	+	Negative
Plasma pepsinogen I.U.	-	-	-	-	-	0-1500
Acid-fast bacteria	-	-	-	-	-	Negative

PARAMETER	CASE NUMBER					NORMAL RANGE
	C11	C12	C13	C14	C15	
HAEMATOLOGY						
P.C.V. %	38	34	30.5	25	34.5	25-35
Hb.g./100 ml.	-	-	11.0	8.5	-	10-14
R.B.C. $10^6/mm^3$	-	-	6.84	4.84	-	6-8
W.B.C. mm^3	9,000	11,400	13,300	12,500	10,900	$7-10^4$
Neutrophils %	58	51.5	74	57	44	25-35
Lymphocytes %	41.5	42	22	36.5	52.5	60-70
Eosinophils %	0.5	0.5	4	6.5	3.5	0-5
BIOCHEMISTRY						
Urea m.mol/l	3.0	2.8	3.7	3.7	3.0	0-8.3
Sodium m.mol/l	146	144	146	144	146	136-151
Potassium m.mol/l	3.9	3.5	5.6	4.9	4.2	3.2-5.8
Chloride m.mol/l	101	92	102	100	96	96-111
Calcium m.mol/l	2.5	2.1	2.6	2.5	2.6	2.3-3.1
Magnesium m.mol/l	1.0	0.6	0.7	0.6	0.9	0.6-1.4
Inorg. PO_4 m.mol/l	1.9	1.7	1.8	2.4	1.9	1.1-2.8
Bilirubin u.mol/l	3.4	3.4	3.4	3.4	1.7	0-8.5
Alk. phosphatase I.U.	50	78	43	71	14	0-100
S.G.O.T. I.U.	45	72	97	74	46	0-100
S.G.P.T. I.U.	26	19	20	25	25	0-50
Total Protein g/l	78	99	94	101	85	50-90
Albumin g/l	28	23	22	26	27	25-40
Globulin g/l	50	76	72	75	58	25-50
OTHER TESTS						
Urine Protein g/l	-	1.8	0.07	0.03	0.11	0-0.5
D. viviparus larvae	0	0	0	0	0	Negative
Strongyle eggs	-	-	-	-	-	0-500
Ppt. to *M. faeni*	+	+	+	+	+	Negative
Plasma pepsinogen I.U.	-	-	-	-	-	0-1500
Acid-fast bacteria	-	-	-	-	-	Negative

PARAMETER	CASE NUMBER					NORMAL RANGE
	C16	C17	C18	C19	C20	
HAEMATOLOGY						
P.C.V. %	34	25	30.5	29	35	25-35
Hb.g./100 ml.	-	7.6	-	9.1	-	10-14
R.B.C. $10^6/mm^3$	-	4.54	-	6.52	-	6-8
W.B.C. mm^3	7,000	6,400	6,300	5,600	13,600	$7-10^4$
Neutrophils %	57.5	20	-	52	-	25-35
Lymphocytes %	36.5	78	-	34	-	60-70
Eosinophils %	6.0	2	-	14	-	0-5
BIOCHEMISTRY						
Urea m.mol/l	2.7	2.0	4.2	3.8	4.3	0-8.3
Sodium m.mol/l	147	143	136	142	146	136-151
Potassium m.mol/l	3.5	5.1	5.5	4.3	4.3	3.2-5.8
Chloride m.mol/l	101	98	92	103	103	96-111
Calcium m.mol/l	2.3	2.5	2.5	2.8	2.3	2.3-3.1
Magnesium m.mol/l	0.6	0.6	0.6	0.7	0.9	0.6-1.4
Inorg. PO_4 m.mol/l	0.9	1.2	1.9	3.0	3.2	1.1-2.8
Bilirubin u.mol/l	12	1.7	5.1	3.4	1.3	0-8.5
Alk. phosphatase I.U.	21	50	43	43	64	0-100
S.G.O.T. I.U.	88	58	83	78	75	0-100
S.G.P.T. I.U.	16	18	29	33	29	0-50
Total Protein g/l	87	78	98	93	105	50-90
Albumin g/l	14	19	22	23	22	25-40
Globulin g/l	73	59	76	70	83	25-50
OTHER TESTS						
Urine Protein g/l	0.05	0.14	0.69	0.20	0.88	0-0.5
D. viviparus larvae	0	0	0	0	0	Negative
Strongyle eggs	-	-	-	-	-	0-500
Ppt. to *M. faeni*	+	+	+	+	+	Negative
Plasma pepsinogen I.U.	-	-	-	-	-	0-1500
Acid-fast bacteria	-	-	-	-	-	Negative

PARAMETER	CASE NUMBER					NORMAL RANGE
	C21	C22	C23	C24	C25	
HAEMATOLOGY						
P.C.V. %	31	30	28.5	36.5	32	25-35
Hb.g./100 ml.	-	10.4	-	-	-	10-14
R.B.C. $10^6/mm^3$	-	5.70	-	-	-	6-8
W.B.C. mm^3	6,000	5,700	8,000	6,600	7,300	$7\text{-}10^4$
Neutrophils %	55	57	56	53	62	25-35
Lymphocytes %	44	43	43	46	32	60-70
Eosinophils %	1	0	1	1	6	0-5
BIOCHEMISTRY						
Urea m.mol/l	1.3	2.8	2.8	2.7	2.8	0-8.3
Sodium m.mol/l	137	149	141	141	142	136-151
Potassium m.mol/l	4.3	4.1	4.5	4.8	4.2	3.2-5.8
Chloride m.mol/l	93	103	95	108	102	96-111
Calcium m.mol/l	2.2	2.4	2.7	2.7	2.5	2.3-3.1
Magnesium m.mol/l	0.6	0.6	0.6	0.4	0.8	0.6-1.4
Inorg. PO_4 m.mol/l	2.1	0.9	1.9	1.0	1.3	1.1-2.8
Bilirubin u.mol/l	5.1	10.0	1.7	6.8	8.0	0-8.5
Alk. phosphatase I.U.	-	41	64	78	93	0-100
S.G.O.T. I.U.	44	75	83	90	554	0-100
S.G.P.T. I.U.	-	21	55	19	35	0-50
Total Protein g/l	89	82	82	91	93	50-90
Albumin g/l	18	20	24	27	20	25-40
Globulin g/l	71	62	58	64	73	25-50
OTHER TESTS						
Urine Protein g/l	0.42	0.77	1.12	0.06	0.04	0-0.5
D. viviparus larvae	0	0	0	0	0	Negative
Strongyle eggs	0	-	-	-	-	0-500
Ppt. to *M. faeni*	+	+	+	+	+	Negative
Plasma pepsinogen I.U.	883	-	-	-	-	0-1500
Acid-fast bacteria	0	-	-	-	-	Negative

PARAMETER	CASE NUMBER					NORMAL RANGE
	C26	C27				
HAEMATOLOGY						
P.C.V. %	30	26				25-35
Hb.g./100 ml.	-	9.1				10-14
R.B.C. $10^6/mm^3$	-	5.15				6-8
W.B.C. mm^3	7,100	3,000				$7-10^4$
Neutrophils %	26	46				25-35
Lymphocytes %	56	52				60-70
Eosinophils %	18	2				0-5
BIOCHEMISTRY						
Urea m.mol/l	4.1	2.4				0-8.3
Sodium m.mol/l	147	150				136-151
Potassium m.mol/l	5.1	4.8				3.2-5.8
Chloride m.mol/l	95	106				96-111
Calcium m.mol/l	2.5	2.5				2.3-3.1
Magnesium m.mol/l	0.7	0.6				0.6-1.4
Inorg. PO_4 m.mol/l	1.9	1.1				1.1-2.8
Bilirubin u.mol/l	1.0	13.0				0-8.5
Alk. phosphatase I.U.	31	30				0-100
S.G.O.T. I.U.	64	67				0-100
S.G.P.T. I.U.	22	23				0-50
Total Protein g/l	110	96				50-90
Albumin g/l	24	19				25-40
Globulin g/l	86	77				25-50
OTHER TESTS						
Urine Protein g/l	0.01	0.27				0-0.5
D. viviparus larvae	0	0				Negative
Strongyle eggs	-	-				0-500
Ppt. to *M. faeni*	+	+				Negative
Plasma pepsinogen I.U.	-	-				0-1500
Acid-fast bacteria	-	-				Negative

APPENDIX 1 - TABLE 1

The relationship between an animal's age, the month respiratory disease was first noticed and the form of disease.

FORM OF DISEASE	AGE (YEARS)	MONTH RESPIRATORY SIGNS NOTICED		
		SEPT. - DEC.	JAN. - MAR.	APRIL - JUNE
Acute	< 6	1	5	5
Chronic	< 6	1	4	2
Acute	> 6	3	3	1
Chronic	> 6	8	6	6
TOTAL		13	18	14

APPENDIX 1 - TABLE 2

The relationship between an animal's age, the system of husbandry and the form of disease.

AGE (YEARS)	ACUTE FORM		CHRONIC FORM	
	BEEF	DAIRY	BEEF	DAIRY
< 6	3	8	1	6
> 6	3	4	6	14
TOTAL	6	12	7	20

APPENDIX 1 - TABLE 3

The relationship between an animal's age, its geographical origin and the form of disease.

AGE (YEARS)	SCOTLAND		ENGLAND		WESTMORLAND	
	ACUTE	CHRONIC	ACUTE	CHRONIC	ACUTE	CHRONIC
< 6	2	2	9	5	8	5
> 6	1	5	6	15	6	9
TOTAL	3	7	15	20	14	14

APPENDIX 1 - TABLE 4

The relationship between an animal's age, the farmer's reaction to mouldy hay dust and the form of disease.

AGE (YEARS)	ACUTE FORM				CHRONIC FORM			
	NO REACTION	POSITIVE REACTION			NO REACTION	POSITIVE REACTION		
		TOTAL	F.L.	O.D.		TOTAL	F.L.	O.D.
< 6	6	5	0	5	1	6	4	2
> 6	2	5	5	0	11	9	7	2
TOTAL	8	10	5	5	12	15	11	4

APPENDIX 1 - TABLE 5

The relationship between the month respiratory disease was first noticed, the system of husbandry and the form of disease.

MONTH RESPIRATORY SIGNS NOTICED	ACUTE FORM		CHRONIC FORM	
	BEEF	DAIRY	BEEF	DAIRY
Sept. - Dec.	2	2	3	6
Jan. - March	2	6	1	9
April - June	2	4	3	5
TOTAL	6	12	7	20

APPENDIX 1 - TABLE 6

The relationship between the month respiratory disease was first noticed, the geographical origin of the animal and the form of disease.

MONTH RESPIRATORY SIGNS NOTICED	ACUTE FORM			CHRONIC FORM		
	SCOTLAND	ENGLAND	W'MORLAND	SCOTLAND	ENGLAND	W'MORLAND
Sept. - Dec.	0	4	4	1	8	4
Jan. - March	2	6	6	2	8	6
April - June	1	5	4	4	4	4
TOTAL	3	15	14	7	20	14

APPENDIX 1 - TABLE 7

The relationship between the month respiratory disease was first noticed, the farmer's reaction to mouldy hay dust and the form of disease.

MONTH RESPIRATORY SIGNS NOTICED	ACUTE FORM				CHRONIC FORM			
	NO REACTION	POSITIVE REACTION			NO REACTION	POSITIVE REACTION		
		TOTAL	F.L.	O.D.		TOTAL	F.L.	O.D.
Sept. - Dec.	3	1	1	0	5	4	2	2
Jan. - March	2	6	3	3	3	7	6	1
April - June	3	3	1	2	4	4	3	1
TOTAL	8	10	5	5	12	15	11	4

APPENDIX 1 - TABLE 8

The relationship between the geographical origin of the animal, the farmer's reaction to mouldy hay dust and the form of disease.

GEOGRAPHICAL ORIGIN	ACUTE FORM				CHRONIC FORM			
	NO REACTION	POSITIVE REACTION			NO REACTION	POSITIVE REACTION		
		TOTAL	F.L.	O.D.		TOTAL	F.L.	O.D.
Scotland	1	2	1	1	1	6	4	2
England	7	8	4	4	11	9	7	2
Westmorland	6	8	4	4	6	8	7	1
TOTAL	8	10	5	5	12	15	11	4

APPENDIX 1 - TABLE 9

The relationship between the system of husbandry, the farmer's reaction to mouldy hay dust and the form of disease.

SYSTEM OF HUSBANDRY	ACUTE FORM				CHRONIC FORM			
	NO REACTION	POSITIVE REACTION			NO REACTION	POSITIVE REACTION		
		TOTAL	F.L.	O.D.		TOTAL	F.L.	O.D.
Beef	2	4	2	2	5	2	0	2
Dairy	6	6	3	3	7	13	11	2
TOTAL	8	10	5	5	12	15	11	4

APPENDIX 1 - TABLE 10

The relationship between the system of husbandry, the geographical origin of the animal and the form of disease.

HUSBANDRY	ACUTE FORM			CHRONIC FORM		
	SCOTLAND	ENGLAND	WESTMORLAND	SCOTLAND	ENGLAND	WESTMORLAND
Beef	1	5	4	1	6	6
Dairy	2	10	10	6	14	8
TOTAL	3	15	14	7	20	14

APPENDIX 1 - TABLE 11

The relationship between the system of husbandry, the breed of animal and the form of disease.

SYSTEM OF HUSBANDRY	ACUTE FORM		CHRONIC FORM	
	FRIESIAN	OTHER BREEDS	FRIESIAN	OTHER BREEDS
Beef	1	5	1	6
Dairy	11	1	9	11
TOTAL	12	6	10	17

APPRENDIX 1 - TABLE 12

The relationship between an animal's age, the month respiratory disease was first noticed and the system of husbandry.

MONTH RESPIRATORY SIGNS NOTICED	< 6 YEARS		> 6 YEARS	
	BEEF	DAIRY	BEEF	DAIRY
Sept. - Dec.	1	1	4	7
Jan. - March	1	8	2	7
April - June	2	5	3	4
TOTAL	4	14	9	18

APPENDIX 1 - TABLE 13

The relationship between an animal's age, its geographical origin and the month respiratory disease was first noticed.

MONTH RESPIRATORY SIGNS NOTICED	< 6 YEARS			> 6 YEARS		
	SCOTLAND	ENGLAND	W'MORLAND	SCOTLAND	ENGLAND	W'MORLAND
Sept. - Dec.	0	2	2	1	10	6
Jan. - March	2	7	7	2	7	5
April - June	2	5	4	3	4	4
TOTAL	4	14	13	6	21	15

APPENDIX 1 - TABLE 14

The relationship between an animal's age, the month respiratory disease was first noticed and the farmer's reaction to mouldy hay dust.

MONTH RESPIRATORY SIGNS NOTICED	< 6 YEARS				> 6 YEARS			
	NO REACTION	POSITIVE REACTION			NO REACTION	POSITIVE REACTION		
		TOTAL	F.L.	O.D.		TOTAL	F.L.	O.D.
Sept. - Dec.	1	1	0	1	7	4	3	1
Jan. - March	2	7	3	4	3	6	6	0
April - June	4	3	1	2	3	4	3	1
TOTAL	7	11	4	7	13	14	12	2

APPENDIX 1 - TABLE 15

The relationship between the month respiratory disease was first noticed, the system of husbandry and the geographical origin of the animal.

MONTH RESPIRATORY SIGNS NOTICED	BEEF			DAIRY		
	SCOTLAND	ENGLAND	W'MORLAND	SCOTLAND	ENGLAND	W'MORLAND
Sept. - Dec.	0	5	5	1	7	3
Jan. - March	1	2	2	3	12	10
April - June	1	4	3	4	5	5
TOTAL	2	11	10	8	24	18

APPENDIX 1 - TABLE 16

The relationship between an animal's age, its geographical origin and the system of husbandry.

SYSTEM OF HUSBANDRY	< 6 YEARS			> 6 YEARS		
	SCOTLAND	ENGLAND	WESTMORLAND	SCOTLAND	ENGLAND	WESTMORLAND
Beef	1	3	2	1	8	8
Dairy	3	11	11	5	13	7
TOTAL	4	14	13	6	21	15

APPENDIX 1 - TABLE 17

The relationship between the month respiratory disease was first noticed, the system of husbandry and the farmer's reaction to mouldy hay dust.

SYSTEM OF HUSBANDRY		FARMER'S REACTION TO DUST			
		NO REACTION	POSITIVE REACTION	FARMER'S LUNG	OTHER DISORDER
BEEF	Sept. - Dec.	3	2	1	1
	Jan. - March	1	2	1	1
	April - June	2	3	0	3
DAIRY	Sept. - Dec.	5	3	2	1
	Jan. - March	4	11	8	3
	April - June	3	6	4	2
TOTAL		18	27	16	11

APPENDIX 1 - TABLE 18

The relationship between an animal's age, its geographical origin and the farmer's reaction to mouldy hay dust.

FARMER'S REACTION TO DUST	< 6 YEARS			> 6 YEARS		
	SCOTLAND	ENGLAND	W'LAND	SCOTLAND	ENGLAND	W'LAND
No reaction	1	6	5	1	12	7
Positive reaction	3	8	8	5	9	8
Farmer's lung	1	3	3	4	8	8
Other disorder	2	5	5	1	1	0
TOTAL	4	14	13	6	21	15

APPENDIX 1 - TABLE 19

The relationship between an animal's age, the system of husbandry and the farmer's reaction to mouldy hay dust.

SYSTEM OF HUSBANDRY	< 6 YEARS				> 6 YEARS			
	NO REACTION	POSITIVE REACTION			NO REACTION	POSITIVE REACTION		
		TOTAL	F.L.	O.D.		TOTAL	F.L.	O.D.
Beef	1	3	0	3	6	3	2	1
Dairy	6	8	4	4	7	11	10	1
TOTAL	7	11	4	7	13	14	12	2

APPENDIX 1 - TABLE 20

The relationship between the geographical origin of the animal, the system of husbandry and the farmer's reaction to mouldy hay dust.

FARMER'S REACTION TO DUST	BEEF			DAIRY		
	SCOTLAND	ENGLAND	W'LAND	SCOTLAND	ENGLAND	W'LAND
No reaction	0	7	6	2	11	6
Positive reaction	2	4	4	6	13	12
Farmer's lung	0	2	2	5	9	9
Other disorder	2	2	2	1	4	3
TOTAL	2	11	10	8	24	18

APPENDIX 1 - TABLE 21

The relationship between the month respiratory disease was first noticed, the farmer's reaction to mouldy hay dust and the geographical origin of the animal.

MONTH RESPIRATORY SIGNS NOTICED	NO REACTION	POSITIVE REACTION		
		TOTAL	F.L.	O.D.
SCOTLAND				
Sept. - Dec.	0	1	1	0
Jan. - March	0	4	2	2
April - May	2	3	2	1
TOTAL	2	8	5	3
ENGLAND				
Sept. - Dec.	8	4	2	2
Jan. - March	5	9	7	2
April - May	5	4	2	2
TOTAL	18	17	11	6
WESTMORLAND				
Sept. - Dec.	5	3	2	1
Jan. - March	3	9	7	2
April - May	4	4	2	2
TOTAL	12	16	11	5

APPENDIX 1 - TABLE 22

The relationship between an animal's age, the breed and the form of disease.

Form of Disease	< 6 Years		> 6 Years	
	Friesian	Other Breeds	Friesian	Other Breeds
Acute	8	3	4	3
Chronic	5	2	5	15
TOTAL	13	5	9	18

APPENDIX 1 - TABLE 23

The relationship between an animal's age, its geographical location and breed.

Breed of Cattle	6 Years			6 Years		
	Scotland	England	W'morland	Scotland	England	W'morland
Friesian	1	12	12	2	7	6
Other breeds	3	2	1	4	14	9
TOTAL	4	14	13	6	21	15

APPENDIX 1 - TABLE 24

The main epidemiological findings of the 45 cases of farmer's lung in cattle.

Case No.	Age (Years)	Breed	System of Husbandry*	Geographical Location +	Month Resp. Disease Noticed	Farmer's Reaction to Dust
A1	6	Friesian	Dairy - B	Westmorland	May	Nil
A2	6	Ayrshire	Dairy - B	Scotland/L	May	Nil
A3	10	Friesian	Dairy - B	Scotland/D	February	Farmer's lung
A4	6	Friesian	Dairy - B	Westmorland	November	Nil
A5	5	Galloway	Beef - L	Scotland/D	February	Other disorder
A6	4	Friesian	Dairy - B	Westmorland	February	Other disorder
A7	10	Friesian	Dairy - B	Westmorland	September	Nil
A8	8	Friesian	Dairy - B	Westmorland	May	Farmer's lung
A9	8	Friesian	Dairy - B	Westmorland	January	Farmer's lung
A10	8	A.A.	Beef - L	Westmorland	November	Nil
A11	9	A.A.	Beef - B	Westmorland	December	Farmer's lung
A12	6	Friesian	Dairy - B	Westmorland	January	Nil
A13	5	Friesian	Beef - B	Westmorland	April	Other disorder
A14	6	Friesian	Dairy - B	Westmorland	January	Other disorder
A15	10	Shorthorn	Beef - B	Westmorland	March	Farmer's lung
A16	5	A.A.	Beef - B	England	April	Nil
A17	2	Friesian	Dairy - B	Westmorland	March	Nil
A18	3	Friesian	Dairy - B	Westmorland	April	Other disorder
C1	10	Ayrshire	Dairy - B	Scotland/D	March	Farmer's lung
C2	10	Friesian	Beef - B	Scotland/L	April	Other disorder
C3	6	Friesian	Dairy - B	Westmorland	January	Farmer's lung
C4	6	Friesian	Dairy - B	Westmorland	January	Farmer's lung
C5	*6	Friesian	Dairy - B	Westmorland	January	Farmer's lung
C6	6	Friesian	Dairy - B	Scotland/D	February	Other disorder
C7	7	Ayrshire	Dairy - B	Scotland/L	November	Farmer's lung
C8	8	Galloway	Beef - B	Westmorland	December	Nil
C9	6	Ayrshire	Dairy - B	Scotland/L	May	Farmer's lung
C10	10	Ayrshire	Dairy - B	Scotland/L	May	Farmer's lung
C11	5	Friesian	Dairy - B	Westmorland	May	Nil
C12	8	A.A.	Beef - L	Westmorland	June	Nil

APPENDIX 1 - TABLE 24 (Cont'd.)

Case No.	(Years)	Breed	System of Husbandry*	Geographical Location+	Month Resp. Disease Noticed	Farmer's Reaction to Dust
C13	5	Friesian	Dairy - B	Westmorland	February	Farmer's lung
C14	9	Friesian	Dairy - B	Westmorland	February	Farmer's lung
C15	8	Ayrshire	Dairy - B	Scotland/L	April	Nil
C16	4	Galloway	Beef - B	Westmorland	November	Other disorder
C17	10	Shorthorn	Beef - B	Westmorland	May	Nil
C18	7	Jersey	Dairy - B	Westmorland	May	Farmer's lung
C19	8	Shorthorn	Beef - B	Westmorland	March	Nil
C20	7	Friesian	Dairy - B	Westmorland	September	Farmer's lung
C21	10	Galloway	Beef - L	Westmorland	November	Nil
C22	10	Jersey	Dairy - L	England	February	Nil
C23	10	Jersey	Dairy - L	England	October	Nil
C24	10	Jersey	Dairy - L	England	October	Nil
C25	10	Jersey	Dairy - L	England	November	Nil
C26	7	Friesian	Dairy - B	England	December	Other disorder
C27	10	Jersey	Dairy - L	England	March	Nil

* B = byre housed, L = loose housed:

\+ Scotland/L = Lanarkshire,
Scotland/D = Dumfriesshire,
England = all counties excluding Westmorland.

APPENDIX 2

RANDOM FARM NO. 1 (R1)

Sample No.	Age	Breed	1970-71		1971-72	
				1:6:71	2:11:71	22:5:72
1	4	A		-	-	-
2	4	A		-		
3	6	A		-	-	-
4	4	A		-	-	-
5	4	A		-	-	-
6	4	A		-	-	-
7	5	A		-	-	-
8	4	A		-	-	-
9	5	A		-	-	-
10	4	A		-	-	
11	6	A		-	-	-
12	11	A		-	-	-
13	5	A		-	-	-
14	4	A		-		-
15	4	A		-	-	-
16	5	A		-	-	-
17	5	A		-	-	-
18	4	A		-	-	-
19	6	A		-	-	-
20	4	A		-	-	-
21	7	A		-	-	-
22	5	A		-	-	-
23	9	A		-	-	-
24	4	A		-		

RANDOM FARM NO. 1 (R1)

Sample No.	Age	Breed	1970-71		1971-72	
				1:6:71	2:11:71	22:5:72
25	6	A		-	-	-
26	8	A		-	-	-
27	6	A		-	-	-
28	6	A		-	-	-
29	4	A		-	-	-
30	6	A		-	-	-
31	6	A		-	-	-
32	6	A		-	-	-
33	5	A		-		
34	8	A		-	-	-
35	5	A		-	-	-
36	9	A		-	-	-
37	5	A		-		
38	4	A		-	-	-
39	6	A		-	-	-
40	5	A		-	-	-
41	5	A		-	-	-
42	5	A		-	-	-
43	5	A		-	-	-
44	10	A		-	-	-
45	4	A		-	-	-
46	9	A		-	-	-
47	6	A		-		-
48	5	A		-	-	-

RANDOM FARM NO. 1 (R1)

Sample No.	Age	Breed	1970-71		1971-72	
				1:6:71	2:11:71	22:5:72
49	5	A		-	-	-
50	6	A		-	-	-
51	5	A		-	-	-
52	9	A		-		
53	9	A		-	-	-
54	6	A		-	-	-
55	4	A		-		
56	4	A		-	-	-
57	5	A		-	-	-
58	5	A		-	-	-
59	10	A		-		
60	6	A		-	-	-
61	4	A		-	-	-
62	4	A		-	-	
63	5	A		-	-	-
64	6	A		-		
65	4	A		-	-	-
66	9	A		-	-	-
67	8	A		-		
68	6	A		-	-	-
69	7	A		-	-	-
70	4	A		-	-	-
71	5	A		-	-	-
72	5	A		-	-	-

RANDOM FARM NO. 1 (R1)

Sample No.	Age	Breed	1970-71		1971-72	
				1:6:71	2:11:71	22:5:72
73	4	A		-	-	-
74	4	A		-	-	-
75	5	A		-	-	-
76		A			-	-
77		A			-	-
78		A			-	-
79		A			-	-
80		A			-	-
81		A			-	-
82		A			-	
83		A			-	-
84		A			-	
85		A			-	
86		A			-	-
87		A			-	
TOTALS				75	76	72

RANDOM FARM NO. 2 (R2)

Sample No.	Age	Breed	1970-71		1971-72	
				26:4:71	4:11:71	25:5:72
1	14	A		-		
2	7	A		+	+	
3	6	A		+		+
4	6	A		-	-	-
5	6	A		-		
6	5	A		-	-	-
7	10	A		+	+	+
8	10	A		+		
9	3	F		+		-
10	5	F		-		
11	4	F		+		-
12	3	F		-	-	-
13	3	A		-	-	-
14	3	F		-	-	-
15	8	A		-		
16	3	F		-	-	
17	3	F		-	-	-
18	4	A.		-	+	-
19	6	A		+	-	
20	5	Her. X		+	-	-
21	6	F		+	+	+
22	4	F		-	-	-
23	8	A		-		
24	6	A		+		

RANDOM FARM NO. 2 (R2)

Sample No.	Age	Breed	1970-71		1971-72	
				26:4:71	4:11:71	25:5:72
25	9	A		+		
26	9	Her. X		+	-	+
27	8	A		-		
28	7	A		+		
29	7	A		-		
30	7	A		+		
31	8	A		+		
32	5	F		+	-	-
33	5	F		-		-
34	4	F		-	-	+
35	7	A		-	-	
36	9	A		-		-
37	4	F		+		+
38	5	F		-		
39	5	F		-		
40	5	A		-	-	-
41	3	F		+	-	
42	6	A		+		
43	8	A		+		
44	8	A		+		
45	6	F		-		
46	10	A		+		
47	10	F		+		
48	10	A		+	+	+

RANDOM FARM NO. 2 (R2)

Sample No.	Age	Breed	1970-71		1971-72	
				26:4:71	4:11:71	25:5:72
49	4	F		+	+	-
50	9	A		+		
51	9	A		-		
52		A			-	
53		A			-	-
54		F			-	-
55		A			-	+
56		A			-	-
57		A			-	-
58		A			-	+
59		A			-	
60		F			-	-
61		A			-	
62		A			-	
63		F			-	-
64		A			-	
65		A			+	-
66		F			-	
67					+	
68		F			-	-
69		F			-	
70		A			-	
71		A				-
72		F			-	

RANDOM FARM NO. 2 (R2)

Sample No.	Age	Breed	1970-71		1971-72	
				26:4:71	4:11:71	25:5:72
73		A			-	
74		F			-	-
75		F			-	
76		F			-	
77		F			+	
78		A			-	
80		A				-
81		A				+
82		A				+
83		A				-
84		A				-
85		A				-
86		A				-
87		A				-
88		A				-
TOTALS				51	48	44

RANDOM FARM NO. 3 (R3)

Sample No.	Age	Breed	1970-71		1971-72	
				10:6:71		
1	4	A		-		
2	7	F		-		
3	7	F		-		
4	6	A		-		
5	2	A		-		
6	2	A		-		
7	4	A		-		
8	4	A		-		
9	3	A		-		
10	3	F		+		
11	4	F		-		
12	9	A		+		
13	3	A		+		
14	6	A		-		
15	3	A		+		
16	6	A		+		
17	3	F		-		
18	6	A		-		
19	3	A		-		
20	3	F		-		
21	9	A		-		
22	3	F		-		
23	10	A		-		
24	5	F		+		

RANDOM FARM NO. 3 (R3)

Sample No.	Age	Breed	1970-71		1971-72	
				10:6:71		
25	9	A		+		
26	10	A		-		
27	9	A		-		
28	7	F		+		
29	8	A		-		
30	2	A		-		
31	3	A		+		
32	10	A		+		
33	4	A		-		
34	4	A		-		
35	4	A		+		
36	3	F		-		
37	3	A		-		
38	6	A		+		
39	6	A		-		
40	6	F		+		
41	4	F		-		
43	4	F		-		
44	4	A		-		
45	7	A		-		
46	7	A		-		
47	3	F		-		
48	8	F		-		
49	9	A		+		

RANDOM FARM NO. 3 (R3)

Sample No.	Age	Breed	1970-71		1971-72	
				10:6:70		
50	8	F		+		
51	3	A		-		
52	7	A		-		
53	6	A		-		
54	10	A		+		
55	4	F		-		
56	3	A		-		
57	6	A		+		
58	3	A		-		
59	3	A		-		
60	4	F		-		
61	7	A		-		
62	7	A		-		
63	8	A		-		
64	7	F		+		
65	3	A		-		
66	6	A		-		
67	8	A		-		
69	6	A		-		
70	9	A		-		
71	3	F		-		
72	4	A		-		
TOTAL				71		

RANDOM FARM NO. 4 (R4)

Sample No.	1970-71		Sample No.	1970-71	
	-	22:3:71		-	22:3:71
1		-	37		-
2		+	38		-
5		+	39		-
6		+	40		-
8		-	42		-
9		+	43		+
10		-	44		-
11		+	46		-
14		-	48		+
16		+	49		-
17		-	51		-
19		-	53		+
20		+	54		+
21		+	55		+
22		-	57		-
24		-	58		+
25		+	59		+
26		+	60		+
27		-	62		-
28		-	63		+
31		+	64		-
33		-	65		-
34		-	66		-
36		-	67		-

RANDOM FARM NO. 4 (R4)

Sample No.	1970-71		Sample No.	1970-71	
	-	22:3:71			
68		-			
69		-			
70		-			
71		-			
TOTAL		52			

POSITIVE SAMPLE FARM NO. 1 (PS1)

Sample No.	Age	Breed	1970-71		1971-72	
			16:10:70	26:3:71	3:11:71	29:4:72
1	6	A	-	-		
2	4	F	-	-	-	-
3	3	F	-	-	-	-
4	13		-			
5	5	F	-	-	-	-
6	4	F	-	-	-	-
7	5	F	-	-	-	-
8	4	F	-	-	+	-
9	11		-			
10	5		-	-	-	
11	4		-	-		
12	5		-	-	-	
13	5		-	-		
14	7		-	+	+	
15	4	A	-	-	-	-
16	6	F	-	-	-	-
17	7	A	-	+	+	-
18	3	F	-	-	-	-
19	5		-	-		
20	4		-	+	+	
21	5	A	-	+	+	-
22	5	F	-	+	+	+
23	4	F	-	-	+	-
24	6		-			

POSITIVE SAMPLE FARM NO. 1 (PS1)

Sample No.	Age	Breed	1970-71		1971-72	
			16:10;70	26:3:71	3:11:71	29:4:72
25	6		-			
26	5	F	-	+	+	+
27	7		-	+		
28	5		-	-		
29	14		-	+	+	
30	11	A	+			
31	4	F	-	+		Broken
32	4		-			
33	4	A			-	-
34	3	A		-	-	Broken
35	6			-	-	
36	6	F	+	+	-	-
37	3			-	-	
38	6	F		-	-	-
39	3	A		-	-	-
40	4	A			-	-
41	3	F			-	-
42	3	F			-	-
43	3	F			-	-
44	4	F			-	-
45	3	F			-	-
46	3	F			-	-
47	4	A			-	-
48	3	F				-

POSITIVE SAMPLE FARM NO. 1 (PSI)

Sample No.	Age	Breed	1970-71		1971-72	
			16:10:70	26:3:71	3:11:71	29:4:72
49	3	F				-
50	3	A				-
52	3	F				-
53	4	A				-
54	3	F				-
TOTALS			32	33	34	32

POSITIVE SAMPLE FARM NO. 2 (PS2)

Sample No.	Age	Breed	1970-71		1971-72	
			14:12:70	17:5:71		
1			-			
2			+			
3	5		-	-		
4	6		-	-		
5			-			
6	6		-	-		
7			-			
8			-			
9	8		-	-		
10			-			
11	8		-	-		
12	6		-	+		
13		Sh. X	+			
14			-			
15			-			
16	3		-	-		
17	3		-	-		
18	3		-	-		
19			-			
20	3		-	-		
21			-			
22			-			
23	6		-	-		
24	9		-	-		

POSITIVE SAMPLE FARM NO. 2 (PS2)

Sample No.	Age	Breed	1970-71		1971-72	
			14:12:70	17:5:71		
25			-			
26	6		-	-		
27	6		-	-		
28			-			
29	6		-	-		
30	4		-	-		
31			-			
32			-			
33	8		-	-		
34	9		+	+		
35			-			
36			-			
37	9		+	+		
38	8		+	+		
39			-			
40	10			-		
42	2			-		
43	4			-		
46	8			+		
47	6			-		
48	4			-		
49	3			-		
50	3			-		
51	5	Her. Bull		-		

POSITIVE SAMPLE FARM NO. 2 (PS2)

Sample No.	Age	Breed	1970-71		1971-72	
			14:12:70	17:5:71		
52	7			-		
53	6			-		
54	9			-		
55	5			-		
56	6			-		
57	3			-		
58	3			-		
59	3			-		
60	3			-		
61	5			-		
62	6			-		
63	9			-		
64	9			+		
65	5			-		
TOTALS			39	43		

POSITIVE SAMPLE FARM NO. 3 (PS3)

Sample No.	Age	Breed	1970-71		1971-72	
			15:12:70	27:4:71		
1	12	G	+			
2	12	G	-			
3	13	G	-	-		
4	12	G	-			
5	13	G	-	-		
6	3	G	-	+		
7	3	G	-	+		
8	4	G	+	+		
9	3	G	-	+		
10	13	G	+	+		
11	5	G	-			
12	13	G	-	-		
13	10	G	+	+		
14	6	G	-	-		
15	4	G	-	-		
16		G	-	-		
17		G	+	-		
18	5	G	+	+		
19		G	+	+		
20	5	G	-	-		
21	4	G	-	-		
22	12	G	+	-		
23	6	G	-	-		
24	2	G	-	-		

POSITIVE SAMPLE FARM NO. 3 (PS3)

Sample No.	Age	Breed	1970-71		1971-72	
			15:12:70	27:4:71		
25	7	G	-	-		
26	2	G	-	-		
27	5	G	-	+		
28	2	G	-	-		
29	5	G	-	-		
30	3	G	-	-		
31	2	G	-	+		
32	2	G	-			
33	4	G	-	+		
34	14	G	+	-		
35	5	G	-	+		
36	18	G	-	-		
37	5	G	-	-		
38	4	G	-	-		
39	5	G	-	-		
40	4	G	-	+		
41	2	G	-	-		
42	2	G	-	-		
43	3	G	-	-		
44	2	G	-	-		
45	4	G	-	+		
46	5	G	+	+		
47	5	G	+	+		
48	2	G	+	-		

POSITIVE SAMPLE FARM NO. 3 (PS3)

Sample No.	Age	Breed	1970-71		1971-72	
			15:12:70	27:4:71		
49	5	G	-	+		
50	5	G	-	-		
51	5	G	-	-		
52	5	G	-	-		
53	5	G	-	-		
54	3	G	-			
55	5	G	-	-		
56	16	G	-			
57	7	G	-	+		
58	5	G	-	-		
59	7	G	-			
60	7	G	-			
61	9	G	-			
62	4	G	-	-		
63	5	G	-	-		
64	8	G	-			
65	7	G	-			
66	6	G	-	-		
67	8	G	-	-		
68		G	+	+		
69	6	G	-	-		
70	7	G	-	-		
71	9	G	-	+		
72	5	G	-			

POSITIVE SAMPLE FARM NO. 3 (PS3)

Sample No.	Age	Breed	1970-71		1971-72	
			15:12:70	27:4:71		
73	11	G	-	-		
74	10	G	-	-		
75	10	G	-	-		
76	10	G	+	+		
77	10	G	-	-		
78	9	G	-	-		
79	5	G	-			
80	5	G	-	-		
81	7	G	-	+		
82	6	G	-	-		
83	6	G	-	-		
84	3	G	-	-		
85	11	G	+	+		
86	4	G	-	-		
87	4	G	-	-		
88	4	G	-	-		
89	8	G	-	+		
90	14	G	-	+		
91	5		-	-		
92	10		-	-		
93	9		-			
94	5		-	+		
95	10		-	-		
96	14		-			

POSITIVE SAMPLE FARM NO. 3 (PS3)

Sample No.	Age	Breed	1970-71		1971-72	
			15:12:70	27:4:71		
97	12		+	+		
98	6		+	-		
99						
100				-		
101				+		
102				+		
103				-		
104				-		
105				+		
106				+		
107				-		
109				-		
110				-		
111				-		
TOTALS			98	93		

POSITIVE SAMPLE FARM NO. 4 (PS4)

Sample No.	Age	Breed	1970-71		1971-72	
			14:12:70	26:4:71		
1	7		-			
2	7		+	+		
3	6		-			
4	6		-			
5	5		-			
6	6		-	-		
7	5		-	-		
8	5		-	-		
9	6		-			
10	5		-			
11	7		+			
12	7		-	-		
13	4		-	-		
14	4		+	+		
15	5		-	-		
16	4		-			
17	4		+	-		
18	3		-	-		
19	5		+			
20	4		+	+		
21	4		-	-		
22	3		+			
23	3		+	-		
24	4		-			

POSITIVE SAMPLE FARM NO. 4 (PS4)

Sample No.	Age	Breed	1970-71		1971-72	
			14:12:70	26:4:71		
25	9		-			
26	6		+	-		
27	7		+			
28	7		+			
29	7		-			
30	7		+			
31	3		+			
32	5		-	+		
33	3		-			
34				-		
35				-		
36				+		
37				-		
38				-		
39				-		
40				-		
41				-		
42				-		
43				-		
44				+		
45				-		
46				-		
47				-		

POSITIVE SAMPLE FARM NO. 4 (PS4)

Sample No.	Age	Breed	1970-71		1971-72	
			14:12:70	26:4:71		
48				+		
49				-		
50				+		
TOTALS			33	32		

POSITIVE SAMPLE FARM NO. 5 (PS5)

Sample No.	Age	Breed	1970-71		1971-72	
			15:12:70	27:4:71		
1	5		+	+		
2	4		+	+		
3	4		-	-		
4	3		+			
5	2	AA	-	+		
6	4		+	+		
7	4		-	-		
8	2		+	+		
9	2		+	+		
10	3		-	-		
11	4		-	-		
12	6		+	-		
13	4	AA	-	+		
14	4	AA	-	-		
15	2	AA	-	-		
16	4		+			
17	2		+	+		
18	2		-			
19	OLD	Highland	-			
20						
TOTALS			19	15		

POSITIVE SAMPLE FARM NO. 6 (PS6)

Sample No.	Age	Breed	1970-71		1971-72	
			14:12:70	27:4:71	20:11:71	7:5:72
1	6	F	+	+	+	+
2	5	F	+	+	-	-
3	5	F	-	-	-	-
4	5	F	+	+	+	
5	3	F	-	+	-	-
6	4	F	-	-	-	-
7	4	F	-	-	-	-
8	5	F	+	+	-	-
9	4	F	+	+	-	-
10	4	F	+	+	-	-
11	4	F	-	+	-	-
12		F	+			
13	6	F	+	+	-	-
14	6	F	-	+		
15	6	F	-	+	-	-
16	6	F	-	-	-	
17	4	F	-	+	-	-
18		F	-			
19	4	F	+	-	-	-
20	4	F	+	-	-	-
21	5	F	-	+	-	
22	6	F	-	+		
23		F	+			
24	6	Sh. X	-	-		

POSITIVE SAMPLE FARM NO. 6 (PS6)

Sample No.	Age	Breed	1970-71		1971-72	
			14:12:70	27:4:71	20:11:71	7:5:72
25	5	F	+	+		
26		F	+			
27		F		+	-	-
28		F		-	-	-
29		F		+	+	+
30		F		+	-	+
31		F			-	-
32		F			-	-
33		F			-	-
34		F			-	-
35		F			-	-
36		F				-
TOTALS			26	26	27	25

POSITIVE SAMPLE FARM NO. 7 (PS7)

Sample No.	Age	Breed	1970-71		1971-72	
						25:4:72
1	5	F				+
2	5	F				-
3	4	F				-
4	3	F				-
5	4	F				-
6	10	F				+
7	4	F				-
8	6	F				+
9	5	F				-
10	8	F				+
11	6	F				-
12	6	F				-
13	3	F				-
14	4	F				+
15	7	F				-
16	5	F				-
17	6	F				-
18	6	F				-
19	6	F				-
20	5	F				-
21	4	F				-
22	3	F				+
23	3	F				-

POSITIVE SAMPLE FARM NO. 7 (PS7)

Sample No.	Age	Breed	1970-71		1971-72	
						25:4:72
24	3	F				-
25	3	F				-
26	3	F				-
27	3	F				-
28	3	F				-
29	3	F				-
30	3	F				-
31	4	F				-
32	3	F				-
33	3	F				-
34	8	F				-
35	3	F				-
36	4	F				-
37	7	F				-
38	5	F				-
39	4	F				-
40	6	F				-
41	13	F				-
42	5	F				-
43	4	F				-
44	6	F				-
45	4	F				+
46	6	F				+

POSITIVE SAMPLE FARM NO. 7 (PS7)

Sample No.	Age	Breed	1970-71		1971-72	
						25:4:72
47	3	F				-
48	5	F				-
49	3	F				-
50	3	F				-
51	4	F				+
52	2	F				-
53	2	F				-
54	2	F				-
56	8	F				-
TOTALS						55

FARMER'S LUNG FARM NO. 1 (FL1)

Sample No.	Age	Breed	1970-71		1971-72	
			27:10:70	18:3:71	11:11:71	16:5:72
1		A	-		-	
2		A	-		+	
3	7		-	-		
4			-			
5	6	A	-	+	-	+
6	4		-	+		
7	10		-	+		
8	4		-	+		-
9		A	-		-	-
10	10		-	-		
11	8	A	-	+	-	
12	8	A	+	+	+	
13	4	F	-	-	-	-
14	10	A	-	+	+	
15	8	A	+	+	+	
16	5		-	+		
17	6	A	+	+	+	
18	4	A	-	+	-	+
19	6		-	-		
20			-			
21	4	F	-	-	-	
22	6	A	-	+	+	+
23	6	A	-	+	+	+
24	8	A	-	+	-	+

FARMER'S LUNG FARM NO. 1 (FL1)

Sample No.	Age	Breed	1970-71		1971-72	
			27:10:70	18:3:71	11:11:71	16:5:72
25	8		-	+		+
26	4		-	-		-
27	4		-	+		
28	4	F	-	+	-	+
29	4	F	-	+	-	+
30		F	-		-	-
31	4	F	-	-	-	-
32	4	F	-	+	-	+
33	4	F	-	+	-	+
34	4	F	-	+		+
35	4	F	-	+	-	+
36	5	A		+	+	+
37	6	A		+		+
38	8			+		
39	4	F		-	-	-
40	7			+		
41		F			-	
42		A			-	-
43		F. Bull			-	
44		F			-	
45		A			+	
46		F			-	+
47		F			-	
48		A			+	+

FARMER'S LUNG FARM NO. 1 (FL1)

Sample No.	Age	Breed	1970-71		1971-72	
			27:10:70	18:3:71	11:11:71	16:5:72
49		A			-	-
50		A			-	
51		A			-	-
52		A			+	+
53		A			+	+
54		A				+
55		F				+
56		A				-
57		A				+
TOTALS			35	34	37	32

FARMER'S LUNG FARM NO. 2 (FL2)

Sample No.	Age	Breed	1970-71		1971-72	
			8:12:70	16:5:71		
1	8	A	-			
2	4	A	-			
3	7	A	-	-		
4	4	F	-			
5	3	A	-			
6	6	F	+			
7	8	A	+			
8	8	A	-	-		
9	8	A	-			
10	6	F	-	-		
11	7	F	+	-		
12	7	A	+	-		
13	3	A	-			
14	3	F	-			
15	7	F	-			
16	3	A	-	-		
17	8	A	+	+		
18	6	F.	-	-		
19	4	A	-	-		
20	5	A	-	+		
21	3	A	+	+		
22	3	A	+			
23	3	A	-	-		
24	5	A	-			

FARMER'S LUNG FARM NO. 2 (FL2)

Sample No.	Age	Breed	1970-71		1971-72	
			8:12:70	16:5:71		
25	3	A	-			
26	3	F	-			
27	5	F	+			
28	7	A	-			
29	5	F	-			
30	5	A	-			
31	6	A	+			
32	6	A	-	+		
33	6	F	-	+		
34	3	A	-			
35	8	F	+			
36	6	A	-			
37	3	A	-	-		
38	8	A	-	-		
39	4	A	-	-		
40		F		-		
41		A		+		
42		A		+		
43		F		-		
44		A		-		
45		A		-		
46		A		-		
47		F		-		
48		A		-		

FARMER'S LUNG FARM NO. 2 (FL2)

Sample No.	Age	Breed	1970-71		1971-72	
			8:12:70	16:5:71		
49		F		-		
50		F		-		
51		F		-		
52		F		+		
53		F		-		
54		F		+		
55		F		+		
56		A		-		
57		A		-		
58		F		+		
59		A		-		
61		F		-		
TOTALS			39	38		

FARMER'S LUNG FARM NO. 3 (FL3)

Sample No.	Age	Breed	1970-71		1971-72	
			12:12:70	27:3:71	25:11:71	1:6:72
1	4		-	+	-	
2	7		-	-	-	-
3	5		-			
4	4		-			
5	5		+			
6	5		-			
7	4		+	+	-	
8	5		-	-		
9	3		+			
10	3		-	-	-	
11	3		+	-		
12	3		+	+	+	
13	3		-	+	-	
14	3		-	+		
15	<3		-	-		
16	<3		+			
17	<3		+	+		
18	<3		-			
19	<3		-	-	-	
20	<3		-	-	-	
21	<3		-	-	-	-
22	<3		-	+		
23	<3		-	+	-	-
24	4		-	+	-	-

FARMER'S LUNG FARM NO. 3 (FL3)

Sample No.	Age	Breed	1970-71		1971-72	
			12:12:70	27:3:70	25:11:71	1:6:72
25	4		-	+	-	-
26	4		-			
27	5		+	+	-	-
28	4		-	+	-	-
29	7		-	+	-	
30	6		-			
31	4		+	+	-	
32	6		+	+		
33	4		-	+		-
34	3		-	-		
35	3		+	+		
36	3		-	+		
37	6	F	-	+	-	
38	3		-	+		
39	< 3		-	-		
40	< 3	F	-	-	-	
41	7		-			
42	7		-			
43	7		+	+		
44	7		+		+	-
45	6		-			
46	6		-	-		-
47	4		-			
48	6		-	-		

FARMER'S LUNG FARM NO. 3 (FL3)

Sample No.	Age	Breed	1970-71		1971-72	
			12:12:70	27:3:71	25:11:71	1:6:72
49	5		-			
50	4		-	-	-	
51	3		-	-	-	
52	4		-			
53	5		+			
54	5		+			
55	4		+		-	
56	4		+	+	+	+
57	4		-	+	-	
58	7		-	+	-	-
59	7		-	+		
61	7		+			
62	7		-	+	-	-
63	3		+	+		
64	< 3		-	-	-	
65	< 3		-	+	-	-
66	< 3		+			
67	6	F	-			
68	3	F	+		-	
69	3	F	-	+	-	
70	< 3	F	-	-	-	-
71	< 3	F	+	+	-	+
72	< 3	F	-	+		
73	3	F	-	+	-	-

FARMER'S LUNG FARM NO. 3 (FL3)

Sample No.	Age	Breed	1970-71		1971-72	
			12:12:70	27:3:71	25:11:71	1:6:72
74	3	F	-	+		
75	3	F	-		-	
76	3	F	-			
77	3	F	-			
78	3	F	-			
79	3	F	-			
80	3	F	-	-	-	-
81	7	A	+			
82	7	A	+			
83	3	F	-	-	-	-
84	<3	F	-	-	-	
85	5	F	+	+		+
86	<3	F	-		-	-
87	<3	F	-	-	-	-
88	<3	F	+	-		
89	<3	F	-	-		-
90		F		-	-	
91		F		-		
92		F		-	-	
93		A		-		
94		F		-	-	
95		F		+		
96		F		+		
97		A		-		-
98		F		-	-	-

FARMER'S LUNG FARM NO. 3 (FL3)

Sample No.	Age	Breed	1970-71		1971-72	
			12:12:70	27:3:71	25:11:71	1:6:72
99		F		-		-
100		A		+		
101		F		+		
102		F		+		
103		F		-		
104		F		-		
105		F		-		
106		F		-		
107		F		-		
108		F		-		
109		F		-		
110		F		-		
111		F		+		
112		F		+		
113		A		-		
114		A		-		
115					-	-
116					-	
117					-	
118						
119					-	
120					-	-
121					-	
122					-	

FARMER'S LUNG FARM NO. 3 (FL3)

Sample No.	Age	Breed	1970-71		1971-72	
			12:12:70	27:3:71	25:11:71	1:6:72
123					-	
124					-	
125					-	-
126					-	-
127					-	-
128					-	
129					-	-
130					-	
131					-	
132					-	
133					-	
134					-	
135					-	
136					-	
137					-	-
138					-	
139					-	
140					-	
141					-	
142					-	
143					-	-
144					-	-
145					-	
146						-

FARMER'S LUNG FARM NO. 3 (FL3)

Sample No.	Age	Breed	1970-71		1971-72	
			12:12:70	27:3:71	25:11:71	1:6:72
147					-	-
148					+	
149					-	
150					-	
151					-	+
152					+	-
153					+	+
154					+	
155						
156					-	
157						-
158						-
159						-
160						-
161						-
162						
163						-
164						-
165						+
166						-
167						-
168						-
169						-
TOTALS			88	82	82	52

FARMER'S LUNG FARM NO. 4 (FL4)

Sample No.	Age	Breed	1970-71		1971-72	
			21:12:70	17:5:71		
1	6	A	+	-		
2	7	F	+	+		
3	8	A	+			
4	3	A	-	-		
5	5	A	+	-		
6	4	F	-	+		
7	5	A	-	-		
8	4	A	-	-		
9	8	A	+	+		
10	5	F	-	-		
11	6	A	-	-		
12	5	F	-	-		
13	4	A	-	-		
14	11	F	-			
15	8	A	+	-		
16	9	A	+			
17	5	A	+	+		
18	5	F	-	-		
19	6	A	-			
20	4	F	+	+		
21	7	F	-			
22	4	A	+	+		
23	5	A	+	+		
24	4	F	+	+		

FARMER'S LUNG FARM NO. 4 (FL4)

Sample No.	Age	Breed	1970-71		1971-72	
			21:12:70	17:5:71		
25	5	A	+	+		
26	4	A	-	-		
27	6	F	-	+		
28	10	A	-	+		
29	8	F	-	-		
30	8	A	-			
31	3	F		-		
32	3	A		-		
33	3	F		-		
34	3	A		-		
35	3	F		+		
36	4	A		+		
37	4	F		-		
38	5	A		-		
TOTALS			30	32		

FARMER'S LUNG FARM NO. 5 (FL5)

Sample No.	Age	Breed	1970-71		1971-72	
			19:12:70	14:5:71	23:11:71	25:5:72
1	14	A	+			
2	3	F	-	-	+	
3	5	A	+		+	
4	3	F	-	-		
5	6	A	-	+	+	
6	3	F	-	-	+	+
7	7	A	+		+	
8	3	F	-	+		
9	5	F	-	+	+	
10	8	A	+	+		
11	7	A	+		+	
12	5	A	+	-	+	+
13	3	F	+	+	+	
14	3	F	-	+	+	-
15	6	A	+	+	+	+
16	3	F	-	+		
17	3	F	-	-	+	+
18	7	A	+		+	
19	13	A	-			
20	3	F	-			+
21	4	F	-	+	+	+
22	4	F	-	-	-	
23	6	F	+			
24	5	A	+	+		

FARMER'S LUNG FARM NO. 5 (FL5)

Sample No.	Age	Breed	1970-71		1971-72	
			19:12:70	14:5:71	23:11:71	25:5:72
25	5	F	+	+	+	+
26	5	F	-			
27	3	F	-	+	+	-
28	7	A	+		+	-
29	7	A	+			
30	9	A	+	+	+	+
31	9	A	+			
32	7	A	+		+	
33	5	F	-	+		
34	5	A	-	+	-	+
35	3	F	-	-	-	+
36	3	F	-	+	+	+
37	4	F	+	+		
38	3	F	-	+	+	+
39	4	F	-	+	+	+
40	5	F	-	+	-	
41	3	F	-		-	-
42	5	A	+	+		
43	3	F	-		+	+
44	3	F	-	+		+
45	3	F	+		+	
46	3	F	-	+		
47	4	A	+	+		
48	3	F	-	+		

FARMER'S LUNG FARM NO. 5 (FL5)

Sample No.	Age	Breed	1970-71		1971-72	
			19:12:70	14:5:71	23:11:71	25:5:72
49	3	A	-	+		
50	5	A	+	+	+	+
51	5	A	+	+	+	
52	5	A	+	+	+	
53	5	A	-	+	+	
54	3	F	-	-	+	+
55	5	F	-	+		+
56	3	F	+		+	+
57	3	A	-	+		
58	3	F	-	+		
59	7	A	+		+	+
60	7	A	+			
61	5	A	+			
62	7	A	+	+	+	+
63	3	F	-	-	-	+
64	3	F	-		-	-
65	4	F	-			
66	6	A	-	+		-
67	6	F	+	+		+
68	9	A	+	+	+	+
69	5	A	-	+	-	
70	9	A	+	+		
71	12	A	+			
72	6	A	+		+	

FARMER'S LUNG FARM NO. 5 (FL5)

Sample No.	Age	Breed	1970-71		1971-72	
			19:12:70	14:5:71	23:11:71	25:5:72
73	5	A	+	+	+	+
74	4	A	+			
75	7	A	+	+		
76	6	A	+			
77	6	A	+			
78	9	A	+	+	+	+
79	7	A	-			
80	6	A	+			
81				+		
82				+		
83				+		
84				+		
85				+		
86				+		
87				+		
88				-		
89				+		
90				+		
91				-		
92				-		
93				-		
94				+		
95				-		
96				+		

FARMER'S LUNG FARM NO. 5 (FL5)

Sample No.	Age	Breed	1970-71		1971-72	
			19:12:70	14:5:71	23:11:71	25:5:72
97				+		
98				+		
99				-		
100				-		
101				+		
102				+		
103				+		
104				-		
105				+		
106				+		
107				+		
108				+		
109					-	-
110					-	-
111					+	+
112					+	+
113					-	+
114					+	+
115					+	
116					+	
117					+	
118		F			+	
119		F			-	-
120		F			+	

FARMER'S LUNG FARM NO. 5 (FL5)

Sample No.	Age	Breed	1970-71		1971-72	
			19:12:70	14:5:71	23:11:71	25:5:72
121		F			-	+
122		F			+	
123		F			-	
124		F			+	-
125		A			+	+
126		F			+	+
127		F			+	
128		F			-	-
129		F			-	
130		F			+	
131		F			+	+
132		A			+	+
133		F			-	-
134		F			+	+
135		F			+	+
136		F			+	+
137		F			+	+
138		F			+	+
139		A			+	+
140		F			-	-
141		F			+	+
142		F			+	+
143		A			+	
144		F			-	

FARMER'S LUNG FARM NO. 5 (FL5)

Sample No.	Age	Breed	1970-71		1971-72	
			19:12:70	14:5:71	23:11:71	25:5:72
145		F				-
146		A				+
147		A				+
148		F				+
149		F				-
150		A				+
151		F				+
TOTALS			80	79	80	63

FARMER'S LUNG FARM NO. 6 (FL6)

Sample No.	Age	Breed	1970		1971	
			22:12:70		5:5:71	
1	9	F	-		-	
2	9	A	-		-	
3	4	A	-		-	
4	9	F	+		-	
5	6	A	-		+	
6	8	F	-		+	
7	7	A	+		+	
8	8	A	-		+	
9	7	F	-		-	
10	8	F	-		+	
11	6	A	-		-	
12	9	A	+		-	
13	8	F	+		+	
14	7	F	-		+	
15	7	A	-		+	
16	3	A	-		+	
17	3	A	+		-	
18	7	A	+		+	
19	7	A	+		-	
20	7	A	+		-	
21	8	A	+		+	
22	7	F	+		+	
23	7	A	+		-	
24	9	A	+		+	

FARMER'S LUNG FARM NO. 6 (FL6)

Sample No.	Age	Breed	1970		1971	
			22:12:70		5:5:71	
25	7	F	-		+	
26	13	A	+		+	
27	4	F	-		-	
28	10	A	+		+	
29	6	A	-		-	
30	10	A	+		-	
31	10	A	+		+	
32	8	A	+		+	
33	8	A	+		-	
34	7	A	+		+	
35	6	A	+		-	
36	5	A	+		-	
37	11	F	-		+	
38	11	A	+		-	
39	8	A	+		-	
40	3	F	+		+	
41	7	F	+		+	
42	7	A	+		+	
43	6	A	+		+	
44	7	A	+		+	
45	6	A	-		-	
46	5	A	+		-	
47	7	A	+		-	
48	8	A	+		+	

FARMER'S LUNG FARM NO. 6 (FL6)

Sample No.	Age	Breed	1970		1971	
			22:12:70		5:5·71	
49	3	A	+		+	
50	7	A	+		+	
51	3	A	+		+	
52	11	A	-		-	
53	3	A	-		+	
54	6	A	-		-	
55	7	A	-		-	
56	9	F	+		+	
57	8	A	-		+	
58	5	F	+		-	
59	4	F	-		+	
60	6	A	+		+	
61	9	A	+		-	
62	6	A	-		+	
63	6	A	+		+	
64	9	A	+		-	
65	9	A	+		+	
66	4	A	+		+	
67	11	A	-		+	
71	7	A	+		+	
72	7	A	-		+	
73	3	A	-		+	
74	4	F	+		-	
75	3	F	-		-	

FARMER'S LUNG FARM NO. 6 (FL6)

Sample No.	Age	Breed	1970		1971	
			22:12:70		5:5:71	
76	3	F	+		+	
77	18	A	+		+	
78	13	A	+		+	
79	7	F	-			
TOTALS			76		75	
N.B.	Sample numbers do not correspond.					

FARMER'S LUNG FARM NO. 7 (FL7)

Sample No.	Age	Breed	1970-71		1971-72	
			11:12:70	13:5:71	25:11:71	4:5:72
1	12	A	-	-		
2	7	A	-	-	-	-
3	3	A	-	-	-	-
4	8	A	-	-	-	-
5	4	A	-	-	-	-
6	5	A	-	-	-	-
7	3	A	-	-	-	
8	3	A	-	-	-	-
9	3	A	-	-	-	-
10	3	A	-	-	-	-
11	3	F	-	-	-	
12	3	A	-	-	-	-
13	5	A	-		-	-
14	6	A	-	-	-	-
15	2	F	-	-	-	-
16	5	A	-	-	-	-
17	11	A	-	-		
18	3	A	-	-	-	-
19	3	A	-	-	-	-
20	3	A	-	-	-	-
21	3	F	-	-	-	-
22	3	A	-	-	-	-
23	5	A	-	-		
24	6	A	-	-	-	-

FARMER'S LUNG FARM NO. 7 (FL7)

Sample No.	Age	Breed	1970-71		1971-72	
			11:12:70	13:5:71	25:11:71	4:5:72
25	4	A	-	-		
26	12	A	-	-	-	-
27	4	A	-		-	-
28	5	A	-	-	-	-
29	5	A	-	-	-	
30	8	A	-	-	-	-
31	8	A	-	-	-	-
32	6	A	-	-	-	-
33	3	A	-			
34	3	A	-	-	-	-
35	12	A	-			
36	9	A	-	+	-	-
37	7	A	-		-	-
38	5	A	-		-	-
39	13	F	-	-	-	
40	5	A	-	-	-	-
41	4	A	-	-	-	-
42	6	A	-	-	-	-
43	4	A	-		-	-
44	5	A	-	-	-	-
45	7	A	-	-	-	-
46	7	A	-	-	-	-
47	6	A	-	-		
48	3	A	-	-	-	-

FARMER'S LUNG FARM NO. 7 (FL7)

Sample No.	Age	Breed	1970-71		1971-72	
			11:12:70	13:5:71	25:11:71	4:5:72
49	3	A	-	-	-	-
50	4	A	-	-	-	-
51	4	A	-	-	-	-
52	9	A	-	-	-	-
53	4	F	-	-	-	-
54	9	A	-	-	-	-
55	4	A	-	-		
56	5	A	-	-	-	-
57	8	A	-	-	-	
58	4	A	-	-	-	-
59	6	A	-			
60	4	F	-	-		
61	4	F	-	-		
62	4	A	-	-	-	-
63	5	A	-			
64		A		-	-	-
65		F		-	-	-
66		A		-		
67		A		-		
68		F		-	-	-
69		A			-	-
70		A			-	-
71		A			-	-
72		A			-	-

FARMER'S LUNG FARM NO. 7 (FL7)

Sample No.	Age	Breed	1970-71		1971-72	
			11:12:70	13:5:71	25:11:71	4:5:72
73		A			-	-
74		A			-	-
76		A			-	-
77		A			-	
78		A			-	
79		A			-	
80		A			-	-
81		A			-	-
82		A				-
83		A				-
84		A				-
85		F				-
86		F				-
87		F				-
88		A				-
89		A				-
90		A				-
TOTALS			63	59	66	67

FARMER'S LUNG FARM NO. 8 (FL8)

Sample No.	Age	Breed	1971		1972	
			26:3:71	20:11:71	6:5:72	1:12:72
1	8	F	+			
2	6	F	+	+		
3	6	F	-	-		
4	7	F	+	+	+	
5	6	F	-	-	-	
6	7	F	+	+	+	
7	4	F	+	-	+	
8	5	F	-	-	-	
9	7	F	+	+	+	
10	6	F	+	+	+	
11	7	F	-	-	+	
12	6	F	+	-		
13	4	F	-			
14	5	F	+	+	+	
15	4	F	+	+	+	
16	4		+	+	+	
17	10	F	+	+	+	
18	6	F.	+	-	+	
19	7	F	+	+	+	
20	6	F	+	-	-	
21	5	F	-	-		
22	6	F	+	-	+	
23	4	F	-	-	+	
24	6	F	+	+	+	

FARMER'S LUNG FARM NO. 8 (FL8)

Sample No.	Age	Breed	1971		1972	
			26:3:71	20:11:71	6:5:72	1:12:72
25	5	F	+	+	+	
26	8	F	+	+		
27	7	F	+	+	+	
28	7	F	+	+		
29	6	F	+		+	
30	7	F	+	+	+	
31	5	F	-	-	+	
32	4	F	+	-	+	
33	4	F	+			
34	5	F	+	-	+	
35	5	F	+	+	-	
36	6	F	+			
37	5	F	+	+		
38	7	F	+	+		
39	6	F	+	+		
40	7	F	+	+	+	
41	7	F	-	-	-	
42	5	F	+	-	+	
43	4	F	+	-	-	
44	4	F	+			
45	4	F	+	-		
46	4	F	+	-		
47	6	F	+			
48	6	F	+			

FARMER'S LUNG FARM NO. 8 (FL8)

Sample No.	Age	Breed	1971		1972	
			26:3:71	20:11:71	6:5:72	1:12:72
49	8	F	+	+		
50	7	F	+	-	+	
51	6	F	+			
52	5	F	+			
53	7	F	+	+	+	
54	3	Her.	+		+	
55				-		
56				-		
57				-		
58				-	+	
59				-	+	
60				-		
61				+		
62				-	-	
63				-	-	
64				-	+	
65				-	+	
66				-		
67				+		
68				-		
69				+		
70				-		
71					+	
72					-	

FARMER'S LUNG FARM NO. 8 (FL8)

Sample No.	Age	Breed	1971		1972	
			26:3:71	20:11:71	6:5:72	1:12:72
73					-	
74					-	
75					+	
TOTALS			54	59	44	

APPENDIX 2 - TABLE 1 The rainfall during the summer months of 1970.

Month	Rainfall (mm)																
	FL1	FL2	FL3	FL4	FL5	FL6	FL8	PS1	PS2	PS3	PS4	PS5	PS6	R1	R2	R3	R4
June	67.1	94.0	55.9	55.9	40.1	60.7	58.2	55.9	59.4	59.4	59.4	59.4	59.4	64.5	55.9	61.0	70.9
July	142.5	176.5	101.9	101.9	78.2	73.4	129.8	101.9	94.0	94.0	94.0	94.0	94.0	82.5	101.9	83.6	78.7
August	99.3	72.9	80.8	80.8	43.7	51.1	81.8	80.8	70.1	70.1	70.1	70.1	70.1	83.3	80.8	75.9	90.7
June + July	209.6	270.5	157.8	157.8	118.3	134.1	188.0	157.8	153.4	153.4	153.4	153.4	153.4	147.0	157.8	144.6	149.6
July + August	241.8	249.4	182.7	121.9	121.9	124.5	211.6	182.7	164.1	164.1	164.1	164.1	164.1	165.8	182.7	159.5	169.4
June + July + August	308.9	343.4	238.6	238.6	162.0	185.2	269.8	238.6	223.5	223.5	223.5	223.5	223.5	230.3	238.6	220.5	240.3

APPENDIX 2 - TABLE 2 The rainfall during the summer months of 1971.

Month	Rainfall (mm)																
	FL1	FL2	FL3	FL4	FL5	FL6	FL8	PS1	PS2	PS3	PS4	PS5	PS6	R1	R2	R3	R4
June	26.8	-	40.1	-	49.5	-	70.3	40.1	-	-	-	-	45.5	36.0	40.1	-	-
July	60.0	-	107.7	-	89.6	-	72.2	107.7	-	-	-	-	59.7	110.7	107.7	-	-
August	79.4	-	142.4	-	117.5	-	179.3	142.4	-	-	-	-	154.2	111.4	142.4	-	-
June + July	122.8	-	147.8	-	139.1	-	142.5	147.8	-	-	-	-	105.2	146.7	147.8	-	-
July + August	139.4	-	250.1	-	207.1	-	251.5	250.1	-	-	-	-	213.9	222.1	250.1	-	-
June + July + August	202.2	-	290.2	-	258.6	-	321.8	290.2	-	-	-	-	259.4	258.1	290.2	-	-

APPENDIX 2 - TABLE 3 The long term (1941-1970) average monthly rainfall.

Month	Rainfall (mm)																
	FL1	FL2	FL3	FL4	FL5	FL6	FL8	PS1	PS2	PS3	PS4	PS5	PS6	R1	R2	R3	R4
June	91	71	72	72	58	68	93	72	59	59	59	59	59	70	72	67	79
July	117	103	91	91	73	85	105	91	73	73	73	73	73	85	91	90	94
August	124	112	109	109	84	99	128	109	96	96	96	96	96	101	109	99	110
June + July	208	174	163	163	131	153	198	163	132	132	132	132	132	155	163	157	173
July + August	241	215	200	200	157	185	233	200	169	169	169	169	169	186	200	189	204
June + July + August	332	286	272	272	215	252	326	272	228	228	228	228	228	256	272	256	283

APPENDIX 2 - TABLE 4 The number of raindays during the summer months of 1970.

Month	Number of Raindays															
	FL1	FL3	FL4	FL5	FL6	FL8	PS1	PS2	PS3	PS4	PS5	PS6	R1	R2	R3	R4
June	9	12	12	-	12	10	12	9	9	9	9	9	13	12	10	11
July	21	23	23	-	16	18	23	20	20	20	20	20	22.	23	19	24
August	8	11	11	-	11	12	11	11	11	11	11	11	14	11	11	12
June + July	30	35	35	-	28	28	35	29	29	29	29	29	35	35	29	35
July + August	30	34	34	-	27	30	34	31	31	31	31	31	36	34	30	36
June + July + August	39	46	46	-	39	40	46	40	40	40	40	40	49	46	40	47

APPENDIX 2 - TABLE 5 The number of raindays during the summer months of 1971.

Month	Number of Raindays															
	FL1	FL3	FL4	FL5	FL6	FL8	PS1	PS2	PS3	PS4	PS5	PS6	R1	R2	R3	R4
June	14	15	-	14	-	16	15	-	-	-	-	12	13	15	-	-
July	12	11	-	11	-	11	11	-	-	-	-	10	11	11	-	-
August	17	19	-	17	-	17	19	-	-	-	-	19	18	19	-	-
June + July	26	26	-	25	-	27	26	-	-	-	-	22	24	26	-	-
July + August	29	30	-	28	-	28	30	-	-	-	-	29	29	30	-	-
June + July + August	43	45	-	42	-	44	45	-	-	-	-	41	42	45	-	-

APPENDIX 3

APPENDIX 3 - TABLE 1

Experiment 4 - the clinical details from periods of constant exposure to mouldy hay dust.

FIRST PERIOD OF CONSTANT EXPOSURE

DURATION OF EXPOSURE	CALF NO.	RESPIRATORY RATE/MIN.	TEMP. °F	COUGHING	OTHER FINDINGS
WEEK 0	4	30	102	-	-
	16	30	101.1	-	-
	17	30	101	-	-
	20	30	101.3	-	-
WEEK 2	4	30	101.7	+	-
	16	40	100.8	-	-
	17	30	102	-	-
	20	30	101.1	-	-
WEEK 5	4	40	101.5	-	-
	16	30	101.6	-	-
	17	40	101.9	-	-
	20	30	101.1	-	-

APPENDIX 3 - TABLE 1 (Cont'd.)

SECOND PERIOD OF CONSTANT EXPOSURE

DURATION OF EXPOSURE	CALF NO.	RESPIRATORY RATE/MIN.	TEMP. °F	COUGHING	OTHER FINDINGS
WEEK 0	4	40	101.2	-	-
	16	30	101	-	-
	17	25	101.6	-	-
	20	25	101.1	-	-
WEEK 1	4	30	101.8	-	Harsh. Crackles on left - A/V.
	16	50	101.6	-	Harsh.
	17	40	101.2	-	Harsh. Hyperpnoea (+)
	20	30	101.6	-	Harsh.
WEEK 2	4	30	101	-	Crackles on left - A/V.
	16	45	101.8	++	-
	17	40	101	-	Harsh.
	20	40	101.5	-	Harsh.
WEEK 3	4	40	101.2	+	Crackles on left - A/V.
	16	40	101.8	-	Harsh.
	17	30	100.8	-	Crackles and rhonchi on left - A/V.
	20	30	101.8	-	Harsh.
WEEK 4	4	40	101.8	+	Crackles on left - A/V.
	16	30	102	-	-
	17	40	101.6	-	-
	20	30	101.5	-	-

APPENDIX 3 - TABLE 1 (Cont'd.)

SECOND PERIOD OF CONSTANT EXPOSURE

DURATION OF EXPOSURE	CALF NO.	RESPIRATORY RATE/MIN.	TEMP. °F	COUGHING	OTHER FINDINGS
WEEK 5	4	50	101.6	+	Crackles on left - A/V.
	16	40	102	-	-
	17	40	102.1	-	-
	20	40	102	-	Occasional crackles on left - A/V.
WEEK 6	4	40	102.2	-	Crackles on left - A/V. Hyperpnoea (+)
	16	40	102.1	-	-
	17	30	101.4	-	-
	20	40	101.3	-	Harsh.

APPENDIX 3 - TABLE 1 (Cont'd.)

THIRD PERIOD OF CONSTANT EXPOSURE

DURATION OF EXPOSURE	CALF NO.	RESPIRATORY RATE/MIN.	TEMP. °F	COUGHING	OTHER FINDINGS
WEEK 0	4	30	101.7	-	-
	16	30	101.6	-	-
	17	30	101.2	-	-
	20	30	101.9	-	-
WEEK 1	4	40	102.1	-	Crackles on left - A/V.
	16	30	101.6	-	-
	17	30	101.3	-	-
	20	30	101.7	-	-
WEEK 2	4	40	101.4	-	-
	16	40	102.2	+	Crackles on left - A/V.
	17	30	101.6	-	
	20	30	101.8	-	
WEEK 3	4	30	102.2	+	-
	16	40	102	++	-
	17	30	101.3	-	-
	20	40	102	-	-
WEEK 4	4	30	101.6	+	Hyperpnoea (+)
	16	40	102	++	-
	17	30	102.5	-	-
	20	30	102	-	Hyperpnoea (++)

APPENDIX 3 - TABLE 1 (Cont'd.)

THIRD PERIOD OF CONSTANT EXPOSURE

DURATION OF EXPOSURE	CALF NO.	RESPIRATORY RATE/MIN.	TEMP. °F.	COUGHING	OTHER FINDINGS
WEEK 5	4	40	102.4	-	Hyperpnoea (+)
	16	30	101.1	-	Hyperpnoea (+)
	17	40	101.6	-	Hyperpnoea (+)
	20	40	102	-	Hyperpnoea (+)
WEEK 6	4	40	102.2	-	-
	16	40	102	-	-
	17	40	101	-	-
	20	40	101.2	-	-
WEEK 7	4	40	101.3	-	-
	16	30	101.9	-	-
	17	30	102	-	-
	20	40	101.9	-	-

APPENDIX 3 - TABLE 2

Experiment 4 - the clinical details following the first massive exposure to mouldy hay dust.

TIME POST-EXPOSURE	CALF NO.	RESPIRATORY RATE/MIN.	TEMP. °F	COUGHING	OTHER FINDINGS
PRE-EXPOSURE	4	30	101.7	-	-
	16	30	101.6	-	-
	17	30	101.2	-	-
	20	30	101.9	-	-
1 HOUR	4	40	102.1	-	Harsh respirations.
	16	30	102.5	-	Harsh respirations.
	17	30	101.3	-	Harsh respirations.
	20	40	101.3	-	Harsh respirations.
2 HOURS	4	30	102.2	-	-
	16	30	102	-	-
	17	30	101.5	-	-
	20	40	102.2	-	-
3 HOURS	4	40	102	-	Crackles on left - A/V.
	16	30	101.7	-	-
	17	30	101.3	-	-
	20	40	102.2	-	-
4 HOURS	4	30	102.3	-	-
	16	40	102.4	-	-
	17	30	102.5	-	-
	20	40	102	-	-

APPENDIX 3 - TABLE 2 (Cont'd.)

TIME POST-EXPOSURE	CALF NO.	RESPIRATORY RATE/MIN.	TEMP. °F	COUGHING	OTHER FINDINGS
5 HOURS	4	30	102.2	-	Slightly dull.
	16	30	102.2	-	-
	17	30	102.3	-	-
	20	40	101.7	-	-
6 HOURS	4	40	102.6	+	-
	16	40	102.3	-	-
	17	30	102.3	-	-
	20	30	102	-	-
7 HOURS	4	40	102.6	-	Crackles left and right - A/V.
	16	40	102.6	-	-
	17	30	102.5	-	-
	20	40	103	-	-
8 HOURS	4	40	102.5	+	Crackles on right - A/V.
	16	40	101.9	-	-
	17	40	102.4	-	-
	20	50	102.7	-	-
9 HOURS	4	30	102.6	-	-
	16	40	101.8	+	-
	17	30	102.1	-	-
	20	50	103	-	-

APPENDIX 3 - TABLE 2 (Cont'd.)

TIME POST-EXPOSURE	CALF NO.	RESPIRATORY RATE/MIN.	TEMP. ^{o}F	COUGHING	OTHER FINDINGS
10 HOURS	4	40	102	-	Crackles on right - A/V.
	16	40	101.7	-	-
	17	30	102.1	-	-
	20	50	102.4	-	-
11 HOURS	4	40	102.3	-	-
	16	40	101.5	-	-
	17	40	101.8	-	-
	20	40	102.7	-	-
12 HOURS	4	30	101.8	-	-
	16	30	101	-	-
	17	40	102	-	-
	20	40	102.5	-	-
24 HOURS	4	40	101.6	+	-
	16	30	101.8	+	-
	17	30	101.4	-	-
	20	40	102	+	Hyperpnoea (+)

APPENDIX 3 - TABLE 3

Experiment 4 - the clinical details following the second massive exposure to mouldy hay dust.

TIME POST-EXPOSURE	CALF NO.	RESPIRATORY RATE/MIN.	TEMP. °F	COUGHING	OTHER FINDINGS
PRE-EXPOSURE	4	30	101	-	-
	16	30	101.1	-	-
	17	30	100.8	-	-
	20	30	100.8	-	-
1 HOUR	4	30	102.3	-	Harsh. Rhonchus on right - A/V.
	16	30	102.5	-	Harsh.
	17	30	101.1	-	-
	20	20.	101.9	-	-
2 HOURS	4	30	102	+	-
	16	30	102.2	-	-
	17	30	102	-	-
	20	30	101.9	-	Slightly dull.
3 HOURS	4	30	102	-	-
	16	30	101.3	-	-
	17	30	101.3	-	-
	20	30	101.4	-	-
4 HOURS	4	30	101.8	+	-
	16	30	101.5	+	Hyperpnoea (+)
	17	30	101.3	-	-
	20	30	101	+	-

APPENDIX 3 - TABLE 3 (Cont'd.)

TIME POST-EXPOSURE	CALF NO.	RESPIRATORY RATE/MIN.	TEMP. °F	COUGHING	OTHER FINDINGS
5 HOURS	4	30	101.6	-	-
	16	30	101.5	-	-
	17	30	101.9	-	-
	20	30	101.6	-	-
6 HOURS	4	30	101.4	+	-
	16	30	101.3	+	Necropsy
	17	30	101.7	-	-
	20	30	101.3	-	Necropsy
7 HOURS	4	30	101.3	-	-
	17	30	101.2	-	-
8 HOURS	4	30	100.8	-	Rhonchus on right - A/V.
	17	30	101.3	-	-
9 HOURS	4	30	102.1	-	-
	17	30	101.3	-	-
10 HOURS	4	30	101.6	-	-
	17	30	101	-	-
11 HOURS	4	30	101.3	-	-
	17	30	101.5	-	-
12 HOURS	4	30	101.7	-	-
	17	30	101.4	-	-

APPENDIX 3 - TABLE 3 (Cont'd.)

TIME POST-EXPOSURE	CALF NO.	RESPIRATORY RATE/MIN.	TEMP. °F	COUGHING	OTHER FINDINGS
24 HOURS	4	30	101.7	-	Necropsy.
	17	30	101.4	-	Necropsy.

APPENDIX 3 - TABLE 4

Experiment 4 - the haematological details following the first massive exposure to mouldy hay dust.

TIME	CALF NO.	P.C.V. %	Hb. g/100 ml.	R.B.C. $10^6/mm^3$	W.B.C. mm^3	N. TOTAL	N. %	L. %	E. %
PRE-EXPOSURE	4	30	9.4	6.13	6,700	1,742	26	74	0
	16	29	9.1	5.88	6,300	1,512	24	74	2
	17	28	9.1	5.84	4,000	1,000	25	74	1
	20	29	9.4	5.90	6,900	2,691	39	57	4
4 HOURS	4	29	9.7	5.96	7,200	1,440	20	79	1
	16	31	10.0	6.48	6,900	966	14	85	1
	17	29	10.0	6.47	5,700	1,311	23	76	1
	20	28	10.4	5.59	8,600	1,290	15	82	3
8 HOURS	4	30	-	5.96	9,500	2,280	24	76	0
	16	30	-	6.61	8,400	2,268	27	70	3
	17	28	-	6.66	6,300	1,386	22	78	0
	20	30	-	5.80	7,200	1,872	26	70	4
12 HOURS	4	30	-	5.65	10,400	2,912	28	70	2
	16	31	-	6.08	7,600	1,672	22	75	3
	17	28	-	6.32	5,400	1,728	32	66	2
	20	30	-	6.06	6,800	1,904	28	68	4
24 HOURS	4	29	-	5.80	7,500	2,550	34	64	2
	16	31	-	6.19	6,700	1,608	24	72	4
	17	27	-	6.20	5,400	1,836	34	64	2
	20	29	-	5.90	6,400	1,792	28	66	6

APPENDIX 3 - TABLE 5

Experiment 4 - the haematological details following the second massive exposure to mouldy hay dust.

TIME	CALF NO.	P.C.V. %	Hb. g/100 ml.	R.B.C. $10^6/mm^3$	W.B.C. mm^3	N. TOTAL	N. %	L. %	E. %
PRE-EXPOSURE	4	27	9.1	5.61	8,000	3,360	42	58	0
	16	31	10.6	6.80	10,300	4,532	44	56	0
	17	28	10.0	6.19	5,200	2,548	49	51	0
	20	30	11.0	6.40	9,000	3,330	37	62	1
2 HOURS	4	26	9.1	6.01	6,400	2,688	42	57	1
	16	29	9.4	6.33	8,400	3,528	42	58	0
	17	27	8.5	6.72	6,200	2,046	33	64	3
	20	28	9.4	5.74	7.700	2,310	30	66	4
4 HOURS	4	27	8.5	5.77	6,500	2,795	42	57	0
	16	29	9.7	6.55	8,900	2,848	32	64	4
	17	27	9.4	6.17	4,200	1,680	40	58	2
	20	29	9.1	6.07	8,400	3,276	39	55	6
6 HOURS	4	26	9.4	5.68	6,900	3,036	44	56	0
	16	30	11.0	6.25	9,600	3,744	39	59	2
	17	33	10.0	6.68	6,500	2,145	33	64	3
	20	28	9.1	5.90	8,600	4,128	48	51	1
8 HOURS	4	32	10.0	6.60	9,400	4,136	44	56	0
	16	NECROPSY 6 HOURS POST - EXPOSURE							
	17	30	10.0	6.89	6,800	3,128	46	53	1
	20	NECROPSY 6 HOURS POST - EXPOSURE							

APPENDIX 3 - TABLE 5 (Cont'd.)

TIME	CALF NO.	P.C.V. %	Hb. g/100 ml.	R.B.C. $10^6/mm^3$	W.B.C. mm^3	N. TOTAL	N. %	L. %	E. %
10 HOURS	4	29	9.7	6.07	8,100	3,645	45	54	1
	17	30	10.4	5.90	6,400	2,880	45	54	1
12 HOURS	4	30	10.0	6.41	8,300	3,901	47	53	0
	17	28	9.4	6.01	5,600	2,352	42	56	2
24 HOURS	4	30	10.4	6.38	8,000	2,880	36	64	0
	17	29	9.4	6.60	6,100	2,623	43	56	1

4 NECROPSY 24 HOURS POST - EXPOSURE

17 NECROPSY 24 HOURS POST - EXPOSURE

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