Differential Diagnosis of Pulmonary Disease in Adult Cattle in Britain

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Introduction

Contagious bovine pleuropneumonia was finally eradicated from Britain in 1898 but within a short time another disease had taken its place as a major hazard to the national herd. The rapid urbanisation of the human population during the Industrial Revolution resulted in the establishment of large, zero-grazed, town dairies and as a consequence of this rapid change to intensivism, bovine tuberculosis became rife. Certain other diseases, such as fog fever and pasteurellosis, were also recognised at this time but with the virtual disappearance of tuberculosis from Britain it has now become obvious that a large number of other, often less dramatic, disorders remain. While none of these problems in any way approach the earlier significance of pleuropneumonia or tuberculosis in terms of prevalence, economic impact, or (in the later case) public health importance, pulmonary disease in adult cattle is still a commonly encountered problem.

As a result of clinico-pathological investigations which we have carried out since 1969, we feel that it is now possible to differentiate between many of the diseases which we have encountered on clinical grounds alone. The following paper briefly summarises the clinical and pathological features of a large and continuing series of cases which we have examined and describes our approach to their clinical differentiation.

Materials and Methods

Source of animals

This paper is based on clinical cases admitted to this veterinary school during a field study of respiratory disease in adult cattle undertaken between 1969 and 1975 (Table 1) and also on other animals and incidents which have been examined and investigated since then. The cattle were all referred to us by practising veterinarians, most of whom were operating in the west and southwest of Scotland and northwest England. All of the subjects were adult cattle (i.e., > 2 years old) and were acquired for detailed clinical study and necropsy examination; in addition, most of the farms from which these animals originated were visited to ascertain the history and background situation, to examine other animals and to purchase further cases whenever necessary. A large number of postmortem specimens have also been examined as a service to practising veterinarians, however, such cases have not been included in this series since we were never able to examine the animals in life.

Clinical terms

The following terms have been used in describing the clinical observations: *fever* — rectal temperature exceeding 39.2°C; *hemoptysis* — the coughing-up of blood; *tachypnea* — increased rate of respiration (i.e., > 30 per minute in the resting animal); *hypernea* - increased depth of respiration; *dyspnea* - severe respiratory distress or difficulty in breathing, regardless of respiratory rate; *rhonchi* — whistling or musical adventitious sounds which usually occur during inspiration and occasionally during both inspiration and expiration; *crackles* — soft or harsh crackling sounds heard most commonly towards the end of inspiration or less frequently during both inspiration and expiration (soft crackles are most often associated with the presence of edema fluid in the airways; harsh crackles, depending on their distribution, are usually indicative of mucopurulent exudate or tenacious mucus in the airways or of interstitial emphysema).

Results

The range and type of disorders referred for investigation are summarised in Table 1. It is convenient to subdivide these disorders into 1. individual animal, and 2. group problems.

Individual Animal Problems

Chronic pulmonary diseases, and in particular chronic suppurative pneumonia and diffuse fibrosing alveolitis, are most frequently encountered; the only other relatively common condition being pulmonary thrombo-embolism following thrombosis of the caudal vena cava, in which the mode of onset is subject to considerable individual variation (see below). Apart from pulmonary thrombo-embolism, other genuinely sudden-onset disorders in individuals are far less common. Fog fever and farmer's lung cases are not infrequently referred as individual cases but further investigations so often reveal that these are the most severely-ill individuals from an affected group that

these conditions have been classified as group problems. The only other sudden-onset disorders in this category are milk allergy (see below) and an as yet unclassified pneumonia associated with widespread pulmonary eosinophilia. It was of particular interest that not a single case of acute bacterial pneumonia was encountered during the period of the survey although a number of cases of chronic suppurative pneumonia were mistakenly referred as such during acute exacerbations.

Chronic suppurative pneumonia (Figures 1 and 2)

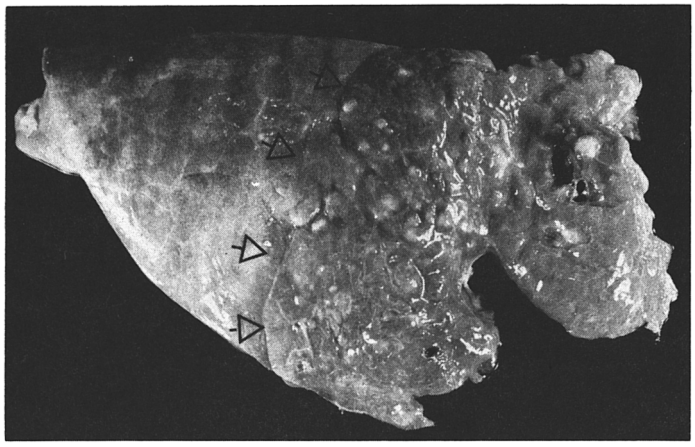

Figure 1. Chronic suppurative pneumonia: extensive consolidation of cranial lung lobes (demarcated by arrows) with small abscesses and localised pleurisy. Compare with Figure 3.

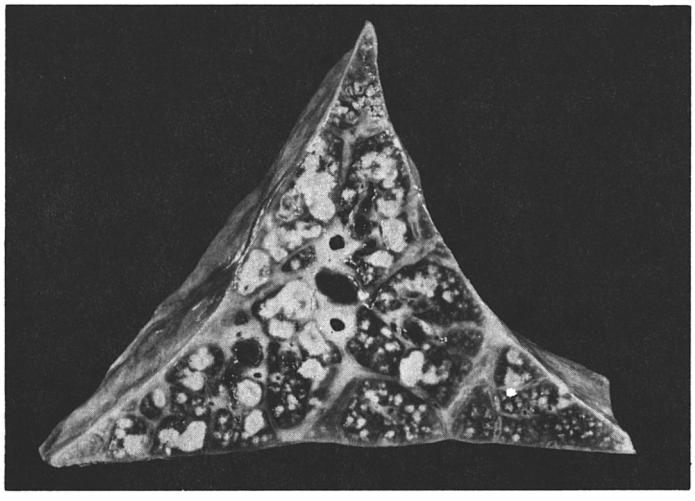

Figure 2. Chronic suppurative pneumonia: cross section of caudal lung lobe. Note consolidation, areas of suppuration and fibrosis of interlobular septa. Compare with Figure 5.

This is a common condition in cattle of all ages but surprisingly few detailed clinical and pathological accounts exist. Usually, the history is of weight-loss and coughing for a period of weeks or months although animals may occasionally be presented with signs of apparently sudden-onset due to exacerbation of a chronic septic focus within the lung.

Typical cases are dull, thin and only intermittently febrile. Frequent, sometimes productive, coughing is present and there is usually tachypnea although this is by no means always a marked feature. Thoracic pain may be obvious or detectable (and sometimes even localised) on percussion; during this procedure it is quite common to precipitate coughing but areas of dullness are rarely demonstrable. When present, rhonchi are usually limited to the cranio-ventral chest. Halitosis is usually a feature only of the small number of cases which proceed to necrotising bronchopneumonia and pleurisy; such cases are usually characterised by sudden deterioration, marked dullness, fever, pain and death within a few days.

It is rarely possible to differentiate on clinical grounds between animals with chronic suppurative bronchopneumonia, multiple lung abscesses, and bronchiectasis, singly or in combinations, and it is useful to use the term chronic suppurative pneumonia to include all these abnormalities. Affected lung segments are clearly demarcated at necropsy and there is often an abundant purulent excudate in the airways with consolidation of dependent lung lobes; multiple, large or small lung abscesses, tubular or saccular bronchiectasis and localised pleurisy may also be found in some cases.

Diffuse fibrosing alveolitis (Figures 3, 4 and 5)

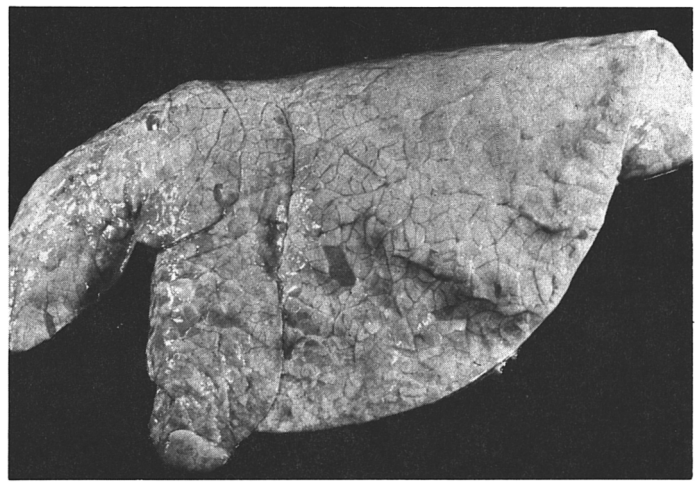

Figure 3. Diffuse fibrosing alveolitis: the lungs are very pale and a few lobules are dark-red and collapsed.

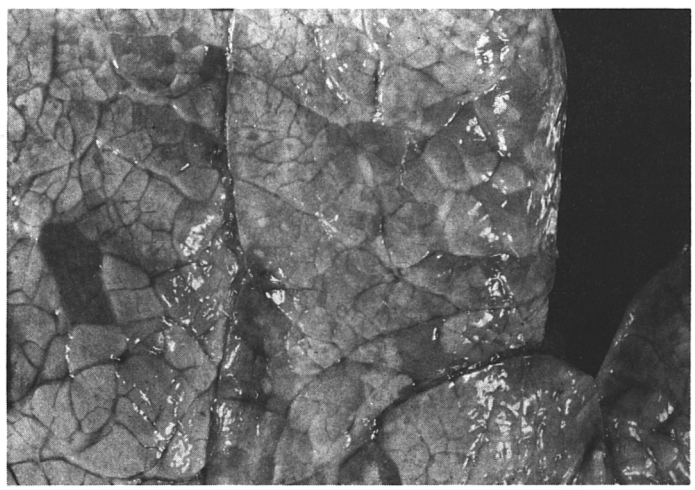

Figure 4. Detail of Figure 3. Note dark lobules depressed below surrounding lung.

Figure 5. Diffuse fibrosing alveolitis: cross section of caudal lung lobe. Note fleshy appearance of lobules and absence of suppuration.

Early in our investigations of bovine respiratory disease, we encountered individual animals with striking pulmonary lesions of diffuse fibrosis and cellular infiltration of interalveolar septa. These animals formed a distinct clinical and pathological group and since their lung lesions closely resembled those of a human disease known as "diffuse fibrosing alveolitis," this name was adopted for the bovine condition.

Diffue fibrosing alveolitis (DFA) usually affects cattle over 6 years of age and cases have been encountered in both beef and dairy herds. The history is usually of chronic, apparently progressive pulmonary disease ranging from a few weeks to two years in duration. Cases of an apparently sudden onset in animals introduced to lush aftermath pasture in the autumn have occasionally been wrongly referred to us as cases of fog fever (see below). In such instances, our further examination has always indicated a long-standing disorder — the animals are often thinner than others in the group and the owners frequently recall the history of coughing and respiratory disease for weeks or months prior to the acute incident.

Typical cases of DFA are thin but remarkably bright considering the severity of their respiratory signs and appetite is usually good; in fact, dullness and inappetance are only to be seen in severe terminal cases with clinical signs of congestive cardiac failure due to chronic *cor pulmonale.* Coughing is always present, tachypnea (40 to 70/min.) and very marked hyperpnea are also found, even at rest; dyspnea may be pronounced even after minimal exercise. Fever and thoracic pain are not a feature. On auscultation, loud rhonchi are frequently heard all over both lung fields and crackles may be heard in the cranio-ventral chest.

The pulmonary pathology of even the most severely disabled cattle is often unimpressive on superficial inspection, but closer examination reveals the presence of severe diffuse lung lesions quite different from those of chronic suppurative pneumonia. The lungs are exceptionally pale, almost white, very firm to cut and extremely heavy, weighing 6 to 16 kg or more, in contrast to a normal weight of 5 kg or less (lungs are weighed without the heart or mediastinal tissues), even in the absence of obvious areas of consolidation. There is diffuse involvement of all lobes of both lungs in the pathological process: most lobules are white and fleshy but, in many cases, one or more lobes contain other grey-red slightly collapsed lobules which exude copious edema fluid when sectioned (Figures 3 and 4); consolidated lobules like those of chronic suppurative pneumonia are not found. Very firm, white or yellow lobules can often be identified in some lungs and these are the result of particularly severe fibrosis, cellular infiltration of interalveolar septa and alveolar epithelial hyperplasia. Excessive volumes of thick mucus are often discovered in the tracheobronchial system but bronchiectasis or abundant purulent exudate are very uncommon (2,5).

Microscopical examination of multiple blocks from every lobe of both lungs reveals diffuse lesions involving the majority of lobules in all segments. The most striking changes are in the respiratory acini where interalveolar septa are severely thickened by fibrosis and cellular infiltration of mature plasma cells, lymphocytes, mast cells and interstitial cells and there is widespread distortion and obliteration of alveolar spaces. Alveolar spaces are filled by large mononuclear cells (a mixture of alveolar macrophages and desquamated alveolar epithelial cells) and there is diffuse alveolar epithelial hyperplasia, the alveoli being lined by cuboidal type 2 pneumonocytes. In some animals, there are multiple foci in which the alveolar epithelium is replaced by tall columnar ciliated cells or by a mixture of ciliated and mucus-secreting cells and in the latter instance the alveoli are often filled with mucus. Bronchitis, bronchiolitis and hypertrophy of the tracheobronchial mucus-secreting apparatus are apparent in many animals and globule leukocytes are common in the tracheobronchial epithelium (2,5).

The etiology of DFA in cattle is unknown. In view of the fact that at least 50% of affected animals have precipitating antibody to *Micropolyspora faeni* it is possible that these may have arisen as a result of chronic farmer's lung (see below). In support of this is the fact that many animals have been admitted from herds with a farmer's lung problem. However, a considerable number of animals having the clinical and pathological features of DFA have no detectable precipitins to *M. faeni* and in these cases it is possible that other etiological factor(s) may be involved.

Thrombosis of the caudal vena cava

Detailed clinical and pathological findings in this intriguing condition have been described recently (2,3)

In approximately 50% of animals there is a history of respiratory signs of only a few days duration. In these cases there is usually rapid deterioration although hemoptysis is commonly absent or overlooked prior to admission to this school. Other animals have a history of weight-loss and coughing for weeks or months before referral. Thoracic pain is often present but respiratory signs are such that many cases initially resemble cases of chronic suppurative pneumonia — that is, until the onset of hemoptysis.

Tachypnea, shallow breathing and coughing are

always present. This latter process often appears to cause pain but many cases show signs of severe intrathoracic pain while walking or even while at rest. Hemoptysis is present in approximately 50% of cases on admission and usually develops within a few days in the remainder. Cases deteriorate rapidly once hemoptysis is present and the majority of animals are dead or have been slaughtered within 10 days of being admitted. As a consequence of hemoptysis, there is often marked mucosal pallor, blood stains are commonly to be found on or around the animal and many also exhibit melena. Widespread rhonchi are frequently detectable on admission and tend to become even more pronounced with deterioration — as does thoracic pain. Hepatomegaly is detectable clinically in about 50% of cases and also becomes more prevalent and obvious with time.

Casts of clotted blood in the tracheobronchial system, ruptured pulmonary arterial aneurysms, multiple pulmonary abscesses and foci of thromboembolism and intra-pulmonary hematomata are to be found in the lungs at necropsy. Examination of the caudal vena cava reveals a thrombus in the intrathoracic portion or in the hepatic part in every case. The pathogensis of these lesions and their relationship to the various clinical signs has been outlined (3).

Pulmonary neoplasia (Figures 6 and 7)

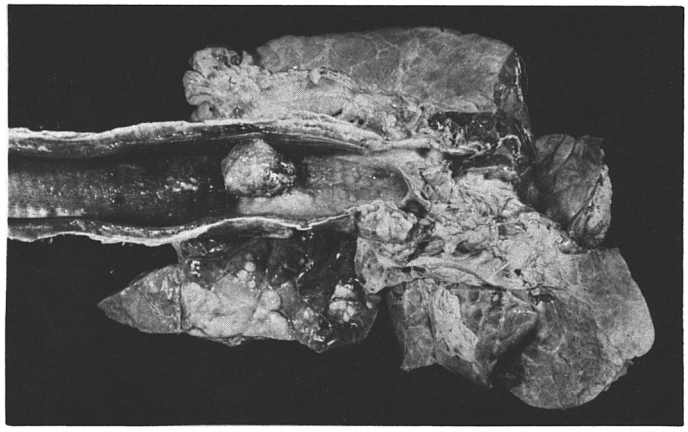

Figure 6. Bronchial carcinoma extending from lobar bronchus of right cranial lobe into the trachea.

Lung tumours are not common. Anderson and Sandison (1), in the most recent survey of pulmonary tumours in British cattle, found 19 primary carcinomas per million cattle in a slaughter house survey, representing 8.3% of all bovine neoplasms in the same study. The affected animals were all females, the majority being over 5 years of age. Secondary lung tumours, mostly lymphosarcomas, were encountered more frequently — the rate being 42 per million cattle examined.

In our survey three cases of bronchogenic carcinoma were found during a six-year period in which a total of 295 pulmonary cases were investigated (Table 1). All

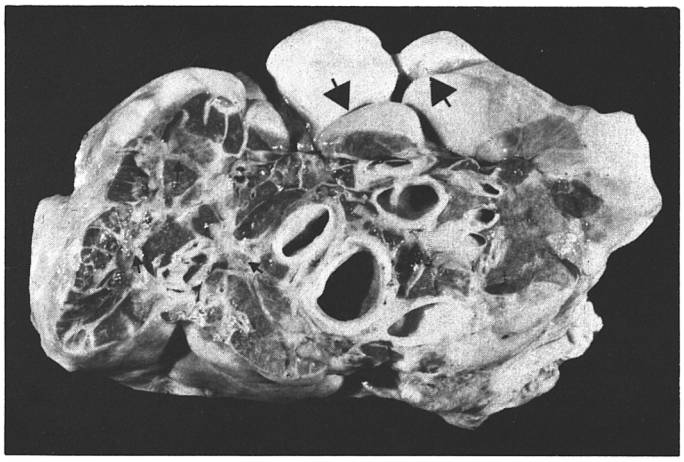

Figure 7. Bronchial carcinoma: the lung is irregularly-scarified by tumour tissue (small arrows). The scirrhous reaction has produced a pseudo-lobulated effect (large arrows).

three animals were presented with signs suggestive of chronic suppurative pneumonia and two were in fact wrongly diagnosed as such. The third was thought to have a lung tumour since percussion and auscultation revealed a large (20 cm diameter) dull and silent area in the right caudal thorax and there were secondary tumour deposits in both eyes. In one subsequent case a tumour partially occluded a major bronchus (Fig. 6) and retrospectively was considered to be the cause of an intermittent, loud sonorous rhonchus. In two earlier cases, the clinical signs were sudden-onset due to tumour erosion of major pulmonary blood vessels and massive hemorrhage into the lung substance or the thoracic cavity.

Milk allergy

The various reports of milk allergy were reviewed by Campbell (4), who demonstrated that the disease was an auto-allergy following sensitisation to alpha-casein in the animal's milk. This condition is probably much more prevalent than is appreciated since so often the clinical features are only of a transient urticaria. However, the syndrome associated with pulmonary signs has much in common with experimentally-induced systemic anaphylaxis and, on occasions, may lead to death.

During the course of our survey, two Ayrshire heifers from different farms succumbed to an apparently identical syndrome and, although its true nature was never defined, milk allergy was retrospectively diagnosed on the grounds of circumstance and probability. Both animals had been grazing good pastures for several weeks and had just been put on to once-daily milking as they were nearing the end of particularly good first lactations. Both developed gross dyspnea just before being milked and almost continual diarrhea and dribbling of urine were noticed in one animal. Skin lesions were not detected. One heifer died within three hours and the other was slaughtered after 24 hours. Post-mortem examination revealed pulmonary congestion, edema, and inter-

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stitial emphysema; there was marked and widespread hyaline membrane formation and some intra-alveolar hemorrhage, but alveolar epithelial hyperplasia was not found, even in the animal which survived for 24 hours.

Two half-sisters of the Jersey breed, both with milk allergy, are currently under investigation in the Department of Veterinary Medicine. Both have a history of episodes of urticaria and respiratory distress associated with milking and similar signs may be induced at will by exposure to alpha-casein. Intradermal injection of alpha-casein produces an immediate response and a large, soft swelling is apparent within 15 minutes.

Differential diagnosis of individual problems

History and background are often of no help in attempts to differentiate between the two commonest conditions which we have encountered, namely chronic suppurative pneumonia and DFA. In both cases owners usually complain of weight-loss and coughing which have often been noticeable for at least some months. Clinical differentiation is usually possible after a detailed physical examination and the most important features to be considered are demeanor, the presence or absence of severe hypernea and/or thoracic pain and also the findings on auscultation. Differences also exist in terms of likely complications.

Uncomplicated cases of DFA are usually bright, they eat normally and chew their cud vigorously; they are in fact surprisingly alert in view of the very marked degree of hyperpnea which is usually present. In contrast, cases of chronic suppurative pneumonia are usually dull (although the degree of depression may vary from day to day), they have poor appetites and their respiratory movements are often very shallow. This latter feature may well be a consequence of thoracic pain, a common feature of chronic suppurative pneumonia but one which is not seen in DFA. Percussion of the thorax in chronic suppurative pneumonia cases may also produce coughing and a pained reaction with grunting. On auscultation of cases of DFA it is quite common to hear loud rhonchi all over both lung fields and harsh crackles may be heard, although less often than rhonchi, in the cranio-ventral thorax. Rhonchi are often absent in chronic suppurative pneumonia during any one examination although they may be detected after exercise or a bout of coughing; when present, they are usually only heard in the cranio-ventral thorax.

Congestive cardiac failure not uncommonly occurs in the later stages of DFA bringing about a fairly rapid clinical deterioration. This complication is only rarely seen in chronic suppurative pneumonia in which sudden deterioration is almost always associated with the development of necrotising bronchopneumonia.

Approximately half of the cases of caval thrombosis have had histories dating back weeks or months and have been clinically indistinguishable from chronic suppurative pneumonia. However, the majority of caval thrombosis cases eventually develop hemoptysis and then diagnosis is simple since in our experience this sign is almost pathognomonic of pulmonary thrombo-embolism and aneurysm rupture following thrombosis of the caudal vena cava. With the onset of hemoptysis, deterioration is usually rapid, thoracic pain is greater and rhonchi are more widespread than in chronic suppurative pneumonia. Occasionally, cattle with a history and signs suggestive of chronic suppurative pneumonia are found to have marked pallor on admission although signs of hemoptysis, that is dried blood on or around the animal or melena, have been absent. Such cases may be tentatively diagnosed as pulmonary thrombo-embolism and vena caval thrombosis and a renewed bout of hemoptysis may be expected within a few days.

It can be seen from Table 1 that the vast majority (approx. 90%) of the individual pulmonary disorders which we encounter are chronic suppurative pneumonia, diffuse fibrosing alveolitis or caudal vena cava thrombosis. Each of these conditions may be correctly diagnosed on clinical grounds on most occasions. While we accept that it may not be possible to diagnose certain other conditions in life, e.g. pulmonary neoplasia, it should be noted that such instances are the exception rather than the rule and make up only about 7% of the cases which were referred to us during the six year study.

Table 1. The prevalence of specific pulmonary diseases of adult cattle examined in the University of Glasgow Veterinary School between July, 1969 and June, 1975.

DIAGNOSIS	NUMBER OF CASES
Individual problems	
Chronic suppurative pneumonia	77
Diffuse fibrosing alveolitis	53
Thrombosis of the caudal vena cava	23
Pulmonary neoplasia	3
Milk allergy	2
Other conditions	9
Group problems	
Fog fever	62
Parasitic bronchitis (i) patent disease	5
(ii) reinfection syndrome	18
Farmer's lung	43
TOTAL:	295

Group Problems

In marked contrast to the pulmonary disorders in individuals, each of the three specific conditions which we have encountered as "group problems" have been intimately associated with management practices. Fog fever and parasitic bronchitis were found in grazing animals during the summer and autumn and farmer's lung developed in cattle exposed to moldy feed indoors in the winter and early spring.

Fog fever (Figures 8, 9, 10, 11)

Fog fever is an acute respiratory distress syndrome with minimal coughing which occurs in adult beef-type cattle shortly after a change to better, often lush, pasture usually in the autumn months from August to November. This disease is similar, if not identical, to acute bovine pulmonary emphysema (ABPE).

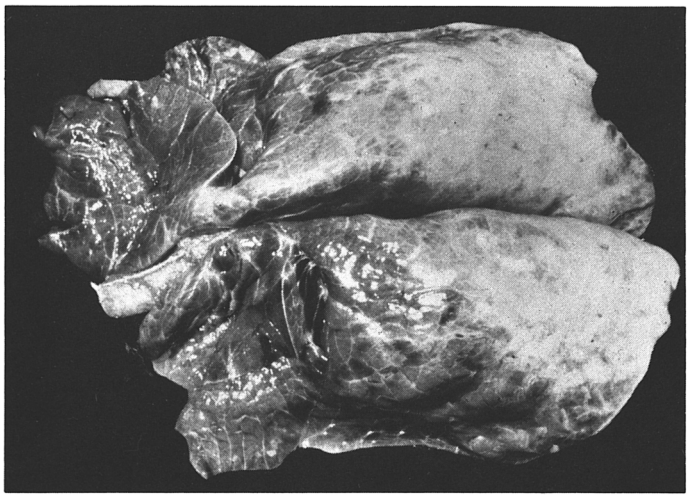

Figure 8. Fog fever: the cranial lobes are dark-red and congested. There is pleural edema and interstitial emphysema in the caudal lobes which are distended by gas bullae. The lungs are from a fatal case.

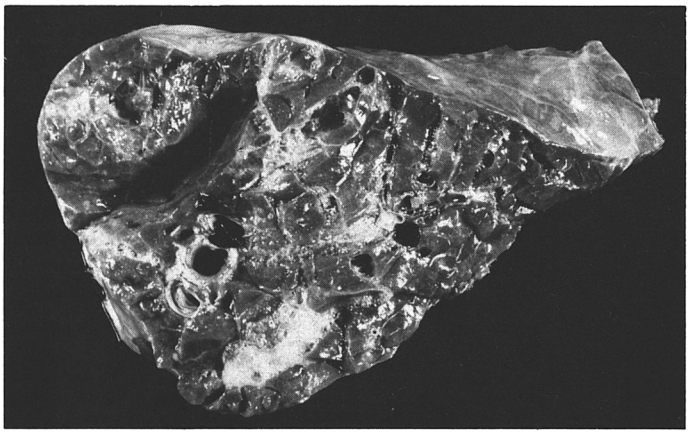

Figure 9. Fog fever: cross section of caudal lung lobe in Figure 8. Interstitial emphysema and gas bullae are evident. The lung lobes are dark-red and have a smooth, shiny cut-surface indicative of the presence of congestion, edema and hyaline membranes.

Figure 10. Fog fever: lungs of a slaughtered animal ill for four days. The lungs were fawn and very heavy.

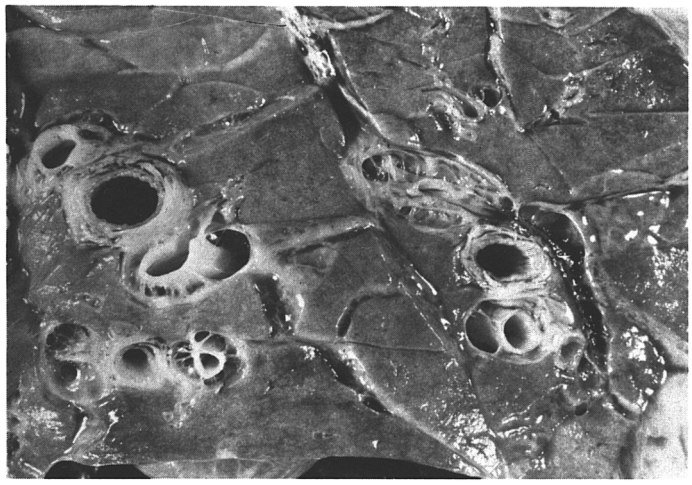

Figure 11. Fog fever: cross section of caudal lobe in Figure 10. The lobules are fawn and fleshy — the result of diffuse alveolar epithelial hyperplasia. Compare with Figure 9.

Almost all outbreaks of fog fever which we have investigated have arisen within two weeks of moving hungry cattle from bare to lush pastures, such as hay or silage aftermath, and the condition has been limited to fat, single-suckler females, usually of the Hereford type. The morbidity rate is variable, but often approaches 50%; 30% of severely affected animals die, usually within two days of the onset of clinical signs. In severe cases there is gross dyspnea, with loud expiratory grunt, frothing at the mouth, mouth-breathing and tachypnea (range 35-75 per minute). On ausculation inspiratory and expiratory sounds are usually surprisingly soft in view of the respiratory rate and crackles are only occasionally detected. Severe cases improve dramatically after three days and in these animals and in others which have not shown severe signs (and which may not be immediately apparent to the inexperienced observer) it is quite common to note only tachypnea (respiratory rate 50-80 per minute) and hyperpnea. Harsh respiratory sounds are common on auscultation and crackles and rhonchi may also be noted, particularly in caudal lung fields, in this later stage. Subcutaneous emphysema may be detected in a few of these convalescing animals. In addition to these signs of respiratory disease within an affected group, there is also a tendency for the demeanor of the group to change so that the animals become more tranquil. It should be particularly noted that coughing is not a dominant feature in affected individuals nor in the group as a whole (6).

In animals that die there are ecchymotic and petechial hemorrhages in the larynx, trachea and bronchi and the airways are filled with frothy edema fluid. Cranial lung lobes are deep-red or purple and the cut surface of the lobules has a smooth, glistening, glass-like appearance, the result of severe congestion, edema and hyaline membranes. Interstitial emphysema with large gas bullae is apparent in all parts of the lung and occasionally may also extend along the back. Pulmonary edema is very noticeable,

especially in the ventral segments of the lungs, and gelatinous yellow edema fluid can be found in the interlobular septa and perivascular connective tissue. Histologically, alveoli and alveolar ducts are usually lined by eosinophilic hyaline membranes; edema fluid, a few eosinophils, neutrophils, alveolar macrophages, and multinucleated giant cells are found in the air spaces. In most animals there is some proliferation of alveolar epithelial cells. In animals that are slaughtered after at least three to four days of illness interstitial emphysema and pulmonary edema are usually minimal. However, all the lung tissue is fawn and rubbery as a result of severe, diffuse, alveolar epithelial hyperplasia, in which the alveoli in all acini are lined by a single layer of cuboidal type 2 pneumonocytes containing frequent mitotic figures. Large mononuclear cells, a mixture of alveolar macrophages and type 2 pneumonocytes, are found in the alveolar spaces, together with condensed hyaline deposits and multinucleated giant cells. Interalveolar septa are edematous and many interstitial cells and eosinophils are apparent. The term "pulmonary adenomatosis" is sometimes used to describe lungs with alveolar epithelial hyperplasia but in our view this can only lead to confusion and the term is best forgotten.

Parasitic bronchitis (i) patent disease (Figures 12 and 13)

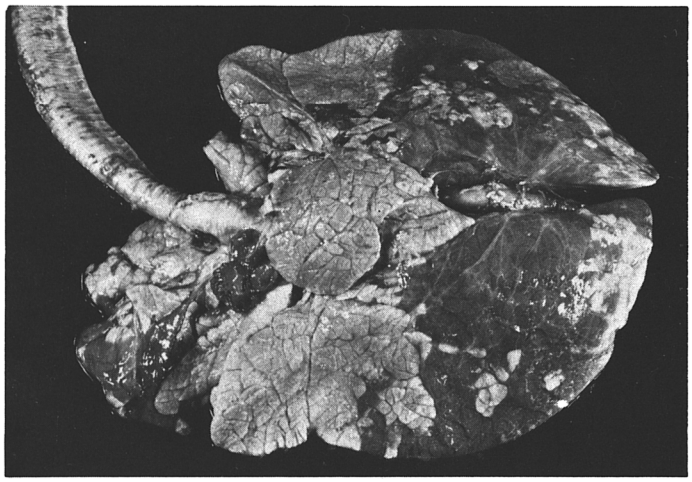

Figure 12. Patent parasitic bronchitis: consolidated lobules in caudo-ventral lung lobes are areas of bronchitis, collapse and reaction to aspirated eggs and larvae. This appearance is typical of patent disease.

Parasitic bronchitis is a familiar and common problem of immature grazing cattle in Britain, even though the disease may easily be prevented by vaccination. There is no clinical or experimental evidence to support the view that age immunity is significant in parasitic bronchitis and we have encountered classic patent parasitic bronchitis in adult dairy cattle that had been shielded from earlier infection. This situation may arise when groups of cattle are moved from regions where parasitic bronchitis is not a problem to areas where the disease is endemic, or when animals

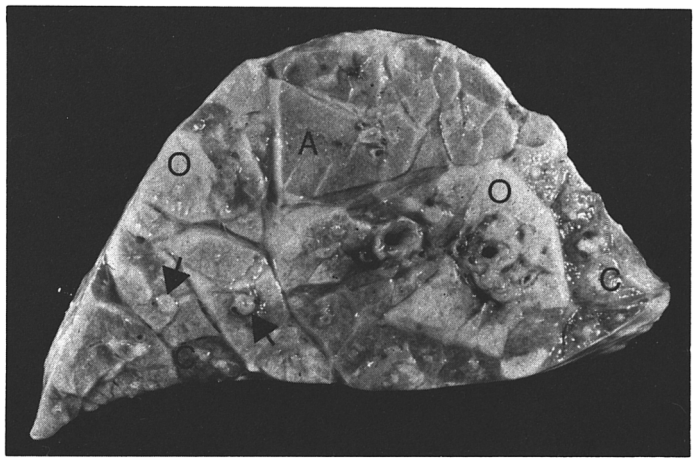

Figure 13. Patent parasitic bronchitis: cross section of caudal lung lobe. Many small bronchi are obstructed by inflammatory reaction and exudate (arrows) leading to overinflation of associated alveoli (0). Other lobules are consolidated by the reaction to eggs and larvae (C) and dorsal lobules are affected by alveolar epithelial hyperplasia (A). Compare this varied appearance with Figure 11.

that have only grazed clean pastures in an endemic area are suddenly exposed to grazing contaminated by other cattle. In both instances, a particular age or management group may be affected within the herd. Apart from the grazing history and epidemiology, the main presenting signs of the patent disease within a group are dramatic drop in milk yield, when dairy cattle are involved, and widespread and frequent coughing. In individuals, the main signs are frequent coughing, marked tachypnea and dullness, together with rhonchi and loud crackles which are often audible over much of the caudal lung fields. *Dictyocaulus viviparus* larvae are present in the feces — 50-250 larvae per gm are not unusual.

At necropsy, many adult lungworms are found in the airways and there is extensive consolidation, particularly of segments in the ventral parts of the caudal lung lobes. There is severe bronchitis and bronchiolitis and aspirated eggs and larvae may be found in the alveolar spaces. Interstitial emphysema, pulmonary edema and hyaline membranes, alveolar epithelial hyperplasia and pulmonary eosinophilia may also be apparent.

(ii) reinfection syndrome (Figures 14, 15 and 16)

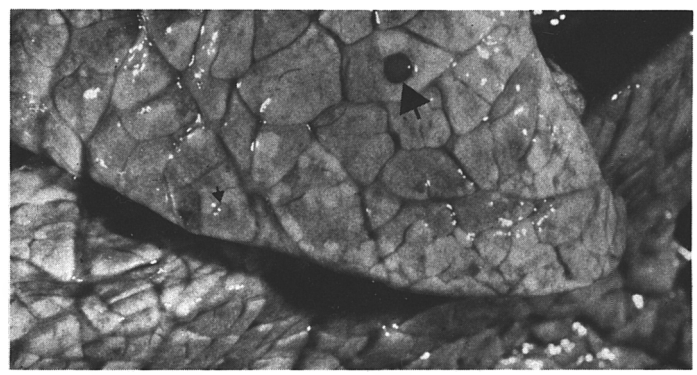

Figure 14. Reinfection syndrome in parasitic bronchitis: large grey (large arrow) and smaller green (small arrow) pulmonary lymphoid nodules.

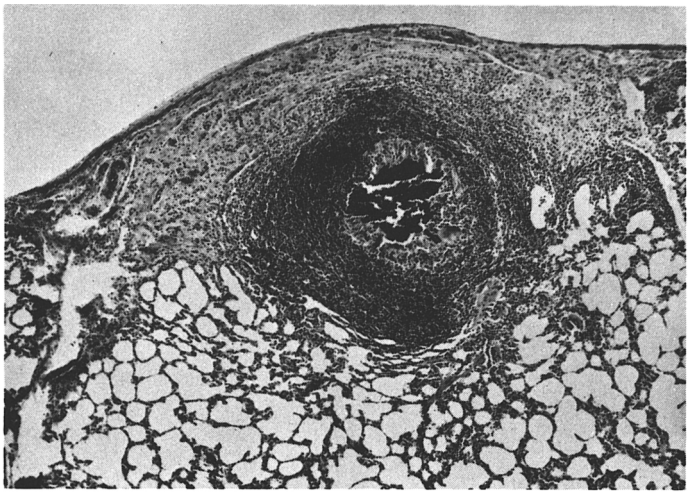

Figure 15. Cross section of subpleural pulmonary lymphoid nodule. Central mass of fragmented eosinophils surrounded by bronchiolar epithelial cells and giant cells within an outer ring of lymphocytes and plasma cells (H/E;x60).

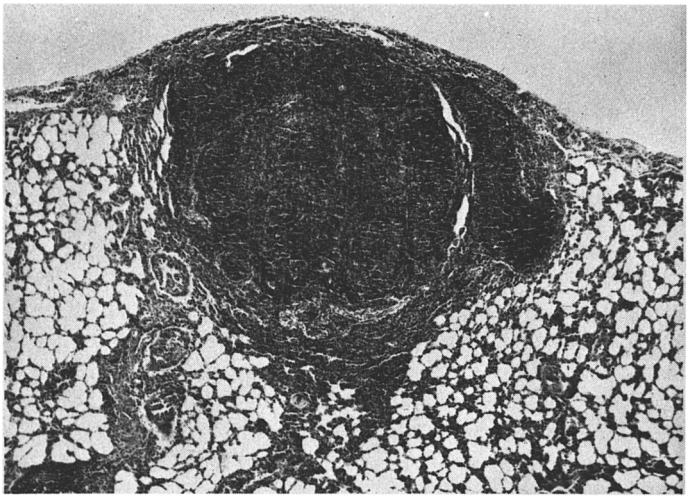

Figure 16. Cross section of mature pulmonary lymphoid nodule composed of lympho-reticular cells: parasitic debris is not apparent (H/E;x60).

The reinfection syndrome occurs on farms on which parasitic bronchitis is endemic and usually develops when adult milking cows graze with, or on fields contaminated by, calves with severe patent disease. It seems likely that the immunity of the adult animals is not able to completely overcome the heavy lungworm challenge and the respiratory signs are the result of a small number of larvae gaining access to the lungs before they are destroyed or expelled. Under these circumstances, severe respiratory signs often occur 14 to 16 days after cattle are introduced to contaminated fields and the main presenting signs are again dramatic drop in milk yield in lactating cattle, and severe coughing in many or all of the animals in the group. In individuals, frequent coughing, marked tachypnea and dullness may be obvious but auscultation only reveals harsh respiratory sounds — rhonchi and crackling are absent. Since egg-laying adults are absent or few in number, *D. viviparus* larvae are not detectable in the feces.

The clinical signs are the result of an immune reaction in which pulmonary lymphoid nodules develop about killed larvae, which are usually in the bronchioles. At necropsy, a number of pulmonary lymphoid nodules, 3 to 4 mm in diameter, is found beneath the visceral pleura of each lung. In the initial stages, the nodules are raised above the lung surface and have a grey-red or greenish-yellow centre (Figure 14). Histologically, this is composed of a central core of brightly eosinophilic parasitic debris surrounded by many proliferating macrophages, multinucleated giant cells and hyperplastic bronchiolar epithelial cells within a ring of eosinophils, macrophages, plasma cells, lymphocytes and giant cells (Figure 15). In time, these nodules form mature lympho-reticular tissue with germinal centres and the parasitic debris is not then apparent (Figure 16). An excessive volume of greenish mucus, heavily infiltrated by eosinophils, is found in the bronchial tree and globule leukocytes are particularly abundant in the tracheobronchial epithelium. Eosinophils are exceedingly numerous both in the bronchial epithelium and in the interlobular septa, where they give the tissue a greenish discoloration. Interstitial emphysema and pulmonary edema are absent. In most animals there are no adult lungworms in the tracheobronchial system and when these are found they are small, stunted and apparently sterile.

Farmer's lung (Figures 17 and 18)

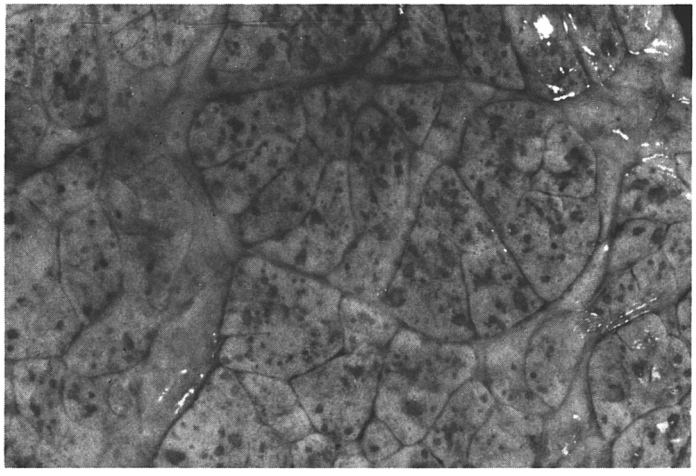

Figure 17. Bovine "farmer's lung": multiple small grey spots beneath the pleura.

Farmer's lung is an allergic respiratory disease which develops after exposure to the dust of moldy hay, cereals or other vegetable matter containing the spores and metabolic products of *M. faeni* and other thermophilic actinomycetes. The disease is a problem in man and cattle only in the western parts of Britain, since these are the areas with the highest summer rainfall. In these regions hay is frequently baled at a high moisture content (i.e., well in excess of 30%), overheating is inevitable and as a consequence, a Thermophilic microflora becomes dominant.

In Britain, farmer's lung disease has only been confirmed in adult cattle; clinical signs usually become

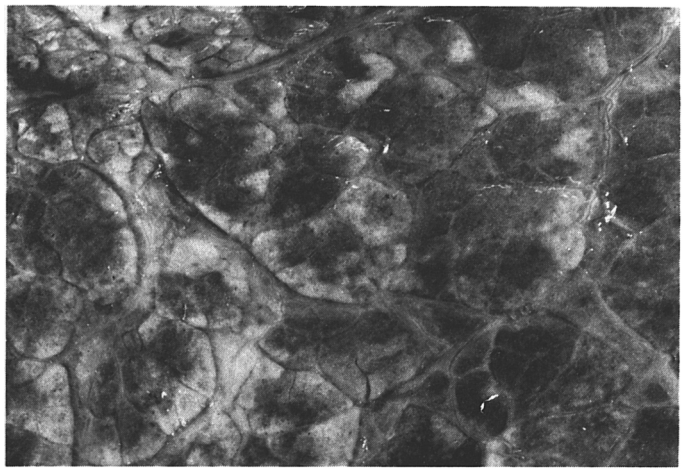

Figure 18. Bovine "farmer's lung": centre of lung lobules in red and slightly collapsed, periphery is pale and overinflated.

obvious during the winter housing period although chronic cases (see below) may not be detected until they are turned out in the spring. The disease is more common in dairy cattle than beef animals. The possibility that the farmer or farm workers might also be affected should not be forgotten.

Clinical signs of farmer's lung disease may develop suddenly (acute farmer's lung), but this form is only rarely seen in more than one animal in a herd at any time. However, successive acute cases may occur in a chronically-affected herd throughout the winter — hence the decision to regard farmer's lung as a group problem.

The clinical features of the acute form of the disease are sudden onset of dullness, decreased appetite and fall in milk yield (where appropriate) (7). Coughing occurs, although this is sometimes overlooked by the owner. On auscultation, crackles may be heard cranio-ventrally. In provocation studies a febrile reaction occurs four to six hours after antigen exposure and lasts for only a few hours; this is perhaps why fever is not a constant finding under field conditions.

Chronic farmer's lung cases may have a history of excessive weight-loss and coughing for several winters with remissions during each grazing season. Other animals may have been recognised as chronic pulmonary cases but eventually may suffer an acute crisis as a result of recent heavy exposure to antigen, unaccustomed exercise, or to the development of congestive cardiac failure. The clinical features of chronic farmer's lung are weight-loss and reduced milk yield (where appropriate) and there is usually frequent coughing, often with the production of copious amounts of green mucus. Tachypnea is usually present and hyperpnea is often very obvious; there is no alteration in thoracic resonance and no obvious or detectable thoracic pain. Auscultation often reveals harsh crackles in the cranio-ventral thorax and widespread rhonchi. Precipitins to *M. faeni* are found in the serum of all cases but the disease cannot be diagnosed on their presence alone since precipitins are only an indication of exposure to the organism.

In acute cases, the lungs may appear surprisingly normal at necropsy, but close examination reveals the presence of a number of small grey spots on the pleural surface of many lobules. The peripheral acini of some lobules are overinflated and this produces a pale-pink, raised edge around a darker-red central portion. On microscopical examination, widespread pulmonary lesions typical of an extrinsic allergic alveolitis can be observed. These include: infiltration of interalveolar septa by lymphocytes, plasma cells and interstitial cells, intraseptal lymphocytic aggregates without germinal centres; characteristic epithelioid granulomata with multinucleated giant cells; bronchiolitis; and bronchiolitis obliterans. If there has been recent natural or experimental exposure to the antigen, there may be foci where the alveoli contain edema fluid, free red blood corpuscles, neutrophils and macrophages and where neutrophils are frequently found in the interalveolar septa along with plasma cells and lymphocytes.

The macroscopic appearance of the lungs in the chronic form is very similar to that of acute cases. However, in some lobules, there is focal fibrosis of the interalveolar septa with localised alveolar epithelial hyperplasia and there may even be focal replacement of the alveolar epithelium by tall columnar ciliated or mucus-secreting cells. The affected lobules are pale white or yellow and firm to cut. This fibrosing change is not diffuse and does not affect the majority of lung segments.

Differential diagnosis of group problems

In marked contrast to disorders in individuals, there is a close association between the group diseases and management practices; the background to outbreaks therefore assumes much greater diagnostic significance. A clear idea of the type of farming operation, the class of livestock involved, the period of housing or recent grazing history are all essential pieces of information. There are a sufficient number of differences between the disorders described to enable clinical differentiation in life but perhaps the most important single piece of information in this respect is the "presenting sign."

Fog fever and both forms of parasitic bronchitis are usually high morbidity disorders which, in Britain, occur in the latter half of the grazing season. Fog fever is classically a disorder of "single-suckling" (i.e., ranched) beef cattle. While alleged incidents of fog fever, involving groups of dairy cattle, have been regularly referred to us, further investigations have so far always revealed that the animals were suffering from one or other of the forms of parasitic bronchitis. We have yet to be called to see an outbreak of parasitic bronchitis in adult beef cattle. In every confirmed (at necropsy) fog fever incident which we have investigated save one, there has been a history that the affected group had recently been *introduced* to better, often lush, grazing and in most cases this grazing was hay or silage aftermath (in many areas the local term for such grazing is "fog" or "foggage,"

hence the name fog fever). The exceptional outbreak involved one animal from a small group of beef cattle on a large area of partially improved and fertilized hill pasture. After a long dry summer, autumn rains promoted an exceptional growth of new grass in improved areas and a fog fever outreak occurred 12 days after the onset of rain. This outbreak emphasises the importance of a detailed grazing history.

Grazing histories in parasitic bronchitis outbreaks have been far less consistent; incidents have occurred in cattle which have grazed a particular area for much of the summer or shortly after (i.e., > 4 weeks) being introduced to heavily contaminated fields. This latter relationship is well demonstrated in outbreaks of the reinfection syndrome occurring 14-16 days after milking cows have been used to graze down a heavily-contaminated calf paddock. In such cases further investigation reveals that the classic patent disease is present in the calves. Outbreaks of patent parasitic bronchitis in adults have usually involved groups of susceptible cattle which have been introduced to farms where parasitic bronchitis has been edemic. This may occasionally arise as the result of a farmer moving a herd to a newly-acquired farm; background information regarding the farm is useful but by no means a necessity in arriving at a diagnosis. Finally, clinical signs of parasitic bronchitis of either type are not uncommonly noticed after a chance of pasture due to infestations acquired prior to the change; since such outbreaks occur in the autumn when dairy cattle are subjected to frequent pasture change, clinical signs may arise after cattle have been moved to hay or silage aftermath. Confusion with fog fever under these conditions should not occur if a detailed grazing history is obtained; in any case there are clear clinical differences between the diseases.

The major clinical difference between fog fever and the two forms of parasitic bronchitis is that in the latter instance, the presenting sign is widespread, frequent and severe coughing. While occasional coughs may be heard in groups of animals in which fog fever is present this is by no means a presenting feature and further investigations usually reveal that the coughing is in the calves at foot, not the adult cattle. Frequent coughing is not a feature of individual cases of fog fever in which the presenting sign is respiratory distress of variable degree.

In both forms of parasitic bronchitis, the presenting sign in the affected group (which may not necessarily be the entire milking herd) and in the individual animal is frequent and severe coughing. In addition there is anorexia and a very marked drop in milk yield; this fact might well explain why all incidents investigated to date have involved dairy cattle since dairy farmers are made much more aware of the illness than would be the case in beef herds. Profound dullness is much more a feature of patent parasitic bronchitis although severe respiratory distress may be seen in either form of the disease. Auscultation, which is often unrewarding in cases of fog fever, is essential if one is to attempt to differentiate between the two forms of parasitic bronchitis. In the patent disease, if one is prepared to examine enough affected animals, it is quite common to hear widespread rhonchi and harsh (emphysematous) crackles but to date such sounds have never been detected in the reinfection syndrome. Finally, an examination of feces will reveal *D. viviparus* larvae only in the patent disease.

The mortality rate in fog fever varies markedly but one or more deaths occur in the majority of outbreaks. In most cases, animals which die have been ill for only a day or two and post-mortem findings are quite characteristic even though they are not pathognomonic. The mortality rate is quite variable in outbreaks of patent parasitic bronchitis; while deaths have been observed, many of the worst affected cattle have been electively slaughtered after a severe illness of up to two weeks duration. In some outbreaks, had it not been for the fact that we were purchasing affected animals for further study it is quite certain that deaths would not have occurred. Similarly, we have yet to see an animal die from the effects of the reinfection phenomenon. In the absence of, and sometimes despite, prompt treatment, recovery may be prolonged after either form of the disease and coughing may continue throughout the following winter. This is not the case with fog fever in that recovery from the classic form of the disease is usually uneventful with almost all cases becoming clinical normal within three or four weeks.

In a clinico-pathological study of adult cattle which developed respiratory signs during the winter-housing period in northwest England and southwest Scotland, Wiseman (to be published) has found that the great majority were suffering from farmer's lung disease. When background information regarding these individuals is examined it becomes clear that this condition is the only specific group disorder recognised and described to date. Differential diagnosis is not, therefore, a problem at the moment although clearly with further study it seems likely that other disorders will be defined (see below). Nevertheless, for a definitive diagnosis of farmer's lung and the possible recognition of other pulmonary diseases in the future it is essential to obtain information regarding the frequency of coughing and/or other respiratory signs in the current and previous winters, the time of onset of coughing or respiratory signs in affected individuals and herds, the type of housing, the winter-feeding regime, whether or not hay is used and, if so, how it has been harvested, stored and fed. In addition, it is necessary to obtain information regarding the serological status of the herd *vis-a-vis* precipitins to *M. faeni* and it is also useful to find out in general terms about the animal attendant's own health record in relation to hay or dust-associated respiratory signs.

Discussion

In general, the history and background in individual cases of respiratory disease are of little help in differential diagnosis. Nevertheless, differentiation is possible in the vast majority of instances following a

detailed clinical examination. Examples of the limited number of occasions on which history and background studies are of use are 1. in chronic suppurative pneumonia after aspiration of foreign material, and 2. in possible *M. faeni* precipitin-negative chronic farmer's lung cases. These might be considered cases of DFA if viewed in isolation but must be regarded in a different light when originating from a herd known to be affected by farmer's lung.

Diagnostic errors in individual disorders have not been common although pulmonary tuberculosis and neoplasia have usually been considered to be chronic suppurative pneumonia. In addition, this latter condition has been wrongly diagnosed in cases which have proved to be DFA at necropsy or in caudal vena caval thrombosis cases which have not presented with hemoptysis. However, with increasing experience such mistakes are becoming less common.

The clear and intimate association between the specific group disorders and husbandry patterns and practices must be re-emphasised. As a result, the clinician's approach to differential diagnosis must be based upon a sound understanding of management techniques. Moreover, he must also operate around a balanced appraisal of what is probable as opposed to what is possible, a balance which may well be subject to national, if not regional, variation. It is our view that a rational approach to differential diagnosis can only arise out of integrated disease-description studies.

On occasion, diagnostic errors have been made in group disorders but if a diagnosis is based upon *situations* as well as clinical *signs* then such mistakes should involve only a small number of incidents. However, diagnostic problems must exist at the limits of specialist knowledge even when detailed clinical studies are supported by extensive pathological investigation. For example, on two occasions, a clinical diagnosis of the reinfection syndrome was made but post-mortem studies did not reveal the expected nodular lesions but rather pulmonary eosinophilia and aggregates of globule leukocytes in the tracheobronchial epithelium. It is possible that these were examples of an undescribed disorder or that the clinical diagnosis was correct and the individuals examined at necropsy did not have typical lesions. After all, little is known of the spectrum of pathological changes in this form of parasitic bronchitis in the partially immune animal. In another instance, a respiratory problem in an entire herd of Jersey cows was found to be a form of extrinsic allergic alveolitis but exhaustive serological testing with fractions of *M. faeni* and a wide variety of organic antigens failed to identify the allergen responsible. The clinical syndrome was identical to that recorded in farmer's lung except that 1. the signs apparently began in the early autumn while the cattle were at grass, and 2. the hay was and had been of excellent quality. Histopathological examination of lung tissue from slaughtered cases confirmed lesions of extrinsic allergic alveolitis including: bronchiolitis, bronchiolitis obliterans, cellular infiltration of interalveolar septa by lymphocytes and plasma cells and the presence of epithelioid granulomata. A more detailed description of these incidents will be published at a later date.

We feel that integrated studies such as we have carried out have resulted in a much clearer picture of the types and patterns of certain bovine pulmonary diseases. Despite the fact that much has still to be learned about the diseases which have been defined and in some instances their aetiologies have still to be established, it is now possible to systematically examine individual cases and outbreaks with some confidence that a sound clinical diagnosis can be made.

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