A Reappraisal of Atypical Interstitial Pneumonia in Cattle

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The term "atypical interstitial pneumonia" (AIP) was introduced by Blood (4) to describe bovine respiratory disorders in which some or all of the following pulmonary lesions were found: congestion, edema, hyaline membranes, interstitial emphysema, alveolar epithelial hyperplasia, fibrosis and cellular infiltration of interalveolar septa. In Canada, acute and chronic clinical forms of the disease were recognized and a number of probable causes were known, but it was proposed that there was sufficient similarity pathologically between all the etiological and clinical forms to justify grouping them as one disease (4), although not all Canadian workers now subscribe to this view (48). In the last decade, much more information has been provided about the diseases grouped under AIP and it has become apparent that there are important differences between the various forms, in terms of clinical signs, epidemiology, etiology and pathogenesis, which justify division of AIP into separate entities. The different syndromes which fall into the morbid-anatomical category of AIP have been described briefly below. The number of references has purposely been kept small since the literature is adequately covered in several reviews (7,19,25,33,43). Differential diagnostic features of the more important syndromes in Britain are discussed elsewhere (45) and this should be read in conjunction with this article.

A. Hypersensitivity diseases

1. *Extrinsic allergic alveolitis (farmer's lung)*

Farmer's lung is an allergic respiratory disease of man which develops after exposure to the dust of moldy hay containing the spores of *Micropolyspora faeni* and other thermophilic actinomycetes. Exposure to *M. faeni* produces a clinical respiratory disease which has been considered to be largely the result of a type III (Arthus) hypersensitivity reaction in the peripheral parts of the lung and precipitating antibodies (precipitins) to *M. faeni* are usually found in the patient's serum. The lung lesions are common to a variety of inhaled organic antigens and are associated with vascular damage by immune complexes at the alveolar level–the term "extrinsic allergic alveolitis" has been used to describe this mechanism. Farmer's lung may occur in both acute and chronic forms in man and severely incapacitates affected individuals.

A disease similar to farmer's lung has been described in cattle exposed to moldy hay and the pulmonary lesions closely resemble those noted in man (36,45). Some confusion between farmer's lung and fog fever (acute bovine pulmonary emphysema) followed the discovery by Jenkins and Pepys (29) of precipitins to *M. faeni* in sera submitted from cattle with respiratory disease and the suggestion that these were possibly of significance in the etiology of fog fever. The clinical signs, epidemiology and pathology of fog fever have since been clearly demonstrated to be different from those of "farmer's lung" in cattle. Furthermore, precipitins to *M. faeni* and other organisms found in moldy hay are absent from the sera of cattle affected by fog fever, although they are frequently present in the sera of adult cattle exposed to hay (7,45). There is no known association between fog fever and "farmer's lung" in cattle.

Occasional case reports have implicated exposure to other moldy feeds, including silage and cornstalks, in incidents of respiratory disease (25,48). Unfortunately, it has not been possible, as yet, to get sufficient data to decide whether these are the result of extrinsic allergic alveolitis, plant toxins, a food contaminant, or as yet unknown factors. There is a great need for detailed research into this area of veterinary medicine and the practitioner should be encouraged to follow up these unusual cases. In this respect, it is perhaps important to point out that while interstitial emphysema is sometimes a dramatic lung lesion at necropsy, it can be produced as an agonal change in animals dying without respiratory disease. Pulmonary edema and congestion may also be seen without underlying respiratory disease, as in left heart failure for example. Undue emphasis should not be placed, therefore, on the occurrence of interstitial emphysema and pulmonary edema, particularly if other organs are not examined in detail. We agree

with Wilkie (48) that the presence of edema and emphysema by themselves do not permit an etiological diagnosis. One should resist the natural tendency to apply an unjustified specific diagnosis such as fog fever or farmer's lung to these cases, although this may be very tempting in some situations, for example when other animals in the herd have clinical or serological evidence of exposure to moldy hay. After all, a cow with farmer's lung will have typical lung lesions of this disease even if it is killed by lightning in the middle of summer and this may mislead the unwary histopathologist!

2. *Milk allergy*

The name "milk allergy" has been applied to a sudden-onset urticarial condition which is sometimes accompanied by respiratory distress, the result of severe pulmonary edema and hyaline membranes, congestion, intra-alveolar hemorrhage and interstitial emphysema (7,10). Cases, a minority of which may terminate fatally, have been encountered in milking cows nearing the end of lactation or subjected to sudden alterations in milking routine. The disease has been found to be an autoallergy, in which the animal becomes sensitive to components of its own milk, principally alpha casein, and the disease has been reproduced experimentally (10).

B. Diseases of unknown etiology

1. *Fog fever and acute bovine pulmonary emphysema*

In Britain, fog fever is an acute respiratory distress syndrome with minimal coughing which occurs in adult (older than two years) beef-type cattle shortly after a change to better, often lush, pasture usually in the autumn months from August to November. The pulmonary lesions, which are obligatory for diagnosis but not pathognomonic, include congestion, edema and hyaline membranes, interstitial emphysema and alveolar epithelial hyperplasia of type 2 pneumonocytes (45). The word "fog" has epidemiological connotations in that the condition is often seen in cattle grazing "fog" pastures (i.e., aftermath, the regrowth after a hay or silage cut); there is no association with atmospheric conditions.

In the USA and Canada, a disease closely resembling fog fever has been recorded many times in adult beef cattle moved from dry summer range onto lush pastures in the fall and occasionally also in the spring (3,33). Many different names have been applied to this syndrome, but acute bovine pulmonary emphysema (ABPE) has been the most widely and frequently used (33). Unfortunately, the term ABPE, like the name fog fever in Britain, has also been applied to a farrago of different respiratory conditions in which interstitial emphysema has been detected clinically or at necropsy. We believe that the terms fog fever and ABPE should be reserved for the pasture-associated diseases alone and this usage is adopted in this article.

With the realisation that fog fever/ABPE is a clear-cut disease entity, it has been possible to consider the question of its etiology in a more rational fashion. Both inhaled and ingested allergens have been suggested as causes of fog fever/ABPE by workers favoring a hypersensitivity theory of etiology, but there is little evidence at the present time to support this view of the origin of the pasture-associated syndrome (7,43). Most recent work has concentrated on the possible role of pasture constituents, since a proliferative alveolitis closely resembling fog fever and ABPE has been produced in cattle given oral doses of the amino acid L-tryptophan, or its metabolites 3 methylindole and indole-acetic acid (see below). A clear demonstration that L-tryptophan in lush grazing is the particular factor involved is still lacking. However, in a recent experiment, fog fever was produced in cattle subjected to abrupt change to lush, lungworm-free pasture in September. Sufficient L-tryptophan was found in the pasture to provide the known toxic dose after only 2-3 days grazing, and 3 methylindole was detected in rumen liquor of affected animals in amounts corresponding to those developing after experimental, oral administration of toxic amounts of L-tryptophan (44). A field trial in the western USA also demonstrated that 3 methylindole was present in ruminal fluid of cattle curing the onset of naturally-occurring ABPE (47).

2. *Diffuse fibrosing alveolitis*

Scadding and Hinson (39) gave the name diffuse fibrosing alveolitis (DFA) to a syndrome of man of unknown and possibly multiple causation, characterised pathologically by a diffuse inflammatory process in the lung beyond the terminal bronchiole. The essential features of this were cellular thickening of the alveolar walls showing a tendency to fibrosis and the presence of large mononuclear cells, presumably of alveolar origin, within the alveolar spaces. This type of pulmonary disease has been discovered more frequently in recent years and among the additional lesions that have been described are alveolar epithelial hyperplasia and metaplasia. Other synonyms for the disease include: diffuse interstitial pulmonary disease, diffuse interstitial pulmonary fibrosis and Hamman-Rich syndrome.

A chronic pulmonary disease characterized by lesions closely resembling those of DFA in man has been recognized in Switzerland (31), Germany (19), Britain (45) and elsewhere in housed and grazing cattle of both beef and dairy breeds. The etiology of DFA in cattle is unknown at present. The presence of precipitating antibodies to *M. faeni* in the sera of some cases suggest that some of these, perhaps the majority, are the result of longstanding extrinsic allergic alveolitis, but the etiology of the remaining portion is obscure. DFA-like conditions in cattle are often assumed to be chronic stages of fog fever or ABPE, but the relationship, if any, is unclear. In Britain, a recent field study of respiratory problems in adult cattle failed to reveal any connection (5,7). In particular, it was not possible to demonstrate that acute signs of fog fever (diagnosed according to the

criteria outlined above) were followed by a chronic illness in any animal, although it was clear that acute exacerbations of DFA were often mistaken for fog fever (5).

3. *Atypical interstitial pneumonia of immature cattle*

Jarrett (26), in Scotland, described an atypical pneumonia of calves in which the pulmonary lesions included interstitial emphysema, edema and hyaline membranes, and alveolar epithelial hyperplasia. A small number of similar cases have since been reported in Britain and an apparently identical acute respiratory syndrome is a well-recognized problem in immature animals in feedlots in North America (30), South Africa (17) and elsewhere, where it is usually referred to as AIP. The etiology of this syndrome is not known and it is quite possible that a number of causes will be discovered and that a number of distinct entities will be identified in different parts of the world. Exposure to moldy feedstuffs was suggested as a cause in South Africa (17). Others believe respiratory syncitial virus infection is responsible. Canadian workers have recently hypothesized that hypersensitivity might be involved, since the pulmonary lesions in their cases were thought to resemble those of a type III pulmonary hypersensitivity reaction, as in extrinsic allergic alveolitis to *M. faeni* (40). If this were so, a substantial proportion of clinical cases might be expected to have serological precipitins to *M. faeni* or other antigens of moldy hay, but we are unaware of any published studies of this aspect of the disease.

Ten years ago, it appeared that AIP in adult cattle was one disease. Subsequent studies in several countries have demonstrated that this is not the case. Unfortunately, little detailed work has been done to analyze the syndromes grouped as AIP in younger animals. Until more information is available, we feel it is only possible to give a general term like "AIP of immature cattle" to the acute respiratory diseases of this age group that are characterized by pulmonary edema, congestion, hyaline membranes, epithelial hyperplasia and interstitial emphysema (although we would carefully distinguish specific entities such as parasitic bronchitis).

C. Parasitic diseases

1. *Dictyocaulus viviparus*

The clinical signs, epidemiology and pathology of both naturally-occurring and experimentally-induced parasitic bronchitis have been fully described (26) and a clear understanding of these is essential for any discussion of AIP. In our European experience, it cannot be emphasized too strongly that this disease should be the first and probably only consideration in diagnosis when acute respiratory distress and coughing occur in groups of immature, unvaccinated calves at pasture in the autumn. In fact, no other condition capable of causing these signs in this class of stock has yet been described in Britain.

The acute clinical signs of parasitic bronchitis are often attributed to other causes, such as fog fever (6), and this is perhaps not surprising since interstitial emphysema, pulmonary edema, hyaline membranes and alveolar epithelial hyperplasia are lesions that may complicate any of the stages of a primary *D. viviparus* infestation (26). In fact, *D. viviparus* infection in cattle is a well-known problem and if it has been established that a respiratory condition is the result of parasitic bronchitis it should not be necessary to introduce another term, such as AIP, into the diagnosis, as though to imply that the signs in question were not solely the result of lungworm infestation. It is particularly unfortunate that the respiratory signs of parasitic bronchitis are so frequently attributed to other causes, since parasitic bronchitis is easy to diagnose, easy to treat and easy to prevent by vaccination (Dictol-irradiated lungworm vaccine, Allen and Hanbury Ltd., England).

2. *Ascaris lumbricoides*

Parasitic bronchitis and pneumonia in cattle is usually the result of *D. viviparus* infection, but interstitial emphysema and pulmonary edema are among the lesions recorded in the lungs of animals infected naturally or experimentally with aberrant parasites such as *A. lumbricoides* (2,34). Regrettably, such cases have often been confused with fog fever or ABPE.

D. Plant poisoning

1. *Ipomoea batatas* (sweet potato)

Incidents of respiratory disease have been reported on several occasions in housed or pastured cattle receiving supplementary feeds of moldy sweet potatoes. Respiratory distress may develop as early as one day after eating infected tubers and death may occur two to five days later. Interstitial emphysema, pulmonary edema, hyaline membranes and alveolar epithelial hyperplasia have been noted at necropsy (37,49).

The condition is believed to be caused by several abnormal metabolites produced by sweet potatoes in response to infection with the fungus *Fusarium solani (javanicum).* Among these toxins are ipomeamarone, ipomeamaranol and a group of substances collectively known as the "lung edema factor" (49). These specific compounds are lethal to mice when given orally or intraperitoneally (49); sweet potato broth cultures infected with *F. solani* have been used to reproduce respiratory disease in cattle (37). It is important to note that the moldy sweet potato-induced disease is a form of poisoning and not a form of extrinsic allergic alveolitis comparable to the respiratory disease that follows exposure to moldy hay.

2. *Zieria arborescens* (stinkwood)

A fatal acute respiratory syndrome in cattle which have eaten leaves of the stinkwood plant *(Zieria arborescens)* has been described in Tasmania. The interval between initial contact with stinkwood and death is about two weeks and interstitial emphysema,

pulmonary edema, hyaline membranes and alveolar epithelial hyperplasia can be discovered at necropsy. The precise toxic compound is not known, but there have been preliminary reports of the isolation of an oil from the leaves which can reproduce these same lesions in rabbits (35).

3. *Perilla frutescens* (purple mint)

Peterson (38) associated respiratory signs and deaths in cattle with ingestions of the leaves and seeds of *Perilla frutescens* (purple mint), a common weed in Arkansas. Attempts were made to reproduce the disease experimentally, by placing adult cattle on *Perilla*-rich pastures, but the results were equivocal, since the clinical signs which developed may well have been the result of sudden access to better grazing–a method which has been used to produce ABPE experimentally. However, just recently it has been discovered that *P. frutescens* contains pneumotoxic "perilla ketone," which is believed capable of producing pulmonary edema and pleural effusion in mice, rats, cattle and sheep (50) and possibly in other species. It seems likely that this weed causes respiratory disease in grazing cattle in certain areas.

4. *Brassicae*

Acute respiratory disease in cattle feeding on rape or kale has been reported in Canada (41) and in Britain comparable signs have been described in hungry adult beef cattle moved from bare pasture to rape or turnip-tops grown for forage (43). At the moment, it is convenient to regard these *Brassica*-associated incidents as being identical to fog fever or ABPE, but it is possible that specific toxic factors will be identified in *Brassicae*, as has been the case with moldy sweet potatoes and *P. frutescens*.

5. *Other Plants*

Hyslop (25) noted reports incriminating the sedge *Carex rostrata* and red clover contaminated by the fungus *Rhizoctonia leguminicola* in the production of bovine pulmonary emphysema but there is little information available.

D. Diseases due to exposure to irritant gases and fumes

1. *Nitrogen dioxide*

Acute exposure of agricultural workers to high concentrations of nitrogen dioxide released from grain or grass silos is an infrequent occupational hazard which invariably results in respiratory disease. In such instances of "silo-filler's disease," pulmonary congestion and edema are the main initial lesions and these may be followed by obliterative bronchiolitis and even progressive interstitial pulmonary fibrosis (20).

There have been reports of apparent nitrogen dioxide poisoning in cattle, but the diagnosis, in all instances, has been conjectural, since there has been no demonstration of nitrogen dioxide in the inhaled air or even methemoglobin in the blood. In two incidents, the respiratory signs were in cattle exposed to corn silage under circumstances believed to be comparable to those of nitrogen dioxide poisoning of man (9,22). However, it has also been suggested that nitrates in plant feedstuffs could release nitrogen dioxide gas during fermentation in the rumen and that subsequent inhalation of nitrogen dioxide in eructated rumen gas could cause interstitial emphysema, pulmonary edema and proliferation of bronchiolar and alveolar epithelial cells. It was considered possible that this might be relevant to the pathogenesis of ABPE (42). These lesions could be produced in cattle forced to inhale nitrogen dioxide gas, but were not found when the gas was introduced into the rumen by a cannula (14). Furthermore, nitrogen dioxide gas could not be demonstrated in the rumen gas of cattle subjected to change from dry to succulent pasture (24) or in animals affected by or recovering from ABPE. Since Cutlip (14) has stated that nitrogen dioxide of rumen origin is probably not involved in respiratory disease in cattle and Blood (4) has also pointed out that circumstances similar to those which cause silo-filler's disease appear to be unlikely amongst cattle, the inescapable conclusion is that inhalation of nitrogen dioxide has very little relevance to bovine pulmonary problems. Clearly, further work is necessary to discover the pathogenesis of the syndromes that have been outlined in cattle housed near silos and, in particular, to distinguish these from extrinsic allergic alveolitis.

2. *Smog*

Acute respiratory distress and deaths were noted in over-fat cattle at the Smithfield Fatstock Show (London) in 1952 and 1963, when there was dense atmospheric fog or smog at the time of the exhibitions. There was considerable coverage in newspaper reports but, regrettably, very few facts appeared in the scientific press. The curious coincidence of acute pulmonary embarrassment and fog has led many people to link the two and it has even been stated that the London fog may be a cause of fog fever. This view is quite erroneous (7).

3. *Zinc oxide fumes*

Congestion and hemorrhage in the trachea, interstitial emphysema and interlobular and pulmonary edema have been noted at necropsy in cattle exposed to fumes of zinc oxide, derived from oxyacetylene cutting and arc welding of galvanised pipe (23).

4. *Chlorine and hydrogen sulfide*

MacDonald, et al. (32), have chronicled the consequences of an accidental release of chlorine gas involving cattle. Emphysema, edema and hyaline membranes were among the lesions discovered post mortem, but the evidence that these were the result of exposure to chlorine was not convincing.

Hydrogen sulfide can be found in the rumen gasses of cattle placed on succulent pastures and it was once considered that inhalation of this gas might be important in the pathogenesis of ABPE (24). Experimental exposure of cattle to hydrogen sulfide did not produce

significant pulmonary lesions even after prolonged exposure to levels regarded as poisonous to man (24).

F. Experimentally-induced syndromes

1. *Systemic anaphylaxis*

Dyspnea, apnea, pulmonary hypertension and systemic hypotension are the main features of experimental acute systemic anaphylaxis in cattle: these signs begin within two minutes of antigen injection and continue until death (usually within 15 minutes of injection) or gradually subside over the next two hours in survivors (1,18). Intra-alveolar hemorrhage, pulmonary congestion, edema and interstitial emphysema are found at necropsy. Alveolar epithelial hyperplasia has only been described as a focal lesion in calves challenged by aerosol (16). Hyaline membranes have been recorded in one animal that survived for 30 hours after challenge (1), but interpretation of the pulmonary responses was made more difficult in this series because the animals were not shielded from infection with *D. viviparus* and approximately 25 per cent of the experimental animals had residual pulmonary lesions of parasitic bronchitis.

Over the years, there have been repeated suggestions that anaphylaxis or hypersensitivity could be the underlying cause of fog fever or ABPE, but there is little evidence to support the view that these factors are involved in the pasture-associated syndrome (7,43). In all probability, the bulk of these suggestions stemmed from the apparent clinical similarity between fog fever/ABPE and well-known anaphylactic reactions, such as those to vaccines and drugs and to larvae of *Hypoderma lineatum* and *H. bovis*–reactions that were recognized long before the immunological basis of type 1 hypersensitivity was established (43). Apart from these, the only well-recognized naturally-occurring condition which closely resembles experimental systemic anaphylaxis is milk allergy.

2. *Bordetella pertussis* infusion

Intravenous infusion of *B. pertussis* suspension into five calves was followed by marked hematological changes and an acute respiratory distress syndrome (5). Severe diffuse alveolar epithelial hyperplasia with pulmonary edema, hyaline membranes and interstitial emphysema was found in one of the five animals at necropsy. The pathogenesis of this is unknown.

3. *Administration of indolic compounds*

A few days after oral administration of the amino acid DL- or L-tryptophan to cattle a respiratory disease may develop which is characterized mainly by pulmonary congestion, edema, hyaline membranes, interstitial emphysema, proliferation of alveolar epithelial cells and infiltration by neutrophils, eosinophils and macrophages (11,15). L-tryptophan, the active isomer, is first broken down in the rumen to indoleacetic acid and then decarboxylated by a *Lactobacillus* species to yield 3 methylindole (3MI), the pneumotoxic derivative (12,13). Tryptamine, indole and other tryptophan metabolites may also be produced in the rumen but have not been found to cause lung disease (28). The only route of metabolism that has been shown to produce pulmonary lesions is that which involves conversion to 3MI. Oral or intravenous dosage with 3MI results in pulmonary lesions similar, but more acute in onset, to those following L-tryptophan administration. The pathogenesis of the pulmonary lesions induced by 3MI is still not fully known, but it appears that 3MI in the blood must first be metabolized by the mixed function oxidase system (responsible for degradation of xenobiotics in liver, lung and elsewhere) before pneumotoxicity is seen. Inhibition or potentiation of the mixed function oxidase system will respectively abolish or enhance the pulmonary lesions produced by 3MI (13).

As mentioned above, there is much evidence to support the view that ingestion of L-tryptophan and its ruminal conversion to 3MI is the cause of fog fever/ABPE. Accordingly, considerable research has been conducted into therapy or prevention of tryptophan-induced disease as a model of the field condition. None of the following drugs, when given before an oral dose of 3MI, appeared to influence the clinical outcome in that most animals became sick or died: mepyramine maleate, acetylsalicylic acid, chloramphenicol, cortisone, diethylcarbamazine citrate, sodium meclofenamate, disodium cromoglycate (unpublished results; 8). In contrast, pretreatment with piperonyl butoxide, an inhibitor of mixed function oxidase activity, prevented 3MI-induced respiratory disease (13). These observations indicated that prevention of 3MI-induced pneumotoxicity appeared more promising than therapeutic treatment of the ensuing pulmonary lesions. Laboratory studies had demonstrated that *in vitro* production of 3MI by ruminal microorganisms could be diminished by antibiotic treatment (13,21). A trial was subsequently conducted with the most promising of these drugs–monensin (Rumensin, Elanco). Adult Hereford cows pretreated with monensin and then dosed with L-tryptophan did not develop clinical signs or lesions of ABPE. Cows in a similar group given L-tryptophan without monensin became sick or died (21). Pretreatment with monensin thus prevented tryptophan-induced ABPE, apparently by diminishing ruminal 3MI production. Further studies are planned to determine whether monensin will also prevent naturally-occurring fog fever/ABPE, an important step in determining if L-tryptophan ingestion is truly the cause of this syndrome. It is worth noting here that monensin is widely used as a growth promoter in feedlot cattle. Those who believe that AIP in immature cattle in feedlots is caused by L-tryptophan ingestion may expect a decrease in disease after a change to monensin-supplemented rations. It will be very interesting to see whether this proves to be the case.

Discussion

The concept of AIP was useful when it was first proposed because it drew attention to a number of increasingly important clinical entities that had some features in common. Unfortunately, the designation AIP and other more specific names, including fog fever and ABPE, have often been misused or regarded as synonyms and this has led to many misunderstandings, particularly amongst those with no experience of the problems. As a result, AIP is now being applied indiscriminately as an appellation for virtually all bovine respiratory disease other than specific infections and neoplasia. The temptation to diagnose pneumonia caused by specific agents (lungworms, migrating ascarid larvae, and viruses, for example) as AIP is perhaps understandable, since the same biochemical mediators of inflammation may ultimately be shown to be involved in all, but it is surely regrettable if it means that specific therapeutic or preventative measures are not adopted–and in our experience this has so often been the case.

Others have also proposed the division of AIP into separate syndromes. The most recent suggestion (40) categorised cases of AIP as either "dietary" (based on epidemiological observations) or "hypersensitivity atypical interstitial pneumonia" (based on histopathological changes). The problem with this approach is that the implication of both diet and hypersensitivity is only a hypothesis and until there is adequate proof that either is involved it would seem unwise to adopt this as the basis of a new classification. The two mechanisms are not, in fact, mutually exclusive, since it is known that dietary change may be quickly followed by the development of hypersensitivity to antigens in the new feedstuffs (46). In Canada, Wilkie (48) has recently pointed out the futility of etiological classification on the basis of morphology in acute and chronic bovine interstitial pneumonias, a point we have been making in Europe for the last ten years. However, we would go further in stressing the futility of etiological diagnosis based solely on morphology, serology or retrospective field studies in the investigation of bovine respiratory disorders. Unfortunately, this is often the case in veterinary medicine, perhaps because there are so few multidisciplinary specialist groups capable of investigating respiratory disease outbreaks in detail at the time they occur and the lone investigator must attempt to assess all the aspects without the advice of more experienced colleagues.

Table 1

An Index of Syndromes Included in Atypical Interstitial Pneumonia of Cattle

A. Hypersensitivity diseases
   1. Extrinsic allergic alveolitis (farmer's lung)
   2. Milk allergy

B. Diseases of unknown etiology
   1. Fog fever and acute bovine pulmonary emphysema
   2. Diffuse fibrosing alveolitis
   3. Atypical interstitial pneumonia of calves

C. Parasitic diseases
   1. *Dictyocaulus viviparus*
   2. *Ascaris lumbricoides*

D. Plant poisoning
   1. *Ipomoea batatas* (sweet potato)
   2. *Zieria arborescens* (stinkwood)
   3. *Perilla frutescens* (purple mint)
   4. *Brassicae*
   5. Other plants

E. Exposure to irritant gases and fumes
   1. Nitrogen dioxide
   2. Smog
   3. Zinc oxide
   4. Chlorine and hydrogen sulfide

F. Experimentally-induced syndromes
   1. Systemic anaphylaxis
   2. *Bordetella pertussis* infusion
   3. Administration of indolic compounds

We believe that the heterogeneous group AIP can be divided into a number of distinct syndromes, which have been considered above in six separate categories (Table 1). These syndromes may be defined in different ways–on a morbid-anatomical basis (e.g., DFA), on an etiological basis (e.g., milk allergy), or on a combined clinical, epidemiological and morbid-anatomical basis (e.g., fog fever, ABPE). In practice, cases may be encountered which are of unknown etiology and in which clinical, epidemiological or pathological findings may not be adequately determined. There is a need for a general term to describe such cattle with acute respiratory signs resulting from pulmonary edema, hyaline membranes, interstitial emphysema and alveolar epithelial hyperplasia, since these lesions are not pathognomonic although their presence may be obligatory for diagnosis of certain conditions. We suggest that this need could be met by the nonspecific term "acute respiratory distress syndrome" (ARDS), which may be defined as any sudden onset respiratory condition with dyspnea that is the result of any combination of the following pulmonary lesions: 1. congestion and edema, 2. hyaline membranes, 3. alveolar epithelial hyperplasia, and 4. interstitial emphysema, other specific causes of respiratory distress, such as parasitic bronchitis, having been excluded. This essentially morbid-anatomical diagnosis may be refined further on an etiological or clinical basis if more information is available; for example, an ARDS occurring in adult, beef-type cattle shortly after a change of pasture in the autumn would be specifically diagnosed as fog fever. In the absence of further facts, the diagnosis would stand alone as "ARDS associated with . . . ." This would avoid any etiological implications and would render terms such as "fog fever-like" or "AIP-like" unnecessary. It would also avoid the applications of the term atypical interstital pneumonia to pulmonary lesions which are not atypical and which do not conform readily to most definitions of interstitial pneumonia.

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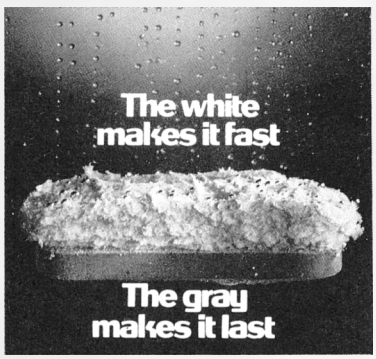

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