Some Current Research on the Emphysema-Adenomatosis Complex of Cattle

*E. O. Dickinson, *D.V.M., Ph.D.*
R. C. Piper, *D.V.M., Ph.D.*

In 1830, French veterinarians described the occurrence of pulmonary emphysema in dairy cattle when they were moved to low, wet meadows containing abundant regrowth (1). There has been increased awareness that this disease is one of major economic significance to the livestock industry in many countries, including the United States. Despite evidence that the disease has been known for over a century and has had considerable economic significance, it remains as a perplexing problem because factors relating to the cause and pathogenesis are unknown. These unanswered questions had led to considerable confusion, frustration and disappointment on the part of both livestock owners and veterinarians who have encountered the problem in cattle. Attempts at control and treatment must be directed toward relief of clinical signs when basic mechanisms are unknown. This approach is not often successful.

In August of 1965, an observation was made which led to productive experimentation in the study of some of the problems regarding this disease. This unexpected event came about as a result of studies being performed on the activities of various liver enzymes in cattle and sheep (2). Following oral administration of large doses of the amino acid D, L-tryptophan, some of the cattle developed acute respiratory distress characterized by polypnea and dyspnea and some of the animals died. At necropsy it was observed that the lesions were strikingly similar to those observed in the naturally occurring disease associated with the grazing of cattle on certain forage crops, sudden change of ration, or the feeding of moldy feeds. The observation that tryptophan had induced the disease was interesting, particularly because this amino acid has been shown to serve as a precusor for several important biological compounds and has been reported in variable quantities in many feeds and forages (3,4). Subsequent research efforts have been directed toward a characterization of the experimental disease and attempts to determine if tryptophan or related compounds might be the agents in the inciting feeds or forages that are responsible for the disease under natural conditions.

Research results have demonstrated that acute respiratory disease can be induced in cattle by oral administration of either tryptophan or a closely related compound, indole-3-acetic acid (5). These inducing agents are given as an aqueous slurry by way of stomach tube directly into the rumen. The dosage levels that most consistently induce the disease in mature cattle are 0.6 to 0.7 grams per kilogram of body weight.

The clinical severity of the respiratory response is variable. Some animals get a very severe response that often leads to death. Others have a mild to moderate transitory response and then apparently recover, whereas still others have little or no reaction following administration of the agents. If signs occur, progressive respiratory decompensation generally begins from one to five days after administration of the inducing agents. The most obvious are signs of increased rate of respiration accompanied by increasing evidence of labored respiration. Dyspnea is most marked at expiration and the more severely affected animals often have an expiratory grunt and stand with the head and neck extended. Cyanosis becomes evident in the terminal stages and death is apparently due to anoxia. Heart rate increases concurrently with the peak of respiratory distress. Temperature generally remains normal or only slightly elevated and the animals often continue to eat until the advanced stages of the disease.

Significant lesions at necropsy are observed in the thoracic cavity; changes in other parts of the body are those associated with terminal hypoxia and congestion. The predominant gross change in the early stages is severe pulmonary edema. All areas of the lung contain considerable quantities of gelatinous fluid which causes considerable distension of interlobular, subpleural, and periarterial tissues. Intersititial emphysema becomes a more prominent feature in animals that die or are killed at later stages of the disease, i.e. beyond 72 hours

**Department of Veterinary Pathology, Washington State University, Pullman, Washington 99163.*
Scientific Paper No. 3723, Washington Agricultural Experimental Stations, Pullman, Project No. 2011.

after administration of the inducing agents (Figure 1). The lungs are large, heavy, very wet, and contain froth in the bronchial tree. Microscopic examination reveals severe pulmonary edema in the early stages and then an increasing tendency for thickening of alveolar septa, formation of dense hyaline membranes, and swelling and proliferation of alveolar lining cells (Figure 2).

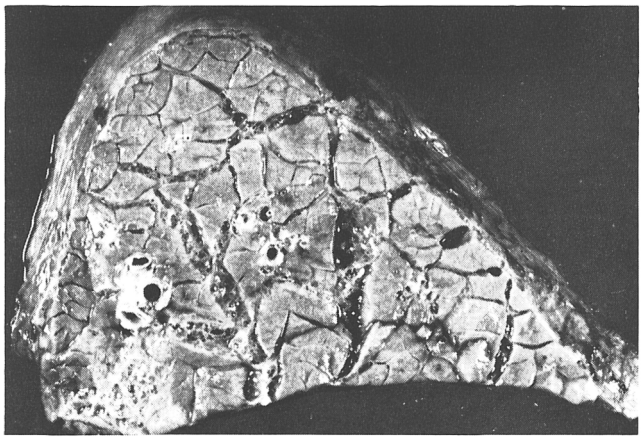

Figure 1. Cross-section of the lung of a cow that died after receiving D, L-tryptophan.

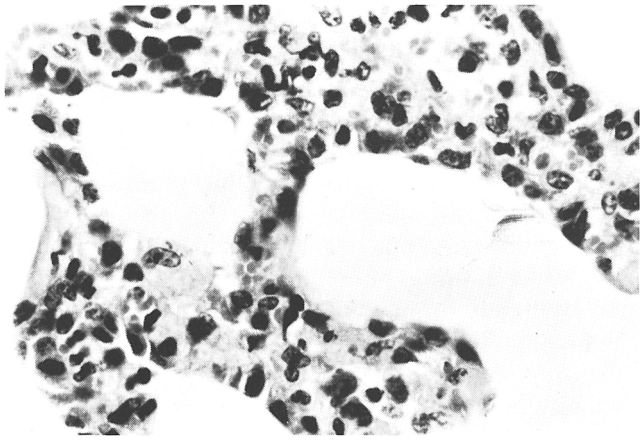

Figure 2. Photomicrograph of the lung changes induced by D, L-tryptophan. Note the thickened alveolar septa, hyaline membrances, and swollen lining cells. H & E. 560X.

The findings of the experimental trials indicate that the onset, course, signs, and lesions of the experimental disease are very similar to those reported for the natural disease. Other interesting correlations between the experimental and natural diseases include the following: (1) The experimental disease has been consistently reproduced only in cattle and the natural disease is known only in cattle. (2) There appears to be a variation in breed susceptibility in the experimental disease that is similar to that observed in the natural disease (6). (3) Older cattle seem to be more susceptible to the effects of the inducing agents. The observations to date suggest that the experimental and natural forms are, in fact, the same disease.

A critical question to ask is whether the experimental procedures can be logically or practically applied to natural conditions. It does seem possible. The association with ration, change of ration, or feeding moldy feeds has been well established in the natural disease. The experimental procedure has a definite dietary relationship because tryptophan, one of the inducing agents used, is a naturally occurring amino acid present in a variety of foods. Indole-3-acetic acid has been regarded as a "plant hormone" or plant growth promoting substance and its activity has been demonstrated in rapidly growing plants of a variety of types. Also, both of the inducing agents are sometimes synthesized by molds (4). Although the absolute identity of the natural and experimental diseases has not been demonstrated, the possibility is suggested that tryptophan, indole-3-acetic acid, or a closely related compound are the causative agent(s) in inciting feeds under natural conditions.

Further studies and analysis of inciting forages for these compounds will be necessary to establish the correlation. Also, additional studies of the pathogenesis of the experimental disease are necessary because at this time it is not known what occurs between the time the inciting agents are administered and the time lung changes begin. When these questions are answered and the mechanisms of the experimental disease are more clearly delineated, a better understanding of the mechanisms of the natural disease should become apparent. It is anticipated that answers to the above questions will allow a more rational approach to the control, prevention and treatment of the natural disease of cattle.

References

1. Delaland, Lecog, Mazure, and Vigney: Obstruction du feuillet, observee sur les vaches laitieres, vulgairement appelee dans nos campagnes empanchure, indegestion des regains. Memoires de la Societe Veterinaire du Calvados et de la Mancha, 1, (1830): 109, 135; cited by Foucher, J.; L'emphyseme des regains dans le Marais Poitevin; essai de traitement. Thesis 45, Ecole Natl. Vet., Alfort, France, (1960).
2. Johnson, R. J. and Dyer, I. A.: Effects of Orally Administered Tryptophan on Tryptophan Pyrrolase Activity in Ovine and Bovine. Life Sci., 5, (1966): 1121-1124.
3. Block, R. J. and Weiss, K. W.: Amino Acid Handbook. Methods and Results of Protein Analysis. Charles C. Thomas, Springfield, Ill., 1956.
4. Meister, A.: Biochemistry of the Amino Acids, Vol. 11, 2nd ed. Academic Press, New York, N.Y., 1965.
5. Dickinson, E. O.: The Effects of Tryptophan on Bovine Lungs. Thesis. Wash. State Univ., Pullman, Washington, (1970).
6. Monlux, W. S., Cutlip, R. C., and Estes, P. C.: Breed Susceptibility to Tryptophan-Induced Pulmonary Adenomatosis in Cattle. Cornell Vet., 60, (1970): 547-551.