PATHOLOGY AND PATHOGENESIS OF THE COMMON DISEASES OF THE RESPIRATORY TRACT OF CATTLE

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THE FOLLOWING IS A BRIEF DISCUSSION of the major lesions which determine the extent and severity of illness in some diseases of the respiratory tract of cattle and a discussion of pathogenetic mechanisms associated with pasteurellosis.

Infectious bovine rhinotracheitis (IBR) may cause a serous or catarrhal exudation in the upper respiratory tract, trachea and bronchi from which an animal is likely to recover. However, if the virus causes more severe damage, necrosis and ulceration of the epithelium may occur. The necrosis begins in small focal areas and appears as white foci against a hyperemic background. The outcome of the disease will be determined by the amount of necrosis which occurs. If the foci become confluent most of the epithelial lining of the respiratory tract may be ulcerated and the surface may become a mass of necrotic debris and inflammatory exudate. Secondary bacterial infection may occur and large amounts of exudate will accumulate in the air passages and cause respiratory insufficiency and secondary pneumonia. The development and extent of lesions is probably related to the immune state of the animal and the virulence of the virus.

Enzootic pneumonia of calves is a clinical entity which can be caused by several agents. The lesions produced is usually a bronchopneumonia or sometimes an interstitial pneumonia; there is some similarity in the gross lesions caused by different agents, particularly in the chronic stages. In the very acute stages, there are histologically recognizable differences with different agents. The main lesion caused is usually a bronchiolitis in the small and medium sized bronchioles. As with IBR the severity of the disease and the eventual outcome will be determined by the degree of damage to the epithelial lining of the bronchioles. If the epithelium becomes ulcerated, the bronchioles are likely to become plugged by necrotic debris and inflammatory exudate. These lesions may be secondarily infected and lead to mucopurulent bronchiolitis or abscesses. In addition there is a danger of organization of the exudate in the bronchioles from the connective tissue below the ulcerated epithelium. Permanent organized plugs of exudate may then remain in the bronchioles (bronchiolitis obliterans) and cause persistent respiratory insufficiency.

The histological lesions of parainfluenza three (PI-3) virus are recognizable in the acute stages by the formation of inclusion bodies in the bronchial epithelium and in characteristic giant cells which form in the alveoli. The lesions of adenoviral induced pneumonia are also recognizable by inclusion bodies in the nuclei of the bronchial epithelium and also in cells in the alveoli. Lesions caused by chlamydia agents are characterized by exudation of large numbers of polymorphonuclear leukocytes primarily into bronchioles but spreading into alveoli. The lesions produced by mycoplasma, rhinovirus, reovirus and enterovirus are not pathologically characteristic.

Some animals with enzootic pneumonia may die in the acute stages and characteristic lesions can be recognized, but most do not die with the acute disease; the eventual outcome is either one, or a combination, of bronchopneumonia, bronchiolitis obliterans, bronchiectasis and abscess formation. Lesions suggestive of the original cause can not usually be recognized in these older lesions nor can the original agent be isolated. The extent of damage in the lung will relate to the immune status of the host and the virulence of the agent.

The terminal lesions of pneumonic pasteurellosis or "shipping fever" are well known. Extensive anteroventral portions of the lungs are dark red, swollen, hard and the dark areas are usually covered by varying amounts of fibrin on the pleural surface. On the cut surface fibrin is also evident between lobules. As the disease progresses, discreetly demarcated small irregular shaped pale areas of coagulation necrosis develop in the parenchyma. *Pasteurella hemolytica* is usually isolated in pure culture in acute untreated cases; however, *Pasteurella multocida* may be found in some cases along with *Pasteurella hemolytica*. Pathologists and clinicians would not differ on the interpretation that the final lesions of pas-

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teurellosis are those of an acute fulminating bacterial pneumonia. There is however, considerable discussion about the agents and mechanisms involved in the early stages of the disease. There has not been a detailed pathological or microbiological investigation of the lung lesions in the early stages of the disease in field cases in order to piece together the pathogenesis or to determine whether or not the early lesions have common features. The immunological status of the host is probably highly significant in terms of the development and extent of severe lesions. There are likely to be differences in lesions based on whether or not the host has been immunized, parenterally or by aerosol, or has encountered a natural infection, or is having a first encounter with the etiological agents.

It has generally been assumed in the veterinary literature that PI-3 virus predisposes and is an integral part of the early stages of pneumonic pasteurellosis. This impression has arisen from circumstantial evidence which indicates that PI-3 infection occurs in cattle which are congregated for shipment, much in the same way that viral respiratory diseases occur in military recruits shortly after they are congregated. There is however, minimal evidence from pathological or microbiological examination of pulmonary lesions to support this contention. Extensive parenteral immunization against either *Pasteurella* or PI-3 virus has not reduced the significance of the disease. Efforts at immunization have been empirical because the pathogenesis of the disease is not known in sufficient detail to determine where to concentrate efforts at control procedures which are economically acceptable to the cattle producer.

Our laboratory has been investigating the possible role of PI-3 virus in the development of pasteurellosis and we have investigated the literature on bacterial-viral interaction in the lungs, most of which pertains to laboratory animals. The general assumption in the literature has been that when a virus is influential in the early stages of a bacterial pneumonia the effect arises from the destruction or impairment of the function of the bronchial epithelium and thus inhibition of the mucociliary clearance mechanism of the lung (6). Bacteria then remain in the lung, and are allowed to accumulate and proliferate to cause inflammation. Recent evidence indicates that this interpretation of the effect of a virus is probably not correct. Rather, evidence has now been presented to indicate that the virus interferes with the phagocytic and/or bactericidal ability of the alveolar macrophages and that the lesions in the bronchioles are not the main problem (2). The mechanism by which a virus interferes with the uptake or the disposal of bacteria in the macrophages has not been clarified and is under investigation. Normally, the alveolar macrophages dispose of bacteria which enter the lower respiratory tract very efficiently. This mechanism which is termed "pulmonary clearance" usually is highly efficient and 80% of a given aerosol dose of bacteria will be removed in four hours and about 95% in eight hours (4, 5, 7).

If the viral agent is given experimentally the peak of virus production occurs at about three days after inoculation, but the inhibition of bactericidal activity occurs at about seven days (3). The bronchial lesions tend to develop at about seven days which is also the time when serum antibody develops. The following circumstances indicate some means of influencing the bacterial-viral interaction (2).

a) If the animals have been immunized via aerosol with the homologous bacterial species prior to inoculation of the virus, the clearance of a bacterial challenge after viral infection is not impaired and the virus has no effect.

b) If the animals have been immunized via aerosol with the virus prior to exposure to the homologous virus and then challenged with a bacterial aerosol, there is little effect on clearance.

c) Bacterial immunization via aerosol prior to a second exposure to the homologous bacterial strain increases the rate of clearance of the bacterial challenge.

Practical considerations for methods of immunization have arisen from this type of research. Calves which had a serum antibody titre to *Pasteurella hemolytica* and were then exposed to PI-3 virus via aerosol did not have impaired clearance over a period of fifteen days even though the virus could be cultured from the lung over this period (1). A similar experiment in calves which are not immune either to the bacteria or to the virus has not been conducted.

The preceding discussion indicates the site at which immunization procedures must be effective in order to prevent lesions. The mechanisms of protection are not clearly understood but sufficient information is available from experiments in laboratory animals to allow practical development of immunization procedures in cattle.

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ABSTRACT

The effects of high calcium diets on the calcium homeostatic mechanisms of the pregnant dairy cow and their possible significance in parturient paresis (milk fever). H. E. Black and C. C. Capen (Coll. Vet. Med., Ohio State Univ., Columbus, Ohio).

The susceptibility of the dairy cow to develop parturient paresis is increased by feeding prepartal diets with a high calcium (CA) content. The objective of this investigation was to determine the effects of a high calcium diet on calcium homeostatic mechanisms in pregnant cows.

Experimental cows fed a high CA diet had a higher blood CA ($> 11.4 \pm 0.4$ mg/100 ml) than controls, but were less able to maintain blood levels at parturition ($< 8.1 \pm 0.3$ mg/100 ml). Plasma parathyroid hormone levels, urinary hydroxyproline and urinary cyclic AMP excretion did not increase with the approach of parturition as occurred in controls. Microradiographic evaluation revealed smooth dense trabecular bone surfaces. Inactive chief cells predominated in the parathyroids of experimental cows and active chief cells in controls. Hyperplasia of ultimbranchial thyroid derivatives occurred in response to the high CA diet. The calcitonin content was 431 ± 34 MRC mU/g thyroid and C-cells had prominent organelles and were partially degranulated. C-cells in the storage phase predominated in controls and the calcitonin activity was 481 ± 17 MRC mU/g thyroid. Differences were detected between the two groups in ^{45}CA uptake by duodenal mucosa *in vitro*. A 130% increase after 20 minutes and 550% increase after 60 minutes incubation occurred in experimental cows compared to a 30% and 20% increase, respectively, in controls. These findings suggest that homeostasis in cows fed a high CA diet is maintained principally by intestinal CA absorption whereas blood CA in cows fed balanced diets prepartum is more under the fine control of parathyroid hormone acting on bone. These results could partially explain why high CA prepartal diets increase the incidence of parturient paresis.

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