Morphological Alterations of the Alveolar Region in Horses with Chronic Obstructive Pulmonary Disease

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Introduction

Chronic obstructive pulmonary disease (COPD) is a naturally occurring respiratory disorder of horses which is morphologically characterized by several alterations of the pulmonary airways, especially the bronchioles. Although the principle lesions are localized in the conducting airways, alveolar changes may occur as the disease progresses. In the literature there is very little information about alterations of the alveolar region with the exception of alveolar emphysema (*Gillespie* and *Tyler*, 1967 a and b, 1969; *Tyler* et *al.*, 1971; *Nicholls*, 1978; *Schoon* and *Deegen*, 1983). Therefore we used electron microscopic methods to investigate alveolar structures in horses with COPD.

Material and Methods

The results deal with the same animals which were presented in the paper by *Drommer* et *al.*, 1985. For evaluation of the alveoli, tissue samples were obtained from the cranial lobe and the anterior, middle and posterior parts of the caudal lobe of each horse.

Results and Discussion

Morphology of the alveolar septa in healthy horses

In healthy horses and other mammalian species except the rat, the alveolar surface is covered by two epithelial cell types which are joined by tight junctions. The squamous alveolar (type I) epithelial cells line the major part (97 %) of the alveolar surface with thin cytoplasmic extensions. The main task of the granular alveolar (type II) epithelial cells is the synthesis and secretion of surface active material, which is called surfactant (*Weibel*, 1973; *Tyler* et *al.*, 1971; *Kaup* and *Drommer*, 1985). In healthy animals, type-II-cells with their apical microvilli and characteristic surfactant containing lamellar bodies occur singly (Fig. 1). The air-blood barrier is formed by thin cytoplasmic sheets of alveolar epithelium and capillary endothelium, the two being separated by a basement membrane. The capillary network is embedded in the alveolar septa. Single apertures of the alveolar septa called pores of Kohn allow collateral ventilation between adjacent alveoli (*Nowell* and *Tyler*, 1971; *Desplechain* et *al.*, 1983).

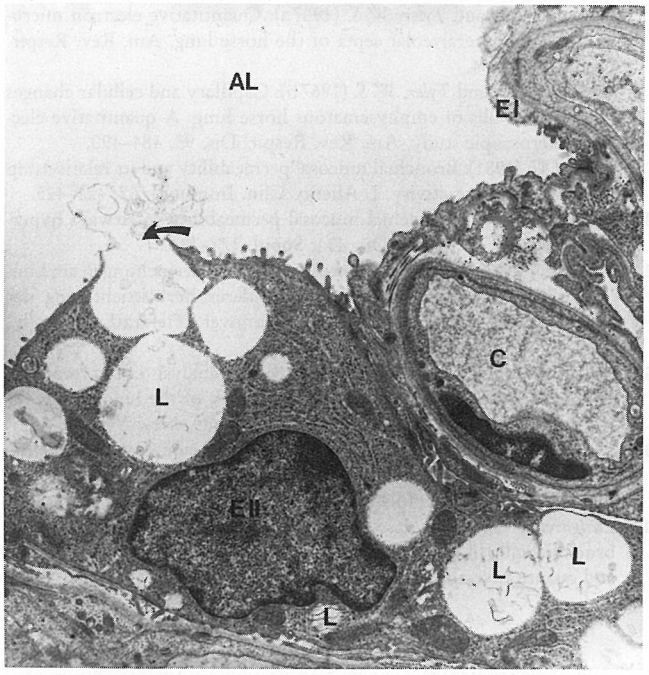

Fig. 1: The alveolar wall of a healthy horse is covererd by squamous epithelial-type I-cells (EI) and epithelial-type II-cells (EII) containing lamellar bodies (L). The electron micrograph reveals the secretion of surfactant (arrow) into the alveolar lumen (AL). C = Capillary. (12,500x.)

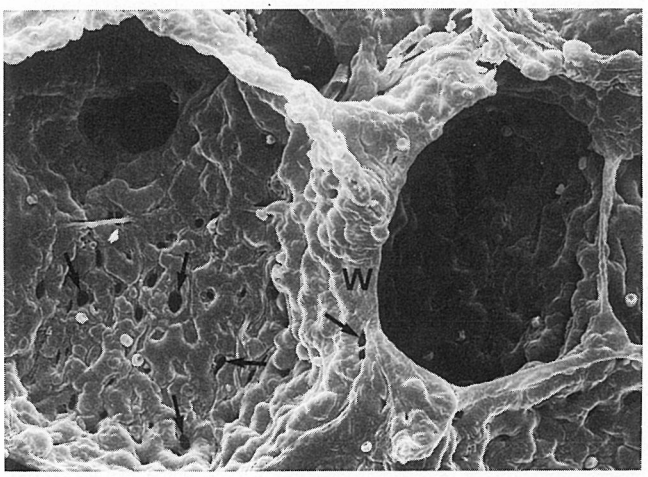

Fig. 2: Pores of Kohn (arrows) are increased in emphysematous lung regions of horses with severe COPD. W = Alveolar wall between adjacent alveoli (1200x).

Pathological changes in horses with COPD

In horses with mild bronchitis only small changes occur in the alveolar region, whereas two main pathological alterations are seen in horses with severe COPD. Alveolar emphysema* with minimal destruction of the alveolar wall appeared in all horses with severe COPD. Scanning electron microscopy revealed an enlargement of alveoli up to four times normal size. The pores of Kohn became larger and increased in number (Fig. 2). Type-II-epithelial cells of dilated regions showed signs of exhaustion with large emp-

* In accordance with the definition set forth by the Ciba Symposium on Emphysema, 1958.

In addition to alveolar emphysema another pathological process was observed in horses with COPD. In cases with mild chronic bronchitis and bronchiolitis the first signs of alveolar fibrosis appeared. The number of collagen fibers was increased and the space between the cytoplasmic sheets of squamous epithelial cells and endothelial cells was broadened. In four horses with a severe course of the disease there was a focal fibrosing alveolitis with thickening of the alveolar septa. The changes started in peribronchiolar regions and spread into adjacent alveolar walls. The alveoli were pushed away by bundles of collagen fibers and mononuclear inflammatory cells including fibroblasts and mast cells. The alveolar surfaces were lined by a cuboidal epithelium and the blood-air barrier was dramatically enlarged (Fig. 4). Transmission electron microscopy revealed a loss of squamous epithelial cells which were replaced by alveolar type-II-cells. These type-II-cells possessed numerous enlarged lamellar bodies. Occasionally there was an accumulation of alveolar macrophages with phagocytosis of surfactant during secretion (Fig. 5). This accumulation of macrophages was perhaps a result of surfactant overproduction which resembles observations of other lung diseases (*Kissler,* 1980). The focal appearance of fibrosing alveolitis may be the reason why only few authors have mentioned similar changes in horses with chronic pulmonary disease (*Sasse,* 1971; *Nicholls,* 1978; *Schoon* and *Deegen,* 1983).

Additionally we discovered interesting cells with intracytoplasmic inclusion bodies between mononuclear inflammatory cell infiltrates (Fig. 6). Transmission electron microscopy revealed that the inclusions had a crystal-like appearance. The crystals had a regular shape and were mainly located in mesenchymal cells but were also seen in smooth muscle cells and epithelial cells (*Iregui,* 1985). They have been observed in all animals, including healthy horses, in different pulmonary regions. But the lungs of horses with severe COPD contain crystals to the highest degree. Sometimes the crystal containing cells were situated in close approximation to eosinophilic granulocytes. Because of the appearance of similar extracellular crystals in tracheobronchial secretions of horses with COPD (*Deconto,* 1983) and humans with bronchial asthma (*Bürrig* and *Pfitzer,* 1985; *Dor* et *al.,* 1984) we assume that these crystals may have been Charcot-Leyden crystals.

In conclusion, our findings demonstrate the appearance of alveolar emphysema and fibrosing alveolitis in horses with severe COPD. Both changes have to be regarded as reactive processes. The emphysema was probably the result of air trapping with collateral ventilation after obstruction of bronchioles. Fibrosis of the alveolar septa could have been induced by peribronchiolar fibrosis which extended to the alveolar sac. The significance of the demonstrated crystals in horses with COPD requires further investigation.

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