Effect of ANS on Severity of Emphysema in BAPN Fed Hamsters

**FIGURE 1.** The degree of emphysema was determined by morphologic examination of gross specimens.

ANS-treated animals as in CDCl₂-BAPN animals without ANS (Fig 1).

The results of the study suggest that the same lung injury might result in either emphysema or fibrosis, connective tissue synthesis during the healing phase being the critical determinant. Furthermore, in the model described, neutrophils do not appear to be essential mediators of the emphysema which developed. We suggest that common lung toxins, such as cigarette smoke, may have important effects upon the healing phase after injury.

**REFERENCES**


**Role of Proteolytic and Oxidative Products of the Neutrophil in Determining the Specificity of the Pulmonary Lesion in Fibrotic and Destructive Lung Disease**


Idiopathic pulmonary fibrosis (IPF) and α₁-antitrypsin deficiency (α₁AT def) are both associated with a chronic influx of neutrophils to the alveolar structures, yet the pathophysiologic consequences of this neutrophil accumulation are strikingly diverse in the 2 disorders. To assess the role of neutrophil proteases and oxidative products in determining the specificity of the lesion associated with a chronic neutrophil alveolitis, connective tissue specific proteases and myeloperoxidase (MPO) were quantitated in the lower respiratory tract (LRT) of normal subjects (n = 14), IPF (n = 42) and α₁AT def (n = 12). Fluid obtained by bronchoalveolar lavage was assayed for MPO, active neutrophil collagenase (C'ase) and elastase (E'ase). While there was no active MPO, C'ase or E'ase in normal LRT fluid, large quantities of MPO and connective tissue (CT) proteases were detected in the LRT of patients with both IPF and α₁AT def. MPO (250 ± 50 units/mg alb), active C'ase (170 ± 40 ng collagen degraded/mg alb), but no active E'ase were recovered from the LRT of the IPF patients. By contrast, MPO (165 ± 20 units/mg alb), active C'ase (120 ± 35 ng collagen degraded/mg alb) as well as active neutrophil E'ase (42 ± 15 µg elastin degraded/mg alb) were recovered from the LRT of α₁AT def patients. In both diseases, the recovery of MPO and active CT proteases correlated well (p<0.001) with the presence of an active neutrophil alveolitis (≥5 neutrophils/100 cells recovered from the LRT). Treatment of normal lung explants with purified MPO at levels comparable to that recovered from patients with chronic neutrophil alveolitis resulted in significant cytotoxicity, providing a mechanism for the neutrophil's direct participation in lung cell injury in IPF and α₁AT def. However, while the oxidant (MPO) mechanism of lung injury is common to both diseases, the distinctive lesion (ie, fibrosis vs destruction of alveolar structures) associated with a chronic neutrophilic alveolitis may be determined by the differential expression of neutrophil CT protease activity within the lung (C'ase in IPF and E'ase + C'ase in α₁AT deficiency).

**Human Neutrophil Elastase within Human Alveolar Macrophages**

Implications for Lung Injury

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