wet: dry weight ratio and lavage fluid total protein were both marginally increased by 10–20 ml/kg VT compared to non-ventilated controls (NVC). However, raising the VT to 30 ml/kg did not further enhance these, suggesting that any increases following 10–20 ml/kg were not due to over-stretching the lungs. Only 40 ml/kg induced substantial increases compared to other groups. Both 40 ml/kg and 30 ml/kg upregulated lavage fluid IL-6, while soluble receptor for advanced glycation end-products (sRAGE) tended to be increased with 10–20 ml/kg but not 30 ml/kg (compared to NVC). Again, only 40 ml/kg VT induced significant upregulation.

Conclusions These data demonstrate that only the highest VT used (40 ml/kg) induced major changes in physiological and inflammatory markers consistent with development of VILI. Signs of injury/inflammation using VT 10–20 ml/kg are likely to result not from substantial lung over-stretch but from other factors, particularly epithelial shear stress secondary to alveolar derecruitment and atelectasis. While such VT may themselves be considered to be "clinically relevant", whether they induce a "clinically relevant" pathophysiology in healthy mice is questionable.

S76 PROTEINASE 3 ACTIVITY IN SPUTUM FROM ALPHA-1-ANTITRYPSIN DEFICIENT SUBJECTS

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Introduction Tissue destruction in emphysema is widely believed to result from an imbalance between serine proteinases and their inhibitors, the antiproteinases. Previous work has studied the role of neutrophil elastase (NE), but there are few studies of proteinase 3 (PR3). PR3 is released from activated neutrophils concurrently with neutrophil elastase (NE), but there are few studies of proteinase 3 inhibitors, the antiproteinases. Previous work has studied the role of myeloperoxidase (MPO), interleukin (IL)-8, and leukotriene (LT)-B4. A selection of patients had CT densitometry performed.

Results In the sample of patients studied, PR3 activity was detected in all of the sol-phase sputum samples (mean 323.90 nm, SEM 72.46) whereas NE activity was detected in only 6 of the samples (overall mean 196.42 nm, SEM 100.59). PR3 activity correlated with IL-8 concentration (p<0.004), NE activity (p<0.001) and total pathogenic bacterial load (p<0.001). There was no significant correlation with myeloperoxidase or LTB4 concentrations. PR3 activity correlated with SGRQ total score (p=0.001) but no correlation was found with lung function parameters or CT densitometry.

Conclusion This pilot study is the first to directly measure PR3 activity in sol-phase sputum. We have shown that PR3 activity can be detected in A1ATD patients, and correlates with the chemotactrant IL-8, NE activity, pathogenic bacterial load and SGRQ total score. PR3 activity should be assessed when evaluating proteinase-mediated airway damage.