

# Inflammation and immune reactions in (ILD) associated with inorganic

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The relationship between mineral dust exposure and alveolitis was explored in subjects with asbestos or silica exposure and implications for the pathogenesis of ILD examined.

Bronchoalveolar lavage (BAL) was performed on three groups: A) 64 subjects (46 smokers; mean age 54) with asbestos exposure and asbestos related disease (ILO classification: stage 0=29; stage 1=22; stage 2+3=13); B) 26 subjects (13 smokers; mean age 52) with mixed dust pneumoconiosis (all with radiographic findings of ILD); C) 23 healthy controls (12 smokers; mean age 35) (reference values [1]).

BAL was performed in the right middle lobe with 5 x 20 ml aliquots of normal saline and in 30 Group A subjects BAL was also performed in the lingula for assessment of interlobar variation of cell differential and asbestos body counts. BAL total cell counts, cell differentials and lymphocyte subpopulations were determined as described previously [1].

An excellent correlation was observed between the two sites for asbestos body counts, % lymphocytes and % neutrophils. In Groups A and B the BAL total cell counts were not significantly different from the controls (non smokers or smokers). Group A, smokers and nonsmokers, had significantly elevated % lymphocytes and neutrophils compared with the respective control groups. The patients with the lowest ILO-stage had the highest % inflammatory cells. In Group B, the inflammatory cells were also mildly elevated but the difference was significant only for the % neutrophils in smokers.

The T4/T8 ratio was increased in some Group A patients (nonsmokers and smokers) and was significantly decreased in some nonsmoking Group B patients (fig. 1.). Group B smokers had a similar decrease in their T4/T8 ratios to control smokers. Leu 7+ natural killer cells were increased in some Group A patients. Tac+, interleukin-2-receptor expressing lymphocytes, were normal in both groups, except for three Group A patients with an elevated %.

This study demonstrated a great uniformity of BAL asbestos body counts in corresponding lobes of the right and left lung and in the distribution of inflammatory cells between these sites. Thus, BAL at one site should give sufficient information on the degree of asbestos burden in the lungs and the profile of inflammatory cells reflecting the type of alveolitis in ILD.

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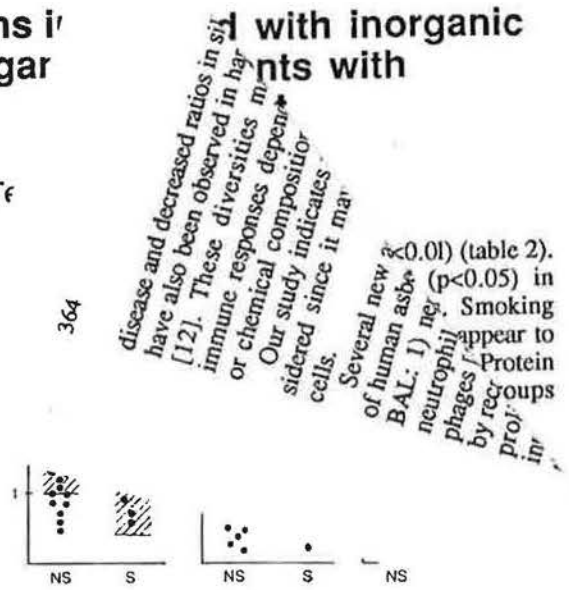


Fig. 1. - BAL lymphocyte subsets in the silica (upper panel) and asbestos (lower panel) exposed subjects. Left: T4/T8 ratio; middle: reactivity of lymphocytes with the monoclonal antibody Leu7 detecting natural killer cells (shown as % total lymphocytes); right: reactivity with the monoclonal antibody Tac detecting interleukin-2 receptors (% total lymphocytes). NS: nonsmokers; S: smokers; BAL: bronchoalveolar lavage.

Our findings confirm previous reports of a mild alveolitis in some subjects with asbestos or silica exposure [2-6]. Lymphocytic alveolitis is frequently found in subjects with known exposure to asbestos but without radiographic or functional signs of ILD. In such subjects BAL lymphocytes are usually higher than in patients suffering from asbestosis. Mean % lymphocytes in our asbestos exposed subjects without disease was 17%, in good agreement with other reports [3, 5]. In asbestosis, we found only mildly elevated neutrophils in agreement with several studies [6, 7] but in contrast to others [5, 8]. Different forms of occupational exposure and types of asbestos fibre may explain these discrepancies. In silicotic data seem to be more consistent [6, 9-11] and concur with our results.

This paper confirms previous data [2] showing elevated T4/T8 ratios in some patients with asbestos

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disease and decreased ratios in silica [12]. These diversities in immune responses depend on chemical composition considered since it may

Several new types of human asbestos (p < 0.01) in BAL: 1) neutrophils appear to be recruited by protein groups

disease and decreased ratios in silicotics. Decreased ratios have also been observed in hard metal workers with ILD [12]. These diversities may indicate different local immune responses depending on the physical structure or chemical composition of the inhaled dust.

Our study indicates that smoking history must be considered since it may affect the profile of inflammatory cells.

Several new aspects concerning the local immunology of human asbestosis and silicosis have been disclosed by BAL: 1) neutrophil accumulation may be explained by neutrophil chemotactic factor release from BAL macrophages [13]; 2) macrophage accumulation may be caused by recruitment of blood monocytes and by increased local proliferation [4]; 3) increased pulmonary gamma-interferon production [14] and release of oxygen radicals that mediate injury to lung parenchymal cells [6, 15] and fibronectin and other growth factors [6, 15] that mediate fibroblast proliferation. Progression from alveolitis to fibrosis may be monitored by measuring procollagen 3 peptide levels in BAL fluid, which show a measurable but moderate increase in patients with asbestosis in contrast to a tenfold increase in patients with active idiopathic pulmonary fibrosis [16].

Enhanced alveolar macrophage Ia antigen expression and enhanced interleukin activity have been observed following asbestos inhalation in rats [17]. An increase in the T-cell subset responsible for interleukin-2 release, namely the T4+ helper lymphocyte, was shown in some patients with asbestosis. In silicosis, however, our studies suggest that the proinflammatory effect of macrophages might be counterbalanced by suppressor T-cells since the T8+ lymphocyte is the predominant phenotype.

In conclusion, BAL studies provide insight into the pathogenesis of mineral dust diseases prompting these questions: 1) What is the clinical relevance of the lymphocytic and/or neutrophilic alveolitis in ILD related to mineral dust exposure; 2) What are the prognostic indicators derived from the BAL pathology for slowly or rapidly progressive fibrosis?

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