

# The mucosal defence capacity against proteolytic leukocyte enzymes

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## SUMMARY

*Antileukoprotease is an important inhibitor of leukocyte elastase and seems to be the primary defence factor against elastase in the respiratory tract. The circulating level of antileukoprotease increases in inflammatory diseases and seems to be related to the degree of inflammation of the lung parenchyma. Antileukoprotease cannot be included among the general acute phase reactants as it does not increase in connection with surgical trauma.*

## INTRODUCTION

Inflammatory diseases of the respiratory tract mucosa result in increased local concentration of leukocytes. Human leukocytes contain a variety of proteolytic enzymes active at neutral pH. These proteolytic enzymes are released from leukocytes in connection with cellular destruction and during phagocytosis. If the enzymes are released in large quantities, tissue destruction may follow.

Bronchial secretions from patients with purulent bronchitis contain large amounts of leukocyte elastase, neutral collagenolytic proteases and chymotrypsin-like enzymes. The main substrates for these enzymes are elastin, collagen and proteoglycans. Leukocyte elastase is important, due to its association with degenerative connective tissue diseases and has been shown to cause lung tissue destruction in experimental animals when infused intratracheally in large amounts.

The effect of the leukocyte proteases is counteracted by a group of protease inhibitors present in plasma as well as in tissues and tissue fluids (Table 1). These inhibitors inactivate the enzymes by forming inhibitor-enzyme complexes. The plasma protease inhibitors  $\alpha_1$ -antitrypsin,  $\alpha_2$ -macroglobulin and antichymotrypsin are found in the respiratory tract. In addition, there is a low molecular weight inhibitor, designated antileukoprotease, as it is a potent inhibitor of leukocyte elastase. Antileukoprotease has turned out to be the dominating elastase inhibitor in the respiratory tract secretions and about 80-90% of the inhibitory capacity is caused by antileukoprotease (Tegner, 1978). A radioimmunoassay for anti-

Table 1. Inhibition specificity of the major enzyme inhibitors in the respiratory tract.

inhibitors	leukocyte enzymes		
	elastase	neutral protease	chymotrypsin-like enzymes
$\alpha_1$ -antitrypsin	+	+	(+)
$\alpha_2$ -macroglobulin	+	+	+
antichymotrypsin			+
antileukoprotease	+		+

leukoprotease was prepared, which allowed quantification of antileukoprotease in human serum (Fryksmark et al., 1981). In healthy blood donors the circulating level is about 125  $\mu\text{g/l}$ .

The aim of this investigation was to follow the plasma levels of antileukoprotease in patients with severe inflammatory diseases of the respiratory tract and lung parenchyma and to elucidate if antileukoprotease functions as a general acute phase reactant or not.

#### MATERIAL AND METHODS

Fifteen patients with pneumonia were studied. All patients had pulmonary X-ray changes, fever above  $38^\circ\text{C}$  and cough or chest pain. Nine patients with cholecystolithiasis, without inflammatory signs, were used as a reference group.

Sera from the patients with pneumonia were drawn every two days during their stay in hospital. Six to twelve weeks after dismissal, the patients returned for follow-up examination.

Sera from the patients with cholecystolithiasis were drawn the day before cholecystectomy and the three following days after the operation.

Sera from all patients were analysed for antileukoprotease, antichymotrypsin and orosomuroid.

#### RESULTS

Sera from patients with pneumonia contained increased circulating levels of antileukoprotease (Figure 1). The values varied from twice to several times the normal level of antileukoprotease in serum. As soon as the patients got adequate therapy the level of antileukoprotease in serum decreased. Most patients had normal circulating levels in serum during follow-up examination. The values of antichymotrypsin and orosomuroid in serum followed that of antileukoprotease. Sera from the reference group of patients with cholecystolithiasis showed normal circulating values the day before cholecystectomy. The three following days after operation there was an increase in serum of antichymotrypsin and orosomuroid, while antileukoprotease remained within normal levels (Figure 2).

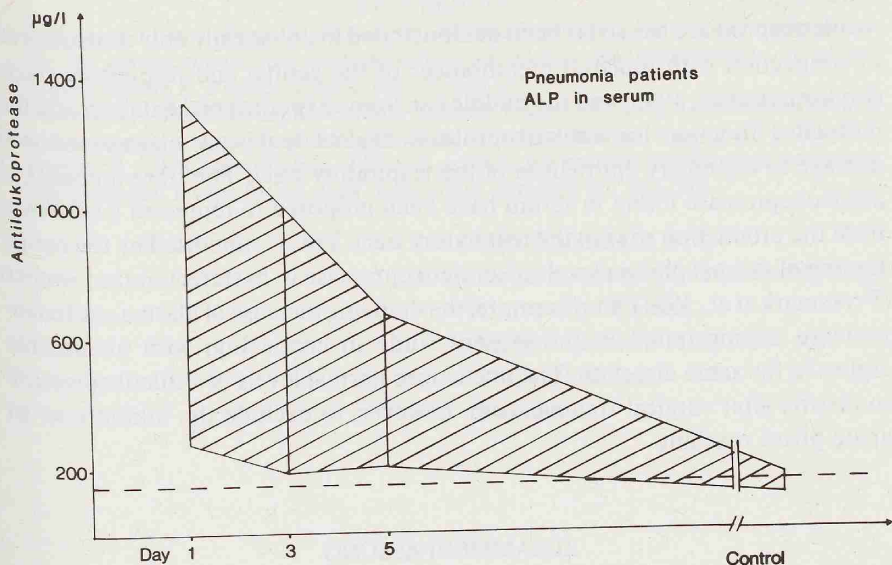


Figure 1. Circulating level of antileukoprotease. The shadowed area shows the range within which antileukoprotease varies in 15 patients. The interrupted line indicates the upper border of the normal range.

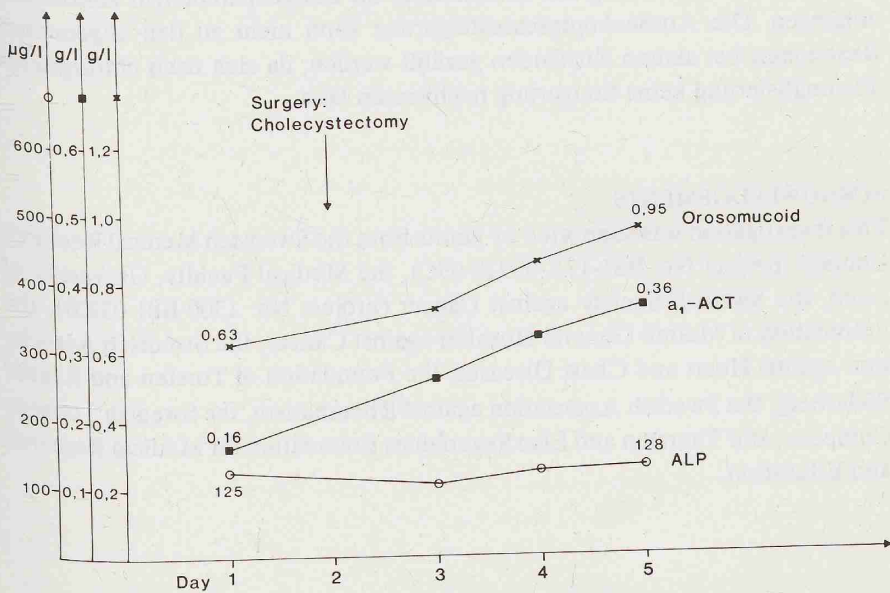


Figure 2. Circulating levels of antileukoprotease, (ALP) antichymotrypsin (a<sub>1</sub>-ACT) and orosomucoid in nine patients with cholelithiasis, before and after surgery. o-antileukoprotease, ■-antichymotrypsin and x-orosomucoid.



## DISCUSSION

Antileukoprotease has so far been demonstrated histologically only in structures in connection with mucosal membranes of the genital and respiratory tracts (Fryksmark et al., 1982) and the middle ear. Some experimental data indicate the protective function for antileukoprotease against leukocyte elastase-induced damage to the ciliary epithelium of the respiratory tract. The trace amounts of antileukoprotease found in serum have been proposed to represent a spill-over from the production sites in the respiratory tract. This is supported by the earlier finding of normal plasma levels of antileukoprotease in hysterectomized women (Fryksmark et al., 1981). Furthermore, the dramatic increase of plasma antileukoprotease demonstrated in the present study in connection with pneumonia argues in the same direction. The unchanged normal levels of antileukoprotease in plasma after surgical trauma seem, however, to exclude the inhibitor as an acute phase reactant.

## ZUSAMMENFASSUNG

Antileukoprotease ist ein wichtiger Inhibitor der Leukozytenelastase und scheint der vorrangige Schutz gegen Elastase in den Luftwegen zu sein. Das Niveau von Antileukoprotease im Kreislauf steigt bei entzündlichen Krankheiten und scheint mit dem Umfang der Entzündung im Lungenparenchym zusammenzuhängen. Die Antileukoproteasesteigerung kann nicht zu den allgemeinen Reaktionen bei akuten Zuständen gezählt werden, da sich nach chirurgischer Traumatisierung keine Steigerung nachweisen lässt.

## ACKNOWLEDGEMENTS

This investigation was supported by grants from the Swedish Medical Research Council (project No. B81-17X-03910-09C), the Medical Faculty, University of Lund, the Swedish Society against Cancer (project No. 1300-B81-03XB), the Foundation of Malmö General Hospital against Cancer, the Swedish Association against Heart and Chest Diseases, the Foundation of Torsten and Ragnar Söderberg, the Swedish Association against Rheumatism, the Swedish Tobacco Company, and Thorsten and Elsu Segerfalde's Foundation for Medical Research and Education.

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