Human Placental Alkaline Phosphatase and Acute Lung Injury

To the Editor:

A specific and sensitive marker for acute lung injury is not available. We believe that serum human placental alkaline phosphatase (hPLAP) is a possible candidate.

For three years we have been involved in research on hPLAP, an oncocetal protein, as a possible marker for gonadal cancer using several monoclonal antibodies for its specific detection. In this context, it was essential to explore the occurrence and localization of this enzyme in normal non-cancerous tissues. hPLAP could be localized on the plasma membrane of some type I pneumocytes and in the unciliated epithelial cells of respiratory bronchioli. Since an increase of serum hPLAP was sometimes observed in heavy smokers, its behavior in several other conditions of acute lung injury was investigated using an enzyme-antigen immunoassay (Innogenetics, Gent, Belgium).

In 88 percent of patients with adult respiratory distress syndrome (n = 17), a significant rise of serum hPLAP could be observed within a 24-hr span before or after clinical onset. The same observation was made in bacterial or viral pneumonia (n = 10), where 100 percent positivity for hPLAP occurred within the same time period. Furthermore, three cases of parquat poisoning all showed a distinct elevation in serum hPLAP at the moment of, or shortly before, overt lung damage. Artificial ventilation also induced serum hPLAP elevation in 88 percent of the patients (n = 8). In these four clinical settings, serum hPLAP levels correlated well with disease progression or regression.

No elevated serum hPLAP levels occurred in 14 patients with chronic aspecific respiratory disease, except for two smokers. We believe that further evaluation of hPLAP as a marker of acute lung injury is worthwhile.

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REFERENCES


Measuring Protease Inhibition

To the Editor:

The report by Fera et al again draws attention to the unresolved issue of inactivation of alpha,-antitrypsin (A1,AT) by tobacco smoke in vivo, an effect that was found by some investigators, among them Fera et al, but not by others. Two types of measurements are usually made to demonstrate the inactivation of A1,AT: 1) functional assay to determine the complete or partial loss of activity to inhibit elastase and/or trypsin; and 2) immunological measurement of A1,AT, usually radial immunodiffusion or nephelometry, that determines the antigenically-reactive protein regardless of its functional state. By dividing the functional activity by the immunologically-determined A1,AT concentration, the specific activity can be calculated.

When these measurements are made in serum or plasma, it is important to realize that the protease whose inhibition is measured interacts with other inhibitors besides A1,AT. The interaction that is of major consequence for the apparent inhibition of a protease is that with alpha,-macroglobulin (A1,M). A1,M forms complexes with proteases that remain enzymatically active against small molecular size substrates such as benzyol-arginine-p-nitroanilide (BAPNA) and

Table 1—Elastase Inhibition by Alpha,-antitrypsin in the Presence of Alpha,-macroglobulin

<table>
<thead>
<tr>
<th>A1,M (ug)</th>
<th>0</th>
<th>25.4</th>
<th>63.5</th>
<th>127.0</th>
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<tbody>
<tr>
<td>Inhibitory activity of 100 ug A1,AT</td>
<td>2.03 ± .06</td>
<td>1.9 ± .06</td>
<td>1.67 ± .03</td>
<td>1.31 ± .04</td>
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<tr>
<td>(units of elastase inhibited)*</td>
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*One unit of elastase is defined as the amount of elastase that solubilizes 1 mg of elastin in 20' at pH 8.8 at 37°C.

1Mean of three measurements ± standard deviation.

Elastase assay was as follows: To 1 ml of Tris buffer (.1M, pH 8.0) was added 20 μl of SAPNA (10 mg/ml in dimethyl formamide) and 2.07 units of porcine pancreatic elastase (Sigma) in .1 ml of Tris buffer. The color development at 405 nm was followed for 5' in a Gilford spectrophotometer with recorder at 25°C. For the inhibition measurements .1 mg of A1,AT in 0.1 ml of Tris buffer containing either no A1-2M or the amounts indicated was added to the cuvette with the elastase (2.07 units) mixed thoroughly and allowed to remain at room temperature for 3'; then 20 μl of SAPNA was added and the reaction was followed by spectrophotometer for at least 5'.