SERUM TRYPSIN INHIBITOR CAPACITY AND PURULENT SPUTUM

Abnormal serum activities of α_1-antitrypsin have been found in association with a variety of pathologic conditions.[1, 2] It has also been shown that the proteinase inhibitor is genetically determined, and 3 values of trypsin inhibitor capacity (TIC: milligrams of trypsin inhibited per ml of serum) have been recognized.[3] For the homozygote-deficient subject, the TIC is less than 0.4 mg per ml; for the heterozygote, the range is between 0.4 and 0.8 mg per ml; and for the normal subject, the TIC value is greater than 0.8 mg per ml; all values were based on enzymatic assay of the serum. Nevertheless, separation of the heterozygote from the normal is not easily achieved since certain disease states, particularly infections, temporarily elevate the TIC in both the heterozygote and normal. Kueppers[4] described the time course of α_1-antitrypsin values after intravenous injections of typhoid vaccine and found little change in the patients who were homozygote-deficient. In the heterozygote, however, the increase was of the same relative magnitude as in normal subjects but was reduced in proportion to the original values. In 7 of 9 patients with pneumonia, Shulman[5] found elevated trypsin inhibitor concentrations that peaked between 4 and 6 days. Similarly, and in somewhat varied situations, an increase in α_1-antitrypsin has been demonstrated in a wide variety of pathologic sera.[2]

Since the early studies by Laurell and Eriksson,[6] α_1-antitrypsin deficiency has been associated with emphysema as an etiologic factor. Much of the screening for this dysproteinemia has been performed on patients with obstructive lung disease, in whom infections of varying degrees of severity are most common.[7, 8, 9] It is therefore quite conceivable that the true prevalence of heterozygosity in these persons may not be evident since the presence of infection may temporarily raise the TIC to the normal range. The purpose of this study was to determine whether the presence of a purulent sputum had any significant effect on α_1-antitrypsin values.

Subjects were selected from among the patients attending the Chest Clinic at West Virginia University Hospital. They were chosen because of a history of chronic bronchitis, acute bronchitis, or bronchiectasis. Two serum samples were drawn from each patient as follows: sample "A" was drawn when the patient was producing purulent sputum; sample "B" was drawn when the patient had been producing mucoid sputum for a minimum of 2 weeks and furthermore was not on a regimen of antimicrobial drugs. The 2 specimens were not drawn in any particular sequence and were separated in one instance by as little as 4 weeks and by as long as 10 months. In no case was the infection considered serious enough to require hospitalization. The sera were separated, divided into several aliquots, and stored at −20°C until ready for analyses. The enzymatic analysis for trypsin inhibitor concentrations was performed according to the method outlined by Eriksson[3] and as previously reported.[10]

The TIC for 16 patients included in this study is shown in table 1. The TIC values when patients were producing purulent sputum were slightly but significantly greater than the TIC values obtained when mucoid sputum was produced ($P < 0.05$). This study, therefore, suggests that serum TIC values during mild tracheobronchial infection should be repeated unless they are clearly within the normal range (i.e., greater than 1.0 mg per ml). Otherwise, a mildly decreased TIC (heterozygote-deficient value) may be unrecognized.

In summary: In 16 patients, the production of purulent sputum without overt signs of more

1 Jacobsson, K.: Scand. J. Clin. Lab. Invest., 1955, *7* (Supplement 14, p. 57).

2 Vogel, R., Trautschold, E., and Werle, E.: Natural Proteinase Inhibitors, Academic Press, New York, 1968, p. 66.

3 Eriksson, S.: Acta Med. Scand., 1965, *177* (Supplement 432, p. 11).

4 Kueppers, F.: Human Genetics, 1968, *6*, 207.

5 Shulman, N. R.: J. Exp. Med., 1952, *95*, 605.

6 Laurell, C. B., and Eriksson, S.: Scand. J. Clin. Lab. Invest., 1963, *15*, 132.

7 Lieberman, J.: New Eng. J. Med., 1969, *281*, 279.

8 Kueppers, F., Fallet, R., and Larson, R. K.: Science, 1969, *165*, 899.

9 Briscoe, W. A., Kueppers, F., Davis, A. L., and Bearn, A. G.: Amer. Rev. Resp. Dis., 1966, *94*, 529.

10 Resnick, H., Lapp, N. L., and Morgan, W. K. C.: J. A. M. A., 1971, *215*, 1101.

TABLE 1

DIAGNOSES AND SERUM TRYPSIN INHIBITOR CAPACITY OF PATIENTS INCLUDED IN STUDY

					Sample A		Sample B	
Patient	Age (years)	Diagnosis*	Race	Sex	TIC† (mg/ml)	Date	TIC (mg/ml)	Date
KC	57	C	W	F	1.08	1-27-71	0.90	2-24-71
OJ	63	C, H	W	M	0.86	3-3-71	0.81	12-2-70
JAL	63	B	W	M	1.18	2-24-71	0.83	3-17-71
MP	67	C	W	F	1.41	2-24-71	1.36	10-21-70
FR	72	C, F, P	W	M	0.93	11-4-70	0.76	6-2-71
HQ	64	C	W	M	0.74	10-21-70	0.66	4-14-70
DW	33	A, D	W	M	1.34	10-28-70	1.04	5-26-71
EC	61	B	W	M	0.84	10-15-70	0.71	6-2-71
AB	59	C, E	W	M	0.86	6-9-71	1.00	9-16-70
KW	72	A, C	N	F	0.98	6-16-71	0.73	10-21-70
GJ	78	A, C	N	M	0.98	4-7-71	1.01	6-30-71
JL	57	C, E	W	M	0.70	3-24-71	0.71	7-28-71
SS	21	B	W	F	1.26	10-15-70	1.69	8-11-71
PY	38	A, C	W	F	1.40	6-23-71	1.24	3-71
WB	34	B	W	F	1.59	11-4-70	0.94	10-5-70
PS	47	C	W	F	0.98	11-3-70	1.01	4-14-71
	Mean difference (TIC of Sample A − TIC of Sample B) = 0.108							
	SD = 0.23							
	t test = 1.84							

*Diagnosis is indicated by following abbreviations: (A) asthma, (B) bronchiectasis, (C) chronic bronchitis, (D) acute bronchitis, (E) emphysema, (F) diabetes mellitus, (H) heart failure, and (P) benign prostatic hypertrophy.

†Trypsin inhibitor capacity of serum.

severe infection, was associated with an increase in serum trypsin inhibitor capacity.

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