Pi^{Pclifton}: a new α_1 -antitrypsin allele in an American Negro family*

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SUMMARY Serum specimens from eight females and two males representing three generations of an American Negro family exhibited an α_1 -antitrypsin phenotype that we labelled MPclifton because of its electrophoretic mobility. The family study and examination of multiple specimens from the same subject indicated that the phenotype represented an α_1 -antitrypsin allele, labelled *Pi*^{Pclifton}. The new genetic variant is not associated with deficiency of α_1 -antitrypsin or of trypsin inhibitory capacity in the serum.

At least 28 variants of α_1 -antitrypsin (α_1 -AT) have been described.¹ Allele *Pi*^z is associated with low serum concentration of α_1 -AT and with early development of pulmonary emphysema² and of hepatic cirrhosis.³ We report a new α_1 -AT variant that is not associated with α_1 -AT deficiency in the serum.

Patients and methods

The proband was an 11-year-old black boy. He was admitted to hospital for his first attack of asthma when his α_1 -AT phenotype was determined. After the initial observation of the unusual phenotype, blood was obtained from the antecubital vein of the boy and of 12 members of his family. Transaminases, bilirubin, and alkaline phosphatase were determined in the serum that was stored at -20°C after the addition of sodium azide (final concentration of 0.02%) for the prevention of bacterial growth.

α_1 -AT concentration was measured by radial immunodiffusion and expressed as mg α_1 -AT/ml serum.⁴

Trypsin inhibitory capacity (TIC) was measured according to Eriksson⁵ and expressed as mg trypsin inhibited/ml serum.

Pi type was determined in three ways. The first method was horizontal discontinuous starch gel electrophoresis at pH 4.95.⁵ The second method was agarose gel electrophoresis at pH 8.6.⁶ The third method was polyacrylamide gel isoelectric focusing electrophoresis (PAG-IEF).⁷ The details of how we

FIG 1 Comparison of PAG-IEF patterns between MPclifton and adjacent phenotypes.

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use these methods have been published.⁸ Crossed immunoelectrophoresis⁹ after PAG-IEF and starch gel electrophoresis, as well as immunofixation¹⁰ after PAG-IEF, were used to verify the protein bands of α_1 -AT.

The proband had one further asthma attack for which he was treated in the emergency room.

Results

Transaminases, bilirubin, and alkaline phosphatase were normal in all specimens of serum. In the serum of subjects with the new Pi type, mean α_1 -AT concentration was $2.32 \text{ mg/ml} \pm 0.35 \text{ 1SD}$, and mean TIC was $0.92 \text{ mg trypsin inhibited/ml} \pm 0.13$

1 SD. These values were normal, the respective control values being 2.74 ± 0.5 , and 0.77 ± 0.2 .

In fig 1, the PAG-IEF pattern of the new Pi type is compared with that of MS, MP, M, MPbudapest, MPst louis, and MV. Fig 1a indicates that the new Pi type migrates faster than S but slower than M and P. Fig 1b indicates that the new Pi type migrates slower than Pbudapest and Pst louis, but faster than MV.

In fig 2, the pattern of acid starch gel electrophoresis is shown. Fig 2a indicates that the new Pi type migrates faster than V but slower than M, S, or P. Fig 2b indicates that the new Pi type migrates slower than Pbudapest.

Fig 3 indicates that on agarose electrophoresis at pH 8.6, the new Pi type migrates at the same rate as M and P. However, the appearance of the new type is a single wide band, whereas that of M or P is a single narrow band.

FIG 2 Comparison of acid starch gel electrophoresis between MPclifton and adjacent phenotypes.

FIG 3 Agarose electrophoresis of MPclifton and adjacent phenotypes.

FIG 4 Immunofixation indicates that Pi type Pclifton is α_1 -AT.