PiPclifton: a new \( \alpha_1 \)-antitrypsin allele in an American Negro family*

GEORGE HUG, GAIL CHUCK, AND MAGNE K FAGERHOL

From the Department of Pediatrics, The Children's Hospital Research Foundation, University of Cincinnati, Cincinnati, Ohio 45229, USA; and the Department of Immunohaematology, Ulleval Hospital, Oslo 1, Norway

SUMMARY Serum specimens from eight females and two males representing three generations of an American Negro family exhibited an \( \alpha_1 \)-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 \( \alpha_1 \)-antitrypsin allele, labelled PiPclifton. The new genetic variant is not associated with deficiency of \( \alpha_1 \)-antitrypsin or of trypsin inhibitory capacity in the serum.

At least 28 variants of \( \alpha_1 \)-antitrypsin (\( \alpha_1 \)-AT) have been described.\(^1\) Allele Pi\( ^2 \) is associated with low serum concentration of \( \alpha_1 \)-AT and with early development of pulmonary emphysema\(^2\) and of hepatic cirrhosis.\(^3\) We report a new \( \alpha_1 \)-AT variant that is not associated with \( \alpha_1 \)-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 \( \alpha_1 \)-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 \(-20^\circ\)C after the addition of sodium azide (final concentration of 0.02%) for the prevention of bacterial growth.

\( \alpha_1 \)-AT concentration was measured by radial immunodiffusion and expressed as mg \( \alpha_1 \)-AT/ml serum.\(^4\)

Trypsin inhibitory capacity (TIC) was measured according to Eriksson\(^2\) 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.\(^6\) 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

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FIG 1 Comparison of PAG-IEF patterns between MPclifton and adjacent phenotypes.
use these methods have been published. Crossed immunoelectrophoresis after PAG-IEF and starch gel electrophoresis, as well as immunofixation after PAG-IEF, were used to verify the protein bands of α1-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 α1-AT concentration was 2.32 mg/ml ± 0.35 1 SD, and mean TIC was 0.92 mg trypsin inhibited/ml ± 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.
Discussion

On PAG-IEF the established phenotype P migrated next to the anodal side of the new Pi type. Thus, according to the rules on nomenclature of the International Pi Committee we label the new Pi type Pclifton.

Ten females and two males belonging to three generations of the affected family were available for testing. Serum specimens from eight females and the two males exhibited Pclifton (fig 5). The phenotype persisted in different specimens obtained from the same affected subject during a period of 2 years. These findings are consistent with the interpretation that Pclifton is the expression of a new $\alpha_1$-AT allele, labelled $P_i^{Pclifton}$. It is probably not a deficiency allele since $\alpha_1$-AT and TIC were not reduced in the serum of the proband or his healthy relatives. The clinical significance of $P_i^{Pclifton}$ is not known.

The new allele has been accepted by the International Pi Committee, 19 July 1979. MPclifton serum will be sent to interested investigators upon their request.

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References


Requests for reprints to Professor G Hug, Department of Pediatrics, College of Medicine, University of Cincinnati, Cincinnati, Ohio 45229, USA.