

PLASMA PROTEIN VARIABILITY IN MZ TWINS

M. MILANI-COMPARETTI, F. SACCUCCI

Institute of Biology and Genetics, Medical School, University of Ancona, Italy

A previous study had shown that only MZ twins are easily exchanged by trained police dogs. This is certainly due to the superimposability of the biochemical basis of body scent. A different approach has now been tried, based on plasma protein fractionating procedures. A pilot study has shown that PolyAcrylamide Gel Electrophoresis (PAGE) results, as expected, in widely different patterns only in DZ twin pairs. Plasma specimens from a sample of 55 supposedly MZ twin pairs were analysed by PAGE. The substantial superimposability of MZ cotwin patterns was confirmed. Analysis of the different fractions indicates the extent of environmental variability. Application to zygosity determination is suggested.

According to the "central dogma" of molecular biology, the genome controls metabolism through protein synthesis. Thus, in a mixture of metabolites, every individual exhibits a prevalence of genetic conditioning, up to the point of permitting biological identification if the components of the mixture are in sufficient numbers. This becomes manifest, e.g., in the identification of individuals through their scent, as performed by trained police dogs. Gedda et al. (1971) have shown that a dog fails to distinguish garments worn by two twins only if they are MZ. This represents a potential method for zygosity determination requiring no blood and feasible even by mail, but of course it cannot be adopted everywhere.

Thus far, most methods of zygosity determination have generally ignored the possible use of modern methods for the fractionation of protein mixtures (essentially plasma, serum or urine). Plasma contains a highly heterogeneous population of protein molecules with a variety of different functions (enzymatic, immunological, transport, etc.), all of which, with the notable exception of the variable part of immunoglobulins, are synthesized under direct genetic control.

In cooperation with Professor Segà's Immunology Lab at Rome's Regina Elena Institute, a pilot study was previously conducted to verify the hypothesis that genetic polymorphisms evidenced by PolyAcrylamide Gel Electrophoresis (PAGE) may reveal the different degree of intrapair concordance in MZ and DZ twins. The preliminary findings (Milani-Comparetti et al. 1975) were encouraging and the study is currently progressing in the laboratories of the Mendel Institute in Rome and the Institute of Biology and Genetics of the University of Ancona.

We took advantage of a recent screening program involving a sample of MZ twins in order to verify the existence and degree of intrapair concordance in the patterns obtained by PAGE according to Ornstein and Davis as modified by Segà et al. (1971). The patterns may be compared either directly or on photographic positives or negatives, or else they may be analyzed densitometrically (Fig. 1); the position of the bands may be expressed in terms of Rf.

Fig. 2 shows a few photographic examples of the 110 gel columns that were exhibited for direct observation during the Congress. The study included 55 twin pairs, all supposed to be MZ: all were concordant as to sex and blood groups A_1A_2BO , M-N, Rh-Hr.

Due to the prevalence of the various classes of immunoglobulins in the Rf area 0-0.33, our study considered especially the possible concordance in bands whose Rf exceeded 0.33. Only three pairs failed to appear concordant; for one of these (no. 4596) four empirical criteria of zygosity concurred in suggesting dizygosity (cf. Gedda et al. 1974). In the other two pairs monozygosity appeared more likely, and further study is required.

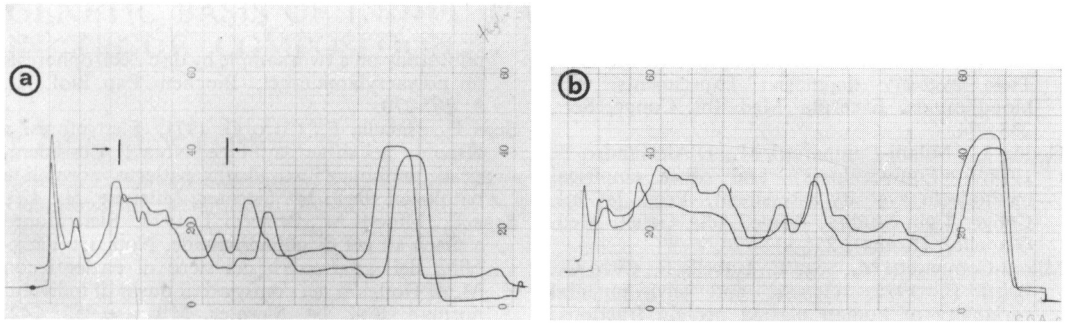


Fig. 1. Comparison of densitometric patterns:

- a. MZ pair: with the exception of the section between arrows (see text) the two patterns are practically superimposable, considering the slightly different total length.
- b. DZ pair: totally different pattern.

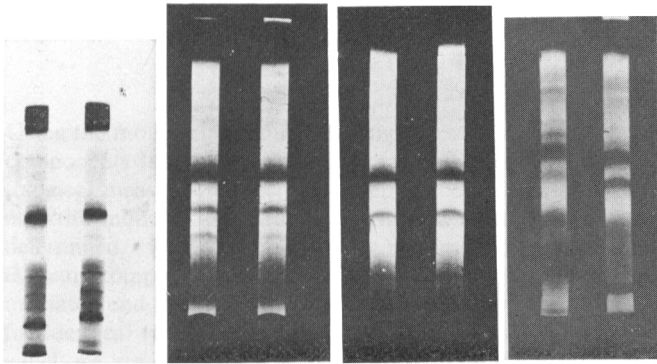


Fig. 2. Comparison of patterns with different photographic techniques: a,b,c. Superimposable patterns of MZ pairs. d. Clearly different pattern of DZ pair.

That chance concordance is a rare occurrence is shown by interpair comparison or by DZ intrapair comparison: concordance seldom occurs, if at all. With improved standardization and the use of additional fractionation techniques (Electrofocusing, TLE, TLC, etc.) we believe that biological identity may come to be established with reproducible certainty. This may bring about a revolution in twin pair zygosity determination, with improved accuracy and reduced costs. The hope that our studies might suggest a useful diagnostic tool for adoption by our colleagues moved us to present this report at the Congress.

A further potential application of our studies to clinical genetics may come from a comparison of fractionation patterns from MZ twins discordant as to various diseases: since the occurrence of abnormal fractions (Sega et al. 1971, 1973) in patients with defined diseases is by now ascertained, our method ought to provide further discrimination between genetic and environmental factors in such diseases, with potential application in preventive medicine and in early diagnosis.

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