Thrombotic Risks: A Clarification

To the Editor:

Rogier M. Bertina has written a clear, timely, and authoritative review of factor V Leiden and other coagulation factor mutations affecting thrombotic risk (1).

I was confused by the fact that the sum of genetic defects in inherited thrombophilia plus the cases with unknown cause add up to 109.7% (Table 1 of reference 1). This could occur due to multiple defects in individual patients. However, it might just be a typographical error, where the unknown cases are 20% rather than 30%.

I would appreciate clarification, as the answer either reduces the number of residual unclassified cases or possibly suggests frequent overlap of thrombophilic states, which would seem to be a new area of inquiry.

Reference

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Dr. Bertina responds:

To the Editor:

In my review of factor V Leiden and other coagulation factor mutations affecting thrombotic risk (1), Table 1 summarized the prevalences of different genetic defects among symptomatic pro-band families with inherited thrombophilia. Burdick is right that by adding up these prevalences one arrives at 109.7%. This is not due to typographical error but reflects the situation that 9.7% of these pro-band families have two different genetic defects. In fact, the present model for familial thrombophilia is that of a multigene disorder (2). Although such a model was already proposed in 1987 (3), it was only after the identification of common genetic risk factors for thrombosis, such as the factor V Leiden mutation (4) and the prothrombin 20210 A allele (5), that experimental support for this model was obtained. Koeleman et al. (6) reported for the first time that factor V Leiden is an additional risk factor for thrombosis in families where both protein C deficiency and the factor V Leiden mutation segregate. Therefore, in these families, individuals that carry two mutations develop thrombosis earlier in life and more frequently than those carrying only one mutation. In the meantime, similar observations have been made by other groups and on other combinations of risk factors (e.g., protein S deficiency and factor V Leiden, antithrombin deficiency and factor V Leiden, and more recently, factor V Leiden and the prothrombin 20210 A allele).

Returning to Table 1 in reference 1, we might expect that, when all the individual genetic risk factors become known, the sum of the various prevalences will approach 200% (each pro-band has at least two different gene defects).

Of course, the concept of familial thrombophilia as a multigenetic disease has important implications for the laboratory analysis of patients who come from thrombophilia families and underlines the need for identification of those genetic risk factors that thus far remain unnoticed.

References

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False-Positive LSD Drug Screening Induced by a Mucolytic Medication

To the Editor:

Since the early 1990s, the ingestion of lysergic acid diethylamide (LSD) as an inexpensive alternative to amphetamine derivatives has once again become widespread (1, 2). Consequently, screening of LSD has gained importance in clinical routine. The drug screening of patients with a severe cranioencephalic trauma showed a positive LSD screening by the homogeneous immunoassay CEDIA® DAU LSD (Boehringer Mannheim). In spite of the 3-h half-life of LSD in plasma (3), the drug screening remained positive for several days. These samples were analyzed by means of fluorescence detection (FLD 1046A, Hewlett-Packard) after solid-phase extraction with HPLC technique (HP 1050, Hewlett-Packard) (4). The positive immunoassay results could not be confirmed. In the following study, we carried out a general screening of medications in urine using the HPLC technique (Remedi HS, Bio-Rad Laboratories). Ambroxol as well as Pirenzepin were detectable.

Because of other unexpected positive LSD results of patients of the same intensive care unit, we carried out a general LSD screening of 10 patients of this ward. All of these 10 samples tested positive by the CEDIA DAU LSD assay but could not be confirmed by the HPLC technique. All those patients had an

Reference