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Is a Nihilistic Attitude to Thrombophilia Screening Justified?

Dear Sir,

Until the 1990s, laboratory testing of haematological risk factors for thrombosis was rare outside the research setting, due to the low yield of positive results. Since the discovery of activated Protein C resistance (1), FV Leiden (2), and other common defects, testing for them (ambiguously termed thrombophilia 'screening') has become one of the fastest growth areas in haematological practice in the United Kingdom.

As in the case of any new medical product, there has been a predictable pattern of response – the sine wave curve. Initial enthusiasm is followed by a phase of disillusion and under-utilisation: eventually, after the careful accumulation of data (which may take many years) the true utility of the intervention becomes clear. Initially, the new "thrombophilia screen" was no doubt over-enthusiastically applied. In the UK we have now entered the second phase of the sine wave: a nihilistic assessment of the value of thrombophilia testing. According to the sine wave hypothesis, this nihilism is no more likely to be justified than the original enthusiasm, and should be treated with equal scepticism. It should certainly not form the basis of health policy or medical education.

The anti-testing argument is based on two premises. The first, as stated by Greaves and Baglin (3), is that a test should be abandoned unless the act of *performing* it is proven (by randomised studies) to improve clinical outcomes via changes in therapy.

The second is that thrombophilia testing generates anxiety in those tested, who cannot cope with the approximate estimate of individual thrombotic risk that the tests provide when combined with properly analysed personal and familial medical histories.

We think both these premises are false. The extremely stringent standard of a proven effect on clinical outcome has rarely, if ever, been applied to tests of haemostasis (e.g. the coagulation screen) or indeed to laboratory tests in general. Most of them would fail it. Moreover we fully concur with Mannucci (4), that such studies are unlikely ever to be undertaken, for they would require very large numbers.

The second premise suggests that the medical profession is not imparting the information to patients in a clear and accessible form. We believe the onus is upon clinicians to improve communication skills, not to abandon the practice of talking to patients about risk.

On the contrary, testing (including family cascade screening) appears to reduce anxiety, for there is often pre-existing concern about the level of thrombotic risk to family members (particularly children) which is allayed by the process of explanation, testing and counselling. In the current climate of openness, doctors should not withhold nor censor information, especially when it is widely available to the public from other, often inaccurate, sources such as the Internet and the popular press. To do so would repeat the error of paternalism recently attributed to clinical pathologists in the UK.

The benefits of thrombophilia testing need restating. Firstly, it provides the best available evidence-based approximation of the risk of recurrence in the proband: secondly, if the defect is genetic, it allows similar thrombotic risk estimation in family members. Of course these approximations are not perfect, but they are better than those based on past clinical events alone. Clinical Geneticists use many markers with similar characteristics and do not find either risk assessment or communicating the degree of uncertainty to their clients impossible. Thrombophilia testing in the proband, and if an inherited defect is found, in family members, allows informed guidance on lifestyle, risk avoidance and future opportunities for thromboprophylaxis. As pointed out by many, this is preventative medicine. It is surely preferable that preventative advice is given on the basis of all accessible information rather than on an empirical, ad hoc basis.

Of course, many requests for thrombophilia "screens" are inappropriate: perhaps misled by the name, clinicians try to "screen" individuals without personal or familial evidence of increased thrombotic risk. Nobody advocates such screening of unselected populations. Testing should be confined to individuals (and families) who demonstrate a high risk of venous thrombosis.

In the field of venous thrombosis there remain many questions, but inhibiting principled investigation (especially through the medium of official guidelines or health policy) is unlikely to lead to better answers. New developments in antithrombotic therapy will provide an expanded range of agents, freeing us from the rigid coumarin risk-benefit paradigm that currently determines debate in this area. We will need more and better individual risk stratification, not less.

We like Mannucci, reject nihilism: it is still an exciting time in the developing field of thrombophilia. In our view, informed assessment and competent communication of the risk of venous thromboembolism to individuals will contribute to a reduced incidence of this dangerous and disfiguring chronic circulatory disease in the future.

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References

1. Dahlback B, Carlsson M, Svensson PJ. Familial thrombophilia due to a previously unrecognised mechanism characterised by poor anticoagulant response to activated protein C. Prediction of a cofactor for activated Protein C. Proc Natl Acad Sci USA 1993; 90: 1004-8.
2. Bertina RM, Koelman BP, Koster T, Rosendaal FR, Dirven RJ, de Ronde H, et al. Mutation in blood coagulation factor V associated with resistance to activated Protein C. Nature 1994; 369: 64-7.
3. Greaves M, Baglin T. Laboratory testing for heritable thrombophilia: impact on clinical management of thrombotic disease. Brit J Haematol 2000; 109: 699-703.
4. Mannucci PM. Genetic hypercoagulability: prevention suggests testing family members. Blood 2001; 98: 21-2.

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