Tests for Hereditary Thrombophilia Are of Limited Value in the Black Population

To the Editor:

We read with interest the recent article by Jerrard-Dunne et al in which they established race-specific ranges for thrombophilia markers in blacks.1 Testing for hereditary thrombophilia has been advocated for a myriad of both arterial and venous disorders and the association with venous thromboembolism (VTE) but not arterial disease has been established in well-conducted studies.2 A common feature in thrombophilia research is the tendency to ignore the potential for ethnicity to influence disease. The conventional hereditary thrombophilia tests performed in the United Kingdom include a range of investigations: genotyping for factor V Leiden (FVL) and prothrombin mutations, and measurement of protein C (PC), protein S (PS), and antithrombin (AT) phenotype. These prothrombotic markers are informative in 30% to 70% of Europeans presenting with VTE and recurrent VTE3 but are rare in black populations.4,5 This is supported by data from our own institution in which only 13 of 142 black subjects (9.1%) with a history of VTE had a thrombophilic marker, compared with 30% of white subjects.6 Of the positive thrombophilia tests in blacks (30% African and 70% Caribbean), 4 had PS deficiency, 6 had PC deficiency, 1 had AT deficiency, and 2 were heterozygous for FVL. In their study, Jerrard-Dunne et al have found that a significant proportion of healthy black controls would be misdiagnosed as having PC, PS, and possibly AT deficiency using reference ranges derived from white populations. This will be of concern to those of us involved in the treatment of VTE in multi-ethnic populations who are aware of both the psychosocial and medical consequences that may associated with the diagnosis of a “genetic disorder.” Negative results in black patients undergoing thrombophilia testing may lead to a false reassurance of normality, and positive results using inappropriate reference ranges should now be viewed as unreliable.

As the genetic basis for hereditary thrombophilia in blacks is poorly characterized but a family history of VTE is as common in blacks as white subjects with VTE,4 it is likely that black populations possess prothrombotic genetic risk factors that are yet to be determined. The Camberwell Thrombophilia Study is a population-based study investigating thrombophilia in the black population. We have recently shown that elevated factor VIII:C (FVIII) level is a major risk factor for VTE in the black population with odds ratio for DVT of 11.1 (95% CI 4.29 to 29.43) for FVIII:C >228 IU/dl. (the 90th centile value in controls).6 Elevated FVIII is also associated with a moderately increased risk of stroke in whites7,8 and has been associated with coronary heart disease and stroke in African-Americans with diabetes.9 Elevated fibrinogen level is an established risk factor for arterial disease2 and has recently been linked to VTE in blacks.10 Thus FVIII and fibrinogen are thrombo-philic markers in blacks that should be considered when assessing risk factors for both venous or arterial thrombosis.

We support the view that an awareness of ethnic differences in reference ranges is vital in order to avoid misdiagnosis of hereditary thrombophilia. More importantly, conventional thrombophilia tests are not generally useful in the black population and may provide false reassurance when negative results are obtained. There is thus an urgent need for further race-specific research into the genetic basis of arterial and venous thrombosis.

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