

25. Palareti G, Legnani C, Cosmi B, Fortunato G, Lunghi B, Bernardi F, et al. D-Dimer test performed after oral anti-coagulation is stopped has a high negative predictive value for recurrence in patients with thrombophilic alterations and previous venous thromboembolism. *Haematologica* 2002; 87(Suppl. to no. 5):55[abstract C137].
26. Andreescu AC, Cushman M, Rosendaal FR. d-dimer as a risk factor for deep vein thrombosis: the Leiden Thrombophilia Study. *Thromb Haemost* 2002; 87:47-51.
27. Palareti G. Can markers of thrombosis after stopping anti-coagulant therapy predict recurrent VTE? 48<sup>th</sup> Scientific and Standardization Committee Meeting of the International Society on Thrombosis and Haemostasis. Boston, Mass, USA. July 18<sup>th</sup>-20<sup>th</sup>, 2002.

---

### Inside Haematologica. Inherited thrombophilia: the impact of our increasing understanding of molecular mechanisms on clinical practice

---

The chapter of genetic thrombophilia was opened in this journal by a landmark article by Bjorn Dahlback.<sup>1</sup> Four years later, Dahlback *et al.*<sup>2</sup> introduced the concept of *thrombophilia as a multigenic disease*. At that time they wrote: "*The realization that thrombophilia is a multifactorial disease, with both circumstantial and genetic risk factors being involved in its pathogenesis, is presumably going to influence the future management of the thrombophilic patient. However, available data are not sufficient for calculation of the thrombosis risk associated with combinations of genetic defects. As most studies are made on selected populations, while accurate prevalence numbers of the different defects in the general population are still lacking, it can only be concluded that individuals with combined defects have higher thrombosis risk than those with individual defects.*"

In subsequent years, *Haematologica* has published several papers on the subject of genetic thrombophilia.<sup>3-16</sup> In this issue of *Haematologica*, two reports deal with genetic predisposition to thromboembolism.<sup>17,18</sup> In particular, De Stefano *et al.*<sup>18</sup> have carefully analyzed the available evidence in order to establish simple guidelines for the management of patients with inherited thrombophilia.

---

### References

1. Dahlback B. Inherited resistance to activated protein C, a major basis of venous thrombosis, is caused by deficient anticoagulant cofactor function of factor V. *Haematologica* 1995; 80 Suppl 2:102-13.
2. Zoller B, Garcia de Frutos P, Hillarp A, Dahlback B. Thrombophilia as a multigenic disease. *Haematologica* 1999; 84:59-70.
3. Vicente V, Gonzalez-Conejero R, Rivera J, Corral J. The prothrombin gene variant 20210A in venous and arterial thromboembolism. *Haematologica* 1999; 84:356-62.
4. Gemmati D, Serino ML, Trivellato C, Fiorini S, Scapoli GL, C677T substitution in the methylenetetrahydrofolate reductase gene as a risk factor for venous thrombosis and arterial disease in selected patients. *Haematologica* 1999; 84:824-8.
5. Singh YS, Arruda VR, Ozello MC, Machado TF, Annichino-Bizzacchi MM. Identification of one novel and three other point mutations in the protein C gene of five unrelated Brazilian patients with hereditary protein C deficiency. *Haematologica* 2000; 85:891-3.
6. Soria JM, Quintana R, Vallve C, Iruin G, Cortes C, Fontcuberta J. A boy with venous thrombosis, homozygous for factor V Leiden, prothrombin G20210A and MTHFR C667T mutations, but belonging to an asymptomatic family. *Haematologica* 2000; 85:1230-2.
7. Aznar J, Vaya A, Estelles A, Mira Y, Segui R, Villa P, et al. Risk of venous thrombosis in carriers of the prothrombin G20210A variant and factor V Leiden and their interaction with oral contraceptives. *Haematologica* 2000; 85:1271-6.
8. Martinelli P, Grandone E, Colaizzo D, Paladini D, Sciannone N, Margaglione M, et al. Familial thrombophilia and the occurrence of fetal growth restriction. *Haematologica* 2001; 86:428-31.
9. Franco RF, Fagundes MG, Meijers JC, Reitsma PH, Lourenco D, Morelli V, et al. Identification of polymorphisms in the 5'-untranslated region of the TAFI gene: relationship with plasma TAFI levels and risk of venous thrombosis. *Haematologica* 2001; 86:510-7.
10. Margaglione M, Brancaccio V, Ciampa A, Papa ML, Grandone E, Di Minno G. Inherited thrombophilic risk factors in a large cohort of individuals referred to Italian thrombophilia centers: distinct roles in different clinical settings. *Haematologica* 2001; 86:634-9.
11. Forastiero R, Martinuzzo M, Adamczuk Y, Varela ML, Pombo G, Carreras LO. The combination of thrombophilic genotypes is associated with definite antiphospholipid syndrome. *Haematologica* 2001; 86:735-41.
12. Soria JM, Baiget M, Castano L, Tejada MI, Perez-Nanclares G, Fontcuberta J. Genetic risk factors for thrombosis in a Basque population and its possible contribution to the analysis of a complex disease such as thrombophilia. *Haematologica* 2001; 86:889-90.
13. Santamaria A, Mateo J, Oliver A, Menendez B, Souto JC, Borrell M, et al. Risk of thrombosis associated with oral contraceptives of women from 97 families with inherited thrombophilia: high risk of thrombosis in carriers of the G20210A mutation of the prothrombin gene. *Haematologica* 2001; 86:965-71.
14. Iolascon A, Giordano P, Storelli S, Li HH, Coppola B, Piga A, et al. Thrombophilia in thalassemia major patients: analysis of genetic predisposing factors. *Haematologica* 2001; 86:1112-3.
15. Tirado I, Mateo J, Soria JM, Oliver A, Borrell M, Coll I, et al. Contribution of prothrombin 20210A allele and factor V Leiden mutation to thrombosis risk in thrombophilic families with other hemostatic deficiencies. *Haematologica* 2001; 86:1200-8.
16. Tormene D, Simioni P, Prandoni P, Luni S, Zerbini P, Sartor D, et al. Factor V Leiden mutation and the risk of venous thromboembolism in pregnant women. *Haematologica* 2001; 86:1305-9.
17. Libourel EJ, Bank I, Meinardi JR, Baljé-Volkers CP, Hamulyak K, Middeldorp S, et al. Co-segregation of thrombophilic disorders in factor V Leiden carriers: the contribution of factor VIII, factor XI, thrombin activatable fibrinolysis inhibitor and lipoprotein(a) to the absolute risk of venous thromboembolism. *Haematologica* 2002; 87:1068-73.
18. De Stefano V, Rossi E, Paciaroni K, Leone G. Screening for inherited thrombophilia: indications and therapeutic implications. *Haematologica* 2002; 87:1095-108.