Dear Sir,

Several case control studies and a recent prospective study showed that in patients with (idiopathic) venous thrombosis mild hyperhomocysteinemia (HH) can be observed 2-3 times more frequently than in controls (1-3). The pathogenetic explanation for this clinical observation is not known. In principal a thrombotic tendency can originate in the blood, in the vessel wall or at the level of thrombocytes. The question that we wanted to answer was whether the thrombotic tendency that might accompany HH is caused by a higher capacity of these persons to generate thrombin. The plasmatic component of a thrombotic tendency might be reflected in the capacity of the platelet poor plasma to generate thrombin. This capacity can be assessed by measuring the endogenous thrombin potential (ETP), i.e. the surface under the thrombin generation curve (4-6). It has been shown that the ETP is significantly increased in such plasma based thrombotic tendencies as deficiencies in AT and mutated Factor V Leiden (6,7). The influence of APC or TM, our data do not support the idea that HH acts via the plasmatic coagulation system. Others suggested a role for factor V or modulin (TM) (10, 11) on the inhibition of the ETP was recently shown deficiencies in AT and mutated Factor V Leiden (6,7). The influence of APC or TM, support of protein C deficiency in the healthy population. Thromb Haemost 1995; 73: 87-93.

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in vivo situation and it is questionable in our opinion whether these in vitro experiments represent the clinical situation. Not finding an association between mild HH and the ETP renders a direct influence of HH on plasmatic thrombin generation improbable. Therefore other factors might be relevant such as the fibrinolytic pathway, enhanced tissue factor activity, enhanced platelet aggregation, increased platelet adhesion on endothelial cells, abnormal nitrogen oxides, abnormal endothelium-derived relaxing factor and inhibition of von Willebrand factor production (1, 15). Most of the studies supporting these hypotheses are however again limited by the high levels of homocysteine used in the in vitro experiments. It has also been shown that homocysteine might induce altered gene expression in endothelial cells, genes that might possibly be related to the process of thrombosis (16, 17).

Until now – to our knowledge – there is however no clear parameter observed in man that might be a clue for the pathogenetic process involved in the association of mild HH and venous thrombosis. We feel such a parameter is urgently needed to proof that the epidemiological association between HH and venous thrombosis can more likely be interpreted as a causative one. Furthermore such a parameter would be very helpful in treatment strategies for HH. Vitamins (folic acid) interpreted as a causative one. Furthermore such a parameter would be very helpful in treatment strategies for HH. Vitamins (folic acid) might possibly be related to the process of thrombosis (16, 17).

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