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Universiteit Leiden



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Title: Pathophysiology of thrombotic thrombocytopenic purpura : pathophysiology of thrombotic thrombocytopenic purpura : the "two-hit" paradigm

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Stellingen

1. The 'two-hit' model of thrombotic thrombocytopenic purpura postulates the existence of a first event (e.g. presence of autoantibodies or mutations) leading to reduced activity of ADAMTS13 and a second event leading to active, widespread microvascular thrombosis. *This thesis*
2. Activity of ADAMTS13 below 10% of normal defines a form of thrombotic thrombocytopenic purpura with distinct clinical behavior. *This thesis*
3. The amount of residual ADAMTS13 activity between acute episodes is a prominent determinant of clinical severity in congenital thrombotic thrombocytopenic purpura. *This thesis*
4. *Ad maiora*: studying ADAMTS13-deficient patients with thrombotic thrombocytopenic purpura can take us much beyond thrombotic thrombocytopenic purpura. *This thesis*
5. Thrombosis is a play of two actors, one is blood hemostasis, the other is the vascular wall (i.e. Virchow's 'dyad').
6. Thrombosis is one disease and as many diseases as the vessels in the circulation.
7. Genetics is '*sub-stantial*' and hence is a preferred way of establishing causality, of '*under-standing*'.
8. Agnostic, high-throughput genetic screening in thrombosis identified causal genes almost exclusively in the hemostatic system. The contribution of genes outside of hemostasis to thrombosis predisposition may be very limited.
9. Humans are overrated. Bacteria have, by all measures, evolutionary superiority over humans. The evolutionary peculiarity of humans is that they are aware of the evolutionary process.
10. Freedom of will is determined by neuronal firing in a complex network (i.e. emergence). Depending on the inherent nature of neuronal firing, 'freedom' of will may be either completely determined or random. But this does not make human life less interesting.