

The EuroClot Collaborative study Genetic Regulation of the End-Stage Clotting Process That Leads to Thrombotic Stroke



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Participants:

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Introduction and Aims

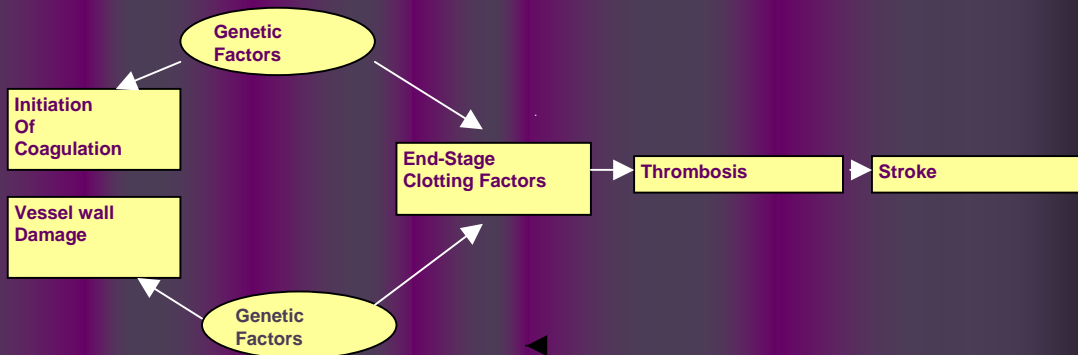
Thrombotic (or ischaemic) stroke is a common and disabling condition affecting an estimated 650,000 Europeans annually with considerable mortality and costing over 30 billion Euros/year. Thrombotic stroke is caused by a blood clot blocking an artery supplying the brain of oxygen and nutrients. Blockage of arteries is caused by thrombus formation due to activation of the coagulation system. The effects of a stroke vary enormously and depend on which part of the brain is damaged and the extent of that damage. For some, the effects can be relatively minor and short-lived, more commonly others die or are left with severe, long-term disabilities.

Aims

EuroClot aims to identify and validate potentially therapeutically useful genes associated with thrombotic stroke and focuses on uncovering the genes that control the end-stage of the coagulation process that leads directly to the production of thrombus (clot) that causes vascular obstruction and tissue death.

Specifically, EuroClot aims to identify the major genes involved in variations of the end-stage clotting process and investigate the role of these novel genes (and existing candidate genes) in the pathogenesis of stroke across Europe.

Scheme of Stages of Thrombosis in Stroke



Materials and methods

Twin studies have shown a substantial genetic component to levels of activation peptides and the final pathway of thrombosis.

Starting from January 2005, for the next 36 months, EuroClot will study stroke intermediate phenotypes in 4,250 individual twins and families from GenomEUtwin project involving various countries: United Kingdom, Holland, Finland, Italy, Sweden and Spain.

2,500 DZ twin individuals will be provided by the *TwinsUK* biobank - London, additional twin pairs will be provided by the Italian group - 350 individuals and the Swedish and the Finnish groups -350 individuals each. In parallel, extended families in Finland -350 individuals and Spain- 350 individuals will be bled.

All samples will be taken in the same way using a standard protocol, namely a fasting venous sample taken within 5 minutes from the co-twin into 0.13 trisodium citrate tube and kept on ice for tests of fibrinolysis and at room temperature for tests of coagulation. Within 1 hour from collection, samples will be centrifuged to obtain platelet- poor plasma, snap frozen in aliquots in liquid nitrogen and stored at -45C until transportation on dry ice to the main phenotyping coagulation centre in Leeds - UK. Further samples collected and stored: plasma EDTA, serum and DNA.

In addition, biochemical risk factor lipids, tryglicerides, glucose and will be measured and any hypertensive medication will be recorded and supplied for the database. Also, clinical data on height, weight, smoking and blood pressure will be obtained from all cohorts and centres.

Conclusions

By the end of 2007 it is anticipated that the groups will identify two novel loci and at least one novel gene or haplotype or gene variant influencing end stage clotting. For geographical variations, it is expected that gene-environment interactions and some differences in gene frequencies and genetic factors across Europe are likely to occur.