

1059 COLD PROMOTED ACTIVATION OF FACTOR VII(CPA) AND PLASMA RENIN ACTIVITY (PRA)

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The CPA phenomenon occurs in about 20% of the population, 60% of women using contraceptive drugs and 90% of pregnant women. Cpa positive plasma samples show at 4°C spontaneous activation of prekallikrein and factor VII, shortening of the Thrombotest^H Time (TT) and consumption of C₄ esterase inhibitor. Since kallikrein may activate prorenin, we related the CPA phenomenon to PRA.

A highly significant correlation was found between the shortening of the TT at 4°C and an increase in PRA during storage of random plasma samples.

It is concluded that special care should be taken when PRA is determined in CPA positive plasma samples in order to avoid erroneously high PRA levels.

1060 ACQUIRED INHIBITORS OF BLOOD COAGULATION IN NON HAEMOPHILIC PATIENTS.

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We report here a study concerning 25 cases of acquired inhibitors of blood coagulation observed in our hospital over the last 3 years. According to their mode of action, these anticoagulants could be divided into 2 groups: only 2 patients' plasmas had an elective effect on anti-haemophilic A factor (AHF), the 23 other inhibitors "lupus-like" were directed against the "Prothrombinactivator complex" of factors Xa, V, and phospholipid and mainly against the phospholipid. These antibodies generally occurred in elderly patients (older than 60 years) but 8 patients were between 15 and 30. Most were women; 13 inhibitors were associated with underlying diseases, well known to induce such abnormality (SLE, neoplastic disease, poly-arthritis, auto-immune haemolysis). If the 2 AHF antibodies induced severe bleeding manifestations, on the other hand, the "lupus-like" inhibitors were generally clinically asymptomatic. These inhibitors have been particularly studied according to their immunological properties by several technics: immuno-neutralization, isolation of immunoglobulins, gel filtration, and for one anti-AHF antibody 125-Iodin radio-labelling step followed by complex dissociation. Their specificity was IgG and/or IgM for the "lupus-like" anticoagulants, IgG for one anti-AHF. The great majority of these inhibitors was still present all over the 3 years follow-up despite of Prednisone treatment for those associated with an underlying disease; the anti-AHF (70 Oxford U.) was successfully treated by Prednisone and Azathioprine. The knowledge of such acquired inhibitors might lead to a further approach in the concept of immune response in man.

1061 CROTALASE AND THROMBIN: COHOMOLOGY OF AMINO ACID SEQUENCES AS EVIDENCE FOR A COMMON ANCESTRAL GENE

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Crotalase is a coagulant enzyme from the venom of *C. adamanteus* which releases specifically fibrinopeptide A from fibrinogen and cleaves the single thrombin-vulnerable bond of prothrombin. Edman degradation of crotalase yielded a six-step N-terminal sequence which contained only one residue in common with the N-terminal sequence of the B-chain of thrombin (Magnusson; Thompson *et al.*). When the two sequences were compared with the N-terminal sequences of the heavy chains of factor IXa (Enfield) and factor Xa (Titani), extensive identity was noted in five of the six positions, indicating evolutionary relationship among the four proteins and the suitability of the crotalase molecule for structure-function studies of thrombin-like actions. Our method for demonstrating that crotalase and thrombin are evolutionarily related is novel and is termed cohomology. We regard two amino acid sequences to be cohomologous when they each exhibit appreciable similarity to one or more different sequences but not to each other. We have

crotalase	Val	Ile	Gly	Gly	Asp	Glu
factor IXa	Val	Val	Gly	Gly	Glu	Asp
factor Xa	Ile	Val	Gly	Gly	Arg	Asp
thrombin	Ile	Val	Glu	Gly	Ser	Asp

found that this approach to the determination of evolutionary relationship, while employed intuitively here, is amenable to rigorous mathematical formulation (to be published).