VITAMIN K AND EXPERIMENTAL TUMOUR METASTASES. P. Hilgard. Universitätsklinik (Tumorforschung) Essen, Federal Republic of Germany.

Evidence has accumulated that anticoagulants can reduce the incidence of metastases from malignant tumours. Coumarin derivatives have been found most effective in various experimental systems, decreased blood coagulability and direct effects on tumour cells have been considered as their mode of action. W. H. Müller described a syngeneic, spontaneously metastasising tumour (Lewis-lung carcinoma) was used in C57/BL mice. Long-term anticoagulation with phenprocoumon resulted in a significant reduction of pulmonary metastases. In contrast, controlled anticoagulation with heparin or anrod was ineffective in the same tumour-host system. In short-term experiments, employing intravenously inoculated tumour cells, it could be demonstrated that the antimetastatic effect of the coumarin-derivative was independent of the effect on blood coagulation and of the drug itself. Under various experimental conditions diet induced vitamin K deficiency was equally effective in reducing metastases as well from primary tumours as from intravenously injected tumour cells.

The present investigations indicate that vitamin K is involved at a cellular level during the early stage of metastasis formation. It is conceivable that vitamin K dependent γ -carboxyglutamic acid residues are located on the cell surface; their absence could substantially influence certain cell characteristics responsible for the lodgement of blood-borne tumour cells.

THE THERAPEUTIC RANGE OF ORAL ANTICOAGULATION. A COMPARISON OF 14 DIFFERENT THROMBOPLASTINS. F. Duckert, G. A. Marbet, S. Christeller, H. Airene, V. Krajnc, I. Morniroli, L. Müller, H. Fässler and T. Morger. Kantonsspital Basel, and Sektion für mathematische Statistik, Hoffmann-La Roche, Basel, Switzerland.

Success and side effects of oral anticoagulation depend on the degree of anticoagulation achieved in the patients. Many physicians are not aware that the therapeutic ranges are different with different thromboplastins. We have compared 13 commercial thromboplastins and a human brain preparation on 100 patients on long term phenprocoumon therapy. Simultaneous sample collection and assays in triplicate for all methods followed exactly the manufacturers' recommendations. Six comparison systems were based on percentage values derived from both manufacturers' and our own standard curves, on clotting time ratios and on the established reference ranges, 15 to 25% with human brain and 5 to 10% with Thrombotest. The statistical analysis included variations of the reference methods and models for linear structural relationships. The data show that the lower limit of the therapeutic range varies widely between 5 and 25% and the upper limit between 10 and 35% for the commercial preparations tested. This study offers the great advantage of a direct comparison of a large number of widely used preparations and allows a much better estimation of the error of each method. It is pointed out that the analysis is only valid for a narrow range where the relationships are truly linear.

COAGULATION AND IMMUNOLOGICAL INVESTIGATIONS IN COMBINED FACTOR V AND FACTOR VIII DEFICIENCY. J. C. Giddings, U. Seligsohn* and A. L. Bloom. University Hospital of Wales, Cardiff, U.K. and *The Chaim Sheba Medical Center, Tel-Aviv University, Israel.

Plasma samples were obtained from patients of two families with inherited combined deficiency of factor V and factor VIII and examined by coagulation and immunological methods for the presence of factor V and factor VIII related antigens. A deficiency of procoagulant factor V was confirmed in all patients although a factor V related antigen was consistently demonstrated in all plasma samples by an inhibitor neutralisation technique using a non precipitating rabbit antibody. A deficiency of procoagulant factor VIII was also confirmed in all patients and factor VIII related antigens were detected by inhibitor neutralisation using human antibody and by electroimmunoassay using a precipitating rabbit antibody. The amounts of factor V and factor VIII related antigens present in the patient's plasma samples were similar to those found in normal human plasma. Ristocetin co-factor assay using washed, fixed human platelets was normal in all patients. The results suggest that inactive antigenic determinants of procoagulant factor V and factor VIII are present in the plasma of these patients and are consistent with the possibility that a common precursor of factor V and factor VIII is defective in these families.