THE EFFECT OF PROCOAGULATIVE PHOSPHOLIPIDS ON THE SYNTHETIC SUBSTRATE DETERMINED THROMBIN GENERATION IN VITRO. F. Schulte, O. Klug, Ursula Roth. Hormon-Chemie München, Munich, Germany.

The effect of procoagulative phospholipids (Procops) with platelet factor-3 like activity on the generation of thrombin in plasma can be determined in vitro with the aid of synthetic chromogenic substrates. Standard citrated plasma of two manufacturers and from different batches incubated with amounts of 2-10 mcg Procops as 1:100 - 1:500 diluted Tachostyptan (micellar Procops in form of a pharmaceutical speciality) was activated. The generated amount of thrombin activity catalyses the hydrolysis of chromogenic substrate to a tripeptide and to p-nitroaniline which was measured kinetically with a spectrophotometer at 405 nm. At optimum concentrations of Procops, activities adequate to 80 (SD + 7, VK 8.8%) - 115 i.u. (SD + 2.5, VK 2.2%) thrombin per ml plasma were measured depending on the conditions of incubation and activation. Having made the basis of appropriate procedures for incubation and activation the in vitro effect of Procops on the thrombin generation in plasma is reproducibly measurable with the aid of chromogenic substrate.

THROMBOREGULATION BY PLATELET PHOSPHOLIPID FATTY ACIDS: EFFECT OF DIETARY LINOLEATE. G. Hornstra. Unilever Research, Vlaardingen, The Netherlands

It is thought that fatty acids, released from certain platelet phospholipids regulate the platelet release reaction and, thereby, thrombus formation. Arachidonic acid (AA) has been shown to be of major importance in this respect, since it is converted by the cyclo-oxygenase (CO-) system to release-inducing substances. However, the AA-CO interaction is inhibited competitively by other poly-unsaturated fatty acids such as linoleic acid (LA). This implies that the ultimate thrombotic response will depend on the ratio between AA and competing fatty acids, released upon platelet activation and, consequently, on the fatty acid composition of certain platelet phospholipids.

In rats, the ratio between AA and LA from platelet phosphatidylcholine is found to be negatively related to the dietary LA content. Since phosphatidylcholine has been shown to be the main source of AA, this finding may explain the well-established anti-thrombotic effect of dietary linoleate.

THE EFFECT OF ENDOTOXIN ON HAEMOSTASIS IN NORMAL AND LEUKEMIC RATS

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Platelet count, fibrinogen and antithrombin levels were studied in normal rats (group A), in rats with the experimental rat leukemia L 5222 in an early phase (group B) and in a final phase (group C) of the disease. The animals were randomized and treated with 0.5 mg endotoxin or placebo as a single i.v. injection. Four hours later blood samples were taken for laboratory tests. The results were as follows: 1. Groups A and B did not differ in the laboratory parameters under investigation 4 hours after injection of saline as a placebo. 2. Leukemic rats of group C treated with saline had significantly elevated levels of fibrinogen and antithrombin as well as reduced platelet count compared to their normal counterparts. 3. The injection of endotoxin resulted in a comparable decrease of platelets in normal and leukemic animals. 4. The injection of endotoxin led to a decrease of fibrinogen levels in all groups. The most pronounced decrease was observed in group B, while there was only a slight fall in group C. The antithrombin levels of group A and B were not influenced by endotoxaemia. The elevated level of antithrombin in group C, however, was completely normalized after a single injection of endotoxin.

It can be concluded from these results that the haemostatic system of rats in the early phase of the leukemia L 5222 is more susceptible to endotoxin than that of normal controls. Possibly due to marked elevated levels of antithrombin rats in the final phase of the disease seem to be protected against the aggravation of the haemostatic defect by endotoxin.