

**INFLUENCE OF ELASTASE ON BLOOD COAGULATION FACTORS: STUDIES IN VITRO, IN RATS AND IN GÖTTINGER MINIATUR PIGS.** U. Kaster\*, U. Artmann, T. Kaethner, H. Burchardi and H. Köstering. Univ. of Göttingen, Dept. of Internal Medicine and Dept. Anaesthesia, Göttingen, W-Germany

The influence of blood coagulation factors in pat. with acute respiratory insufficiency of adults, especially of the so called "pancreatitis lungs" is still unknown. In order to find out the effect of elastase, possibly activated by trypsin in pat. with acute pancreatitis, on blood coagulation factors, we performed some studies. In vitro elastase induces in plasma and blood in correlation to the dosages enhancement of thrombin generation in the TGT, a shortening of PTT, Thrombin time and of r- and k-time in the TEC, a loss of fibrinogen and an increase of fibrin monomer complexes. In another study, elastase (960 U/kg b.w.) was injected intravenously in rats. 30 min. later there was found a loss of fibrinogen, number of platelets, Prothrombin and a prolongation of PTT and Thrombin time and an increase of fibrin monomer complexes, especially in these rats, which received beside elastase Kalikreininhibitors or antifibrinolytic drugs. After repeated injections (5 times within 50 h) we found histomorphologically thrombi as well as bleeding complications. In another study we performed (150 min) an infusion of elastase (333 U/kg b.w./h) to 9 pigs. We determined a loss of fibrinogen of platelets, of F. II, F. VII and F. XIII, a prolongation of PTT, F. VIII and F. V remained within the normal range. But there was found an enhancement of Thrombin generation in the TGT, too. Comparing the results of blood coagulation tests and of histomorphological findings, elastase induced a DIC. We have to discuss their influence on ARIA and "Pancreatic lungs".

**A NEW FACTOR CONTROL PLASMA FOR ESTABLISHING CALIBRATION CURVES FOR FACTOR-ASSAY IN EXTRINSIC AND INTRINSIC SYSTEM.** R. Spaethe, A. Lampart\*, M. Naumann, J. Strauss. Scientific Department of the American Hospital Supply Deutschland GmbH, Munich, Federal Republic of Germany.\*Merz + Dade AG, Duedingen, Switzerland.

We present a lyophilised human plasma which is optimal for calibration curves and factor control in extrinsic as well as in intrinsic system. Comparative assays were carried out between factor control plasma and a fresh plasma pool which was frozen at  $-70^{\circ}\text{C}$  from 15 normal young men. The fresh plasma pool and the factor control plasmas for the calibration curves were diluted with Owren's veronal buffer pH 7,35 in a geometric sequence. All deficiency plasmas (American Dade, Division of American Hospital Supply Corporation) were used according to the instructions of the manufacturer. All assays were carried out by two independent investigators.

For the extrinsic system Thromboplastin C and FS (American Dade) were used. With this thromboplastin the calibration curves for the fresh plasma pool and the factor control plasma showed an identical course when plotted semilogarithmically. The calibration curves for the factors II, V, VII, and X showed a good correlation to normal plasma pool.

For the intrinsic system the PTT-reagent Actin (American Dade) was used. The measuring times for the calibration curves of the factor control plasma are slightly longer than of the fresh plasma pool.

When factors determined in factor control plasmas are read from the fresh plasma calibration curves, the range of normal values is from 90 to 105% for the factors in extrinsic system and from 80 to 105% in intrinsic system. According to these assessments, the factor control plasma seems to be appropriate for establishing calibration curves for factor assays as well as for calibration of thromboplastin time. This is a contribution to further standardization of coagulation assays.

**EFFECT OF T-2 MYCOTOXIN ON THE COAGULATION MECHANISM.** P.A. Gentry and M.L. Cooper. Department of Biomedical Sciences, Ontario Veterinary College, University of Guelph, Guelph, Ontario, Canada.

Corn and wheat stored under low temperature conditions can become contaminated by the mold *Fusarium Trincinctum*. Animals affected with corn toxicosis develop symptoms of epistaxis, anorexia and hemorrhagic lesions of the intestinal and urinary tracts. Controversy exists concerning which of the several metabolites produced by the mold is responsible for the hemorrhagic syndrome. Studies from this laboratory have shown that one of the metabolites produced by the fungus, T-2 toxin (4,15-diacetoxy-8-[3 methylbutyloxy]-12, 13-epoxy- $\Delta^3$ -tricothecene-3-ol), can induce a prolongation of the plasma clotting time when determined by either the activated partial thromboplastin time assay or the one stage prothrombin time assay. A single intravenous administration of T-2 toxin to either rabbits or calves, at a dosage of 0.50 and 0.25 mg per kg body weight respectively, results in a decrease in the plasma activity of Factors VII, IX, X and XI of 40-50 percent of pre-treatment values. The maximal decrease in activity is observed 24 hrs after toxin administration and the activity remains depressed for the next 48 hrs before gradually returning to initial values. Plasma fibrinogen concentration decreases from 498 gm/l to 395 gm/l by 24 hours and to a minimum of 351 gm/l by 54 hrs before showing a partial recovery. Platelet counts remain unchanged. Preliminary data indicate that the T-2 toxin does not act directly as a vitamin K antagonist in producing the alteration in procoagulant activity.

**BLOOD COAGULATION DISTURBANCES DURING OLIGURIA AND POLYURIA OF ACUTE RENAL FAILURE IN MAN.** J. Schrader, H. Köstering, H. Kaiser, P. Kramer and F. Scheeler. Department of Nephrology, University Medical Clinic, Göttingen, W.-Germany.

The blood coagulation system makes a significant contribution to renal damage in many disease processes. Intrarenal coagulation appears to occur in a wide variety of diseases as a primary or secondary event. As there is evidence that intraglomerular coagulation is a significant factor in the development and maintenance of oliguria in acute ischemic renal failure, blood coagulation investigations were performed in 20 patients with acute renal failure of varied etiology. The investigations were done on a daily basis from the onset of oliguria (urine flow  $<20$  ml/h) until serum creatinine declined to less than 2,0 mg%. Thus, we were able to detect changes in blood coagulation during oliguria and polyuria. We found an enhanced thrombin generation in both oliguria and polyuria. Fibrin monomer complexes were significantly increased in both states, but more predominantly in polyuria. Factor VIII and alpha-1 antitrypsin activities were also elevated. PTT and r- and k-time in TEG were shortened more in polyuria than in oliguria, whereas fibrinogen was elevated more in oliguria than in polyuria. Factor XIII activity and prothrombin complex activity (Quick's test) were lowered in both states, the lowest values of the former being found in polyuria, the lowest values of the latter in oliguria with a normalizing tendency in the following days. Fibrinolytic activity was also decreased. No significant changes were found in plasminogen, antithrombin III, alpha-2 macroglobulin, factor V and thrombin time. In summary, we found a hypercoagulability in these patients with acute renal failure, which was more predominant during polyuria and which correlated with the tendency to thrombosis and to shorter dwelling periods of i.v. catheters in this state. Consequently, the changes in blood coagulation of 3 patients with acute postrenal failure were not as significant as those found in the other patients. The treatment with anticoagulants in patients with acute renal failure will be discussed.