## 405 INHIBITION OF FIBRINOLYSIS IN ENDOTOXIN SHOCK OF THE PIG

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Fibrin deposites play an important role in the pathophysiology of ARDS. We used an endotoxin shock of the pig (10µg/kg.h lipopolysaccharide from S.abortus equi for 6 h) to follow up plasma levels of t-PA, PAI and fibrin monomers (fm) in an experimental model of this disease. Previous described functional tests of t-PA, PAI and fm were modified for porcine plasma. 9 pigs received endotoxin compared to 3 control animals receiving physiologic NaCl solution.
We found a 10-fold increase of t-PA activity after 2 hours (3 IU compared to human melanoma t-PA) followed by plasma levels below starting point. PAI and fm showed a continuous increase until the end of experiment(PAI: 25 ± 9 to 91 ± 11 arb. units; fm: 61 ± 43 to 458 ± 101 ng/ml ). Basic levels of these parameters were not influenced by NaCl infusion in the controls.
We conclude that functional determinations of t-PA, PAI and fm are helpful to investigate the role of fibrinolytic activator and inhibitor capacity in septic shock. Fibrinolysis seemed to be impaired by exhaustion of t-PA and increase of PAI.

## 406 PLASMINOGEN ACTIVATORS AND INHIBITORS IN RABBIT CONNECTIVE TISSUES

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The medial collateral ligament (MCL), anterior cruciate ligament (ACL), patellar tendon (PT), and achilles tendon (AT) of immature, adolescent and mature rabbits were assayed for plasminogen activator (PA) using previously described caseinolytic and zymographic assays. Zymographic analysis detected one major band of PA activity corresponding to a high molecular weight urokinase (HMW UK) (Mr = 48,000). An additional band of activity at 88,000 daltons was shown to consist of a complex between HWM UK and a 40,000 dalton binding protein. Leupeptin was shown to inhibit complex formation, thus implicating interaction of the binding component to the active site of enzyme. The caseinolytic assay demonstrated PA activity to vary along the length of both the MCL and ACL with higher activity at the ligament insertions as compared to the midsubstance. This polarity in PA activity was maintained when the outer synovial lining on the ligaments was removed. In contrast, the PT and AT showed no polarity and quantitatively lower PA activity. As the rabbit matured, the PA pattern was unaltered, however, the level of PA activity increased with age in all the connective tissues studied. Urokinase-type PA expression in connective tissues could be altered by the environment in that immobilization or exercise of the limb has been shown to decrease and increase u-PA activity respectively. These results indicate that these connective tissues, particularly the ligaments, are dynamic systems and that PA expression by these tissues may be actively involved in maintaining homeostasis through modulation of matrix components. (Supported by the Canad. Arth. Soc., the Alberta Children's Hospital and AHFMR).

## 407 PMN-ELASTASE RELEASE BY BETA-FXIIa AND THE EFFECT OF INCREASED C1-INHIBITOR LEVELS

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It is known that the addition of beta-FXIIa to plasma leads to an increase in plasma kallikrein levels. In order to study the changes in PMN-elastase levels we added 150 ug beta-FXIIa to 500 ml of human plasma. In these experiments FXII levels were not significantly altered, whereas prekallikrein levels fell from 43% to 37% after the infusion of this enzyme. Kallikrein like activities increased immediately after beta-FXIIa administration from 51 U/l to 78 U/l. Elastase-alpha-1-proteinase-inhibitor-complexes rose significantly from 111 ug/l to 1482 ug/l.
In order to establish successful therapy C1-inhibitor levels were increased by the addition of 1500 plasma units of C1-inhibitor to plasma before enzyme infusion.
Concerning components of the kallikrein-kinin-system and elastase-alpha-1-proteinase-inhibitor complexes changes seen in these series were not significantly different to experiments without enzyme administration. These results suggest that in clinical situations with contact activation infusion of C1-inhibitor might be a helpful therapy.