1068 ENDOTHELIAL RECEPTOR-MEDIATED CLEARANCE OF THROMBIN: COMPARISON WITH TWO ACTIVE SITE-INHIBITED DERIVATIVES.

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Thrombin binds to a receptor on human umbilical vein endothelial cells in vitro (Awbrey, B., Hoak, J., and Owen, W., J. Biol. Chem. in press). We studied the fate of ^{125}I-thrombin and diisopropylfluorophosphoryl-^{125}I-thrombin (DIP-^{125}I-thrombin) in rabbits to determine whether the thrombin receptor plays a role in removing thrombin from the circulation. One unit of DIP-^{125}I-thrombin, or ^{125}I-thrombin was injected rapidly into the ear vein or carotid artery. When injected via either route, 70% of ^{125}I-thrombin and 90% of DIP-^{125}I-thrombin disappeared from the circulation within one minute. Clearance of either active or DIP-thrombin was inhibited by prior injection of excess unlabelled DIP-thrombin. DIP-thrombin given intra-arterially was found in organs in proportion to their blood supply. Both DIP-thrombin and thrombin given intravenously went predominantly to the lungs with subsequent removal to other organs. Thrombin, however, had a shorter half-life in the lung than DIP-thrombin (2.5 vs 25 minutes). Intravenous p-guanidino-benzoyl thrombin, which is a reversible acyl-enzyme complex (half-life for dissociation at 37° of 8 min), had a half-life in the lung of 5 min. The rapid uptake of both thrombin and DIP-thrombin by vascular beds and the saturability of the process support the hypothesis that the thrombin receptor is involved in the clearance mechanism. The rapid exchange of active thrombin, after its initial deposition, may reflect interaction with plasma components.

1069 ACUTE PANCREATITIS IN MAN AND BLOOD COAGULATION DISTURBANCES

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The pathogenesis of blood coagulation-disturbances in patients with acute pancreatitis in man is still unknown. Therefore we studied repeatedly the blood coagulation system of all patients with acute pancreatitis, who were admitted to our clinic or were transferred from other hospitals after complications occurred. 19 patients with a severe pancreatitis were studied. Most of them showed oliguria, pancreatic lungs, thrombosis or haemorrhage. Only 9 determinations (in 5 patients) resulted an enhancement of thrombin generation in the Thrombin-Generation-Test (TGT). All the other patients showed already hypocoagulability in the TGT and severe signs of DIC and consumption coagulopathy with a loss of platelets, fibrinogen and prothrombin complex. In 9 patients, who died, we found histomorphologically fibrin deposites and hyaline thrombi. In comparison to 58 patients with elevated amylases but no severe pancreatitis we found, that the initial alteration of blood coagulation system in pancreatitis is a hypercoagulability, possibly caused by trypsin, phospholipase A or elastase.

1070 THE EFFECT OF HALOTAN AND ETHER ANAESTHESIA ON SOME PARAMETERS OF BLOOD CLOTTING AND FIBRINOLYSIS.

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The effect of anaesthesia with halotan and ether /100 and 80 cases respectively/ on some parameters of blood clotting and fibrinolysis was investigated. The influence of the drugs on blood clotting and fibrinolysis in vitro was also investigated. Halotan anaesthesia caused decrease in fibrinogen, prothrombin, factor V and number of platelets. Platelet adhesiveness was increased. Ether anaesthesia increased fibrinolytic activity and platelet stickiness. Halotan in vitro shortened r + k and prolonged ma in TEG. The both drugs induced reversible platelet aggregation with subsequent "refractory state" of platelets to ADP. Ether in vitro increased fibrinolytic activity. The results show that the influence of anaesthetic drugs on blood clotting and fibrinolysis should be taken into account in the choice of the proper anaesthetic in patients with impaired haemostasis.