ties. Disc electrophoretic resolution was carried out on columns of polyacrylamide gel[10] containing 0.15 *M* e-aminocaproic acid.

Results and discussion. The electrophoretic profile in Figure 1 shows that purified human plasminogen (1 mg/ml) at pH 6.5, and after incubation at 25 °C for 30 min migrated as a single polydisperse major zone (profile A). When incubated with porcine heart plasminogen activator (0.01 mg/ml) at pH 6.5, the human plasminogen migrated in at least 4 zones (profile B). When porcine heart DNA-human plasminogen complex was incubated with porcine heart plasminogen activator, the mixture migrated in at least 2 zones. Profile C of Figure 1, shows also reduced number of migrating zones, indicating limited activator activity. Under these experimental conditions, with the quantities used, the porcine heart activator was not detected on the polyacrylamide gel.

Progressive decrease in the release of caseinolytic activity is seen in Figure 2, curve a, where 3 μg of porcine heart plasminogen activator was added to incubation solutions of human plasminogen and increasing amounts of porcine heart DNA. Stronger inhibition of the release of caseinolytic activity is shown by curves b and c, where 5 μg and 30 μg of the plasminogen activator were added.

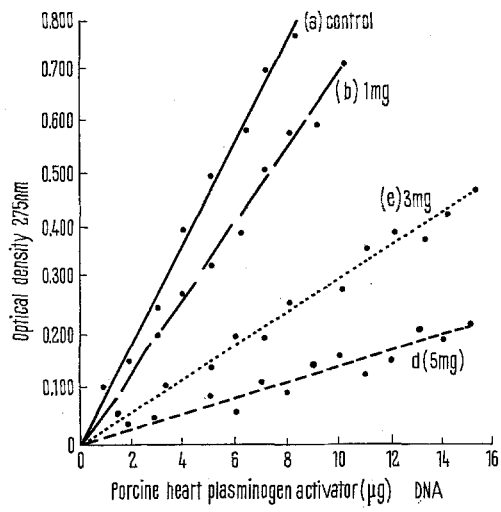

Fig. 4. Inhibition of porcine heart activator-activation of human plasminogen by porcine heart DNA. Human plasminogen was first incubated with 1, 3, and 5 μg of porcine heart DNA to 1 mg of human plasminogen, at pH 6.2 and 25 °C for 30 min. Increasing quantities of the porcine heart plasminogen activator was then added. Incubation was continued for additional 30 min. The esterolytic (LMe) hydrolytic activity of each was finally determined[9].

The inhibitory effect of increasing amounts of porcine heart DNA on the catalytic release of esterolytic (LMe) activity from human plasminogen is shown in Figure 3. Progressive inhibition of plasminogen activation followed by the assay of the activated enzyme, plasmin activity released from the action of 3, 15 and 20 μg of porcine heart plasminogen activator indicate possible complex DNA-plasminogen formation. The esterolytic activity of plasminogen-activator-activated human plasminogen in 30 min incubated solutions is a function of the concentration of the activator. However, the esterolytic activity decreases by the addition to the plasminogen solution of porcine heart DNA. The degree of inhibition depends on the ratio of plasminogen to DNA. The inhibitory effect of DNA on the release of esterolytic activity from human plasminogen is shown in Figure 4.

The results described could be interpreted as follows: Human plasminogen combined with porcine heart DNA forming a complex. The formation of this new class of DNA complexes was first suggested by the work of HOFSTEE[11] in which he described the ability of chymotrypsinogen to form soluble stoichimetric complexes with DNA. The present preliminary observations demonstrated the formation of plasminogen-DNA complexes, and suggested the ability of the DNA to protect the zymogen from the action of a tissue plasminogen activator. Studies are in progress aimed at the ability of the DNA in the complex to protect the zymogen from the action of various plasminogen activators.

Résumé. Les résultats de ces études démontrent la formation de «complexes» entre l'acide désoxyribonucléique et la plasminogène. L'acide désoxyribonucléique inhibe l'action catalytique de la plasminogène humaine sur la plasmine.

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Fibrinolytic System, Fibrinogen Degradation Products and Soluble Fibrin Monomer Complexes of Renal Venous and Aortal Blood

Renal venous blood obtained from rabbit, dog or man during surgery by direct puncture under general anaesthesia shows an elevated fibrinolytic activity[1–3]. High values of fibrinogen degradation products (FDP) were found[3] in dog renal blood obtained by venous puncture. These experiments suggested an enhanced continuous fibrinolysis originating in renal vessels. A continuous secretion of plasminogen activator into the systemic circulation was postulated.

Recently several investigators found that renal venous blood obtained by selective catheterisation had a slightly higher fibrinolytic activity than arterial and peripheral venous blood[4,5]. The comparison of these literature data indicates that renal venous blood obtained by direct puncture always showed much higher fibrinolytic activity than the renal venous blood obtained by catheterization.

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Fibrinolytic system FDP and SFMC in aorta and renal venous blood

	Area of circulation Aorta		Left kidney vein		Right kidney vein	
	M	S.D.	M	S.D.	M	S.D.
Fibrinogen mg/100 ml	297	±147	302	±147	320	±106
Euglobulin fibrinolysis min	200	± 84	196	± 84	196	± 81
Plasminogen units	0.83	± 0.23	0.80	± 0.15	0.87	± 0.15
Antiplasmin % inhibition	30	± 13.3	38	± 13.2	33	± 11.6
Thrombin time sec	17	± 2.14	17	± 2.70	17	± 1.77
Antithrombin VI time sec	29	± 2.8	29	± 2.1	29	± 2.6
PS precipitate from plasma O.D.	0.38	± 0.16	0.37	± 0.14	0.38	± 0.14
PS precipitate from serum O.D.	0.08	± 0.02	0.08	± 0.018	0.09	± 0.014
Staphylococcal clumping titer	18.3	–	13.4	–	13.1	–
FDP titer immunoassay	3.7	–	4.0	–	3.7	–

M, mean values of 13 determinations and standard deviation.

Our recent studies[6,7] demonstrate that renal venous blood obtained by very cautious catheterization has the same fibrinolytic activity as peripheral venous blood. In the present paper our earlier study was completed by determination of fibrinolytic activity, FDP and soluble fibrin monomer complexes (SFMC) level in blood drawn from aorta and renal veins by catheterization.

13 patients with arteriosclerosis (2), renovascular hyper tension (6), pyelonephritis (1), obesity (1), hypertensive disease (2) and colon cancer (1) were examined. The catheters were introduced through the femoral arteria and femoral vein respectively according to the SELDINGER's method[8]. Serum and citrated or oxalated plasma were obtained by immediate centrifugation and deeply frozen (−50 °C). All tests were performed simultaneously. Fibrinogen was determined according to QUICK[9], euglobulin fibrinolysis by the methods of KOWALSKI et al.[10], antiplasmin by the method of HAGAN et al.[11], plasminogen was determined by the MITCHELL's method[12] and the results expressed in units according to ALKJAERSIG et al.[13].

Thrombin time and antithrombin VI time were examined according to WOROWSKI et al.[3]. The amount of SFMC in oxalated plasma and sera was evaluated using the turbidimetric method of LIPINSKI and WOROWSKI[14,15]. This method consists of selective precipitation of SFMC by protamine sulfate at final concentration of 0.1%. The increase of optical density at 6190 Å was recorded.

The amount of FDP and SFMC in blood sera were also evaluated by immunoassay[16] and by staphylococcal clumping method[17]. Results are presented in the Table. The values of fibrinolytic activity, fibrinogen, plasminogen, antiplasmin, FDP and SFMC found in aortal and renal venous blood were quite similar.

Our experiments do not support hypothesis of the prominent role of the kidney in the activation of fibrinolysis in the organism and in the continuous formation of FDP in the kidney circulation. These observations do not exclude the possibility that kidney may release a large amount of plasminogen activator into the circulation in such situations as stasis, stress, or vasodilatation. This would be in good agreement with HOLEMANS and MLYNARCZYK[18] who found a similar release of plasminogen activator following perfusion of both dog kidney and leg with histamine solution. Also MENON et al.[5] found elevation of fibrinolytic activity in kidney venous blood after perfusion with papaverin. It seems that discrepancies between the results of various experiments in which the elevated fibrinolytic activity in renal venous blood was or was not observed may be dependent on the technique of blood drawing. The degree of activation of fibrinolysis in renal venous blood may be connected with such factors as traumatization of the kidney vessels, stasis or stress. On the other hand, renal venous blood does not show, under physiological conditions, higher fibrinolytic activity than that of other areas of circulation. The physiological importance of local fibrinolysis in kidney tissue is not disproved.

Zusammenfassung. Im durch Katheterisierung gewonnenen Nieren- und Aortenblut wurden Euglobulinfibrinolyse, Fibrinogen, Plasminogen, Antiplasmin, Fibrinogendegradationsprodukte und deren lösbare Fibrinmonomerenkomplexe bestimmt. Signifikante Unterschiede bezüglich des Verhaltens sämtlicher Komponenten des fibrinolytischen Systems konnten in den untersuchten Gefässgebieten nicht festgestellt werden.

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