noted that the rise in plasma amino acid nitrogen of diabetic rats was markedly reduced by adrenalectomy. Cortisol restored and increased the rate of rise of plasma amino acids of adrenalectomized-diabetic rats. It was also noted that injection of adrenal steroids increases the free amino acid concentrations of liver[19] and muscle[17,20]. In the present investigation, riboflavin deficiency has been found to elevate the free amino acid nitrogen concentrations in liver as well as in plasma and muscle. It is therefore possible that, apart from accumulation of free amino acids in liver due to reduced oxidation of amino acids, there occurs mobilization of amino acids from the breakdown of peripheral tissue proteins, resulting in elevation of free amino acid nitrogen concentrations of liver, muscle and plasma in riboflavin deficiency. This is probably effected by the increased adrenal cortical secretions in riboflavin deficiency[21].

Zusammenfassung. Männliche Albino-Ratten, 45 Tage bei riboflavinarmer Nahrung, zeigten erhöhten Gehalt freien Aminosäure-Stickstoffs in Leber, Muskel und Plasma. Die Erhöhung scheint durch eine gesteigerte Aktivität der Nebennierenrinde beim Riboflavinmangel herbeigeführt zu sein.

A. K. Chatterjee and B. B. Ghosh

Department of Physiology, University College of Science, Calcutta-9 (India),
8 March 1968.

[19] H. N. Christensen, in *Mammalian Protein Metabolism* (Ed. H. N. Munro and J. B. Allison; Academic Press Inc., New York 1964), vol. 1, p. 113.
[20] S. A. Kaplan and C. S. N. Shimizu, Endocrinology *72*, 267 (1963).
[21] Acknowledgment. The authors wish to express their sincere gratitude to Prof. S. R. Maitra, Head of the Department of Physiology, Calcutta University, for constant encouragement and for providing the laboratory facilities. They also acknowledge the financial assistance rendered by the Ministry of Education, Government of India.

The Kidney and Fibrinolysis in Man

It is commonly known that oxygen consumption by the kidney is very high. Both histochemical studies and determinations in renal homogenates revealed the highest known activity of various enzymes in renal tissue. The presence of a potent trypsine inhibitor and a plasminogen activator (urokinase) was demonstrated in urine, both being supposedly produced by the kidney. All these circumstances justified an idea of a possible role of the kidney in maintenance and regulation of blood fibrinolytic activity. When Buluk et al.[1,2] demonstrated in rabbits the potent effect of the ureter obstruction or of renal ischaemia on the fibrinolytic activity in venous blood from the corresponding kidney, we decided to study this problem in man.

It was done in 2 different ways: (a) the blood plasma fibrinolytic activity and urinary plasminogen activator were determined in a large group of patients with various renal diseases and compared to those in healthy subjects. (b) Direct determinations of fibrinolytic activity in the blood plasma from renal veins.

The urokinase was determined according to the procedure described in another paper[3] while the plasma fibrinolytic activity in the euglobulin fraction according to Kowalski et al.[4]. In the first series it was found[3] that no distinct difference in blood plasma activity occurs between the healthy subjects and most of those with renal disease. In uraemia and nephrosis the fibrinolytic activity was decreased ($p < 0.01$). The urokinase elimination, however, decreased distinctly ($p < 0.01$) in chronic glomerulonephritis, nephrosis and uraemia (Figure 1). A similar phenomenon seemed to appear in renovascular obstruction but the small number of patients did not allow a convincing evaluation.

In the second series the blood was drawn by veinpuncture in patients operated on because of a unilateral renal disease (hydronephrosis, TB, nephrocirrhosis). The plasma fibrinolytic activity in cubital and renal veins (the latter on the side of the lesion) was determined. The urine from the sick kidney was taken by the pelvic puncture while from the other it was collected through a catheter inserted after the opposite ureter had been ligated. We were not able to demonstrate any difference in the fibrinolytic activity between the renal and the cubital veins while the urine from the damaged kidney showed much lower content of the urokinase than that from the healthy one (Figure 2).

After some pilot experiments we abandoned further study and these data have not yet been published, because – facing convincing and opposite results of Buluk research – we had many doubts as to the technique of our experiments; it is well understandable that during surgical procedure the kidney and its vessels were maltreated, our approach was difficult and all was done in a hurry in order not to disturb the surgeons.

Now, after many years we have returned[5] to the problem when a modern technique of selective catheterization of various vessels has become available. We took the opportunity of catheterization performed in order to assess the renin activity in 17 patients suspected to have reno-vascular hypertension. The renal artery obstruction was previously demonstrated by selective arteriography and the % of artery narrowing was calculated. Two catheters were inserted in both renal veins, the third in the hepatic vein and the fourth in the vena cava just above its bifurcation. The details of the procedure are reported in the paper by Kokot et al.[6]. They have found the typical behaviour of renin activity in horizontal and

[1] K. Buluk and M. Furman, Experientia *18*, 146 (1962).
[2] K. Buluk and M. Malofiejew, Acta physiol. pol. *14*, 371 (1963).
[3] A. Nowak and B. Zahorska-Markiewicz, Polskie Archwm Med. wewn. *35*, 653 (1965).
[4] E. Kowalski, M. Kopeć and S. Niewiarowski, J. clin. Path. *12*, 215 (1959).
[5] A. Nowak, F. Kokot, J. Dosiak and Z. Czekala, in preparation.
[6] F. Kokot, J. Kuska, Z. Czekala and A. Nowak, Z. inn. Med., in press.

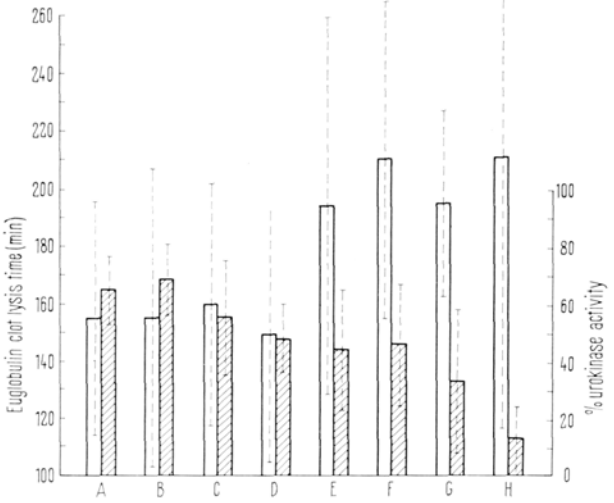

Fig. 1. Fibrinolytic blood activity (open area), and urokinase content in urine (shadowed area) in: A, 32 healthy subjects; B, 6 cases of acute glomerulonephritis; C, 13 cases of pyelonephritis; D, 10 chronic glomerulonephritis; E, 9 nephroso-nephritis; F, 14 nephrosis; G, 11 reno-vascular disease, H, 20 uraemia.

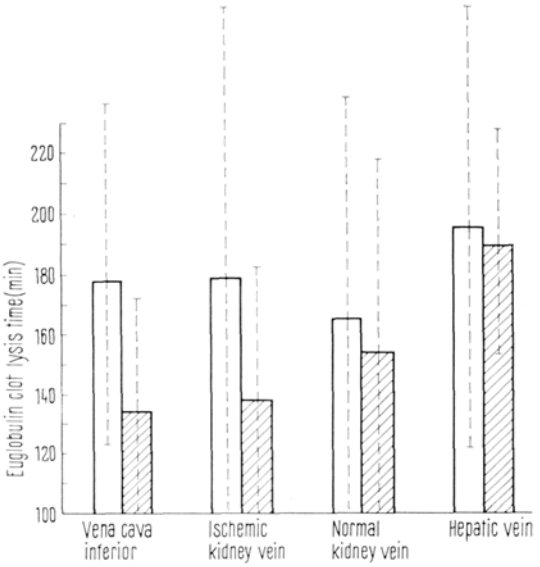

Fig. 3. Fibrinolytic activity in the blood samples simultaneously taken by selective catheterization. Open area: first sample taken in the horizontal position (mean values from 17 patients). Shadowed area: second sample drawn after 30 min of tilting to 80° (mean from 9 cases).

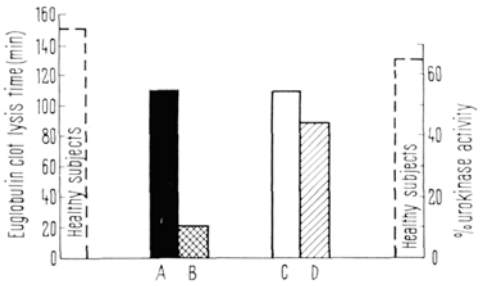

Fig. 2. (C), fibrinolytic activity in the blood drawn from cubital vein and (A) from the damaged kidney (3 cases). (D), urokinase in the urine from the healthy kidney and (B) from the sick kidney (9 cases).

vertical positions as is known in the unilateral kidney ischemia.

No distinct difference was found, however, in the plasma fibrinolytic activation between both renal veins, vena cava and hepatic vein (Figure 3). Neither did tilting of the patient produce a higher elevation of this activity on the side of ischemia than in the other kidney. The same range of activation was found in the blood drawn from vena cava. However, the return to the normal plasmin activity in the blood that passed through the liver was a constant and significant phenomenon. No interrelation was found between the renin and fibrinolytic activities in the same blood samples from those patients.

The possible significance of plasminogen activation by a renal activator as well as its potentiation due to the ischaemia, recently became the starting point for a new conception of the possible mechanisms of renovascular hypertension[7,8]. We cannot support it nor are we able to admit a prevalent role of the kidney in the maintenance and regulation of plasma fibrinolytic activity in man. The liver seems to play an important role in restoring the elevated fibrinolytic activity to normal limits.

Contrary to seemingly non-eminent role of the renal activator in the regulation of fibrinolysis in the blood, its secretion on the other side of the renal barrier, i.e. to the urine, is clearly demonstrable. So in man the renal activator passes easily into the urine (when it is named urokinase) but vanishes from there in serious kidney lesions; maybe it does not penetrate so easily into blood circulation and cannot play there a major role in the regulation of the fibrinolytic activity. Some evidence exists that the activator secreted into the blood is different from that secreted into the urine[9,10,11].

Zusammenfassung. Während Nierenoperationen vorgenommene Messungen ergaben, dass eine in der Funktion stark eingeschränkte Niere weniger Urokinase in den Urin ausscheidet, ohne dass jedoch die fibrinolytische Aktivität im Venenblut zunimmt. Es wird daraus geschlossen, dass die Nieren keine erheblichen Mengen Plasminogen-aktivierender Stoffe an das Blut abgeben.

K. Gibiński and A. Nowak

3rd Medical Clinic, Francuska 20, Katowice (Poland),
25 March 1968.

[7] J. Prokopowicz, K. Worowski, A. Poplawski, M. Myśliwiec and S. Niewiarowski, Experientia *23*, 224 (1967).
[8] S. Niewiarowski, J. Prokopowicz, K. Worowski, A. Poplawski and Gabryelewicz, Thromb. Diath. haemorrh. *17*, 1 (1967).
[9] Ch. Kuciński and A. Fletcher, Fedn Proc. Fedn Am. Socs exp. Biol. *25*, 194 (1966).
[10] D. McConnel, J. G. Johnson, R. Holemans and L. A. Cohen, Fedn Proc. Fedn Am. Socs exp. Biol. *25*, 194 (1966).
[11] This study was supported in part by a grant from the Polish Academy of Sciences. – The authors are deeply indebted to Dr. A. Szkodny for his valuable help in taking blood samples during surgery.