

ELEVATED AMINOPEPTIDASE ACTIVITY IN THE URINE
IN ACUTE RENAL FAILURE

F. Scheler and H. Bergmann*

The aminopeptidase is located similarly to the alkaline phosphatase in the luminal portion of the cytoplasm of proximal tubular cells (1,2). An increase of the activity of these enzymes in urine is to be expected if the proximal tubular cells are damaged. Indeed Amador et al. (3) have found an elevated activity of the alkaline phosphatase in urine in those patients with diseases of the renal parenchyma, such as acute and subacute glomerulonephritis, renal lupus erythematosus, renal infarction, and acute tubular necrosis. We mostly studied the aminopeptidase activity and excretion in urine in patients with different forms of acute renal failure, and with subacute and chronic glomerulonephritis and chronic pyelonephritis.

Aminopeptidase is defined as the enzyme or enzymes which are able to split l-leucyl-beta-naphthylamine. Beta-naphthylamine is measured after formation of a red dye with Echorot 3 GL. The activity is defined in mU/ml. (conforming to the International Union of Biochemistry). See details of method, deviations of method, influences of different urinary abnormalities in our earlier papers (4,6). In order to simplify the activity of enzymes in urine it will be expressed in percentage of normal. We found different increases of the aminopeptidase in acute renal failure and in subacute glomerulonephritis. We want to record our observations especially about the value of the urinary aminopeptidase activity in the diagnosis and prognosis of acute renal failure.

Figure 1 shows a characteristic course of acute renal failure induced by toxic influences. There is a high activity of aminopeptidase concentration and alkaline phosphatase concentration during the toxic influences (in this case the lesion occurred after the injection of contrast substances in a patient with reduced cardiac output). In the oliguric and the early polyuric phase the activities of both enzymes are at a low level. In this case a single injury was followed by an acute renal failure. In comparison we find only a small increase of the urinary aminopeptidase concentration in the course of the acute renal failure induced by postoperative circulatory shock (Figure 2).

These observations could be correlated with Oliver's findings (7). Toxic influences mostly induce proximal tubular necrosis; circulation shock induces diffuse tubularrhesis without important lesions of the proximal tubules. By the urinary aminopeptidase concentration we can obtain some information about the causes of acute renal failure if we can get the urine for examination early enough, that means immediately after the injury.

The urinary aminopeptidase excretion shows an increase at the same time as the urine volume and the clearance of creatinine (Figure 2). Evidently the enzyme remains in the temporarily damaged nephrons which do not produce urine at this time. When these nephrons (or at least a part of them) begin their urine production the enzyme excretion shows a marked increase. These observations may point to the fact that during the acute renal failure the polyuric phase begins because of the participation in urine

*From the Department of Medicine and of Dermatology, University Hospital, Gottingen.

production of the temporarily injured and temporarily functionless nephrons. For the diagnosis and prognosis the figure of the urinary aminopeptidase excretion doesn't give us any more information so that we need not consider it any more.

Generally patients with acute renal failure come to us in an advanced state of disease. If there is still an increase of the urinary aminopeptidase activity it means a complicated renal failure (Figure 3). A lasting high aminopeptidase concentration during the oliguric phase indicates the continuance of a morbidic agent or an additional injury, and must be considered as an unfavourable prognosis. Not only the activity of aminopeptidase in the urine but also the renal function have to be regarded. We have seen patients with an increase of enzymes in spite of an improvement of the renal function. There were often side effects of drugs (such as streptomycin, colistine, tetracycline) which produced an increase of the urinary aminopeptidase concentration. Indeed Wright and Welch ⁽⁸⁾ have found necrosis of the proximal tubular cells in rats by colistine. Such side effects of drugs have been found with or without an acute renal failure. We found such increases of the enzyme activity because of toxic influences also in chronic renal failure but seldom in patients with normal renal function.

Patients undergoing cardiovascular surgery, too, may have a high concentration of aminopeptidase without always having an acute renal failure. The injurious influences by haemolysis and other metabolic products may be the cause. Some results of patients with acute renal failure are summarised in Table I. It shows the highest urinary aminopeptidase concentrations in patients with a severe form of the condition. It shows that a prognostic statement is possible by the determination of the urinary aminopeptidase activity.

An elevated activity of aminopeptidase was found not only in the acute renal failure but also in the subacute glomerulonephritis. We find already very high values in an early state of subacute glomerulonephritis before renal insufficiency starts. The gradual course of subacute glomerulonephritis is reflected by the activity of aminopeptidase in the urine (Figure 4). The aminopeptidase concentration in the serum remains independent of urinary enzyme concentration at a constant normal level. These high values of enzyme activity demonstrate the early involvement of the proximal tubular cells, as demonstrated histological by fatty degeneration of the proximal convoluted tubules ⁽⁹⁾. Proximal tubular epithelial necrosis and regeneration has been found too in acute diffuse membranous glomerulonephritis ⁽¹⁰⁾. The determination of urinary aminopeptidase activity may give some help in separation of chronic renal insufficiency from acute inflammatory influences as will be found in acute and subacute glomerulonephritis.

A diminished activity of enzymes was found in patients with chronic glomerulonephritis and chronic pyelonephritis, also in the advanced uremic state (Table II). The cause may be the diminished number of nephrons.

The determination of the activity of aminopeptidase in urine, as of the alkaline phosphatase, may give some help of great value in the diagnosis and prognosis of an early renal failure. Moreover the determination of these enzymes in urine allows the early recognition of toxic influences to the proximal tubular cells before the development of diminishing renal function.

REFERENCES

1. Nachlas, M. M., Goldstein, T. P., Seligman, A. M. (1962). Arch. Biochem. 97, 223.
2. Gomori, G. (1954). Proc. Soc. exp. Biol. (N. Y.) 85, 570.
3. Amador, E., Zimmermann, Th. S., Wacker, W. E. C. (1963). J. Amer. med. Ass. 185, 953.
4. Scheler, F., Bergmann, H. (1963). Verh. dtsch. Ges. inn. Med. "69", 732.
5. Bergmann, H., Estrich, S., Scheler, F., Schmidt, M. (1963). Ärztl. Lab. 9, 255.
6. Bergmann, H., Scheler, F. (1964). Klin. Wschr. 42, 275.
7. Oliver, J., (1962) in Glomeruläre und tubuläre Nierenerkrankungen, Stuttgart: Thieme 128.
8. Wright, W. W., Welch, H. (1959/60). Antibiot. Ann. 61.
9. Garci - Cáceres, U. (1959). Amer. J., Path. 35, 755.
10. Allen, A. C. (1962). The Kidney: Medical and Surgical Diseases. II Edition, New York: Grand and Stratton.

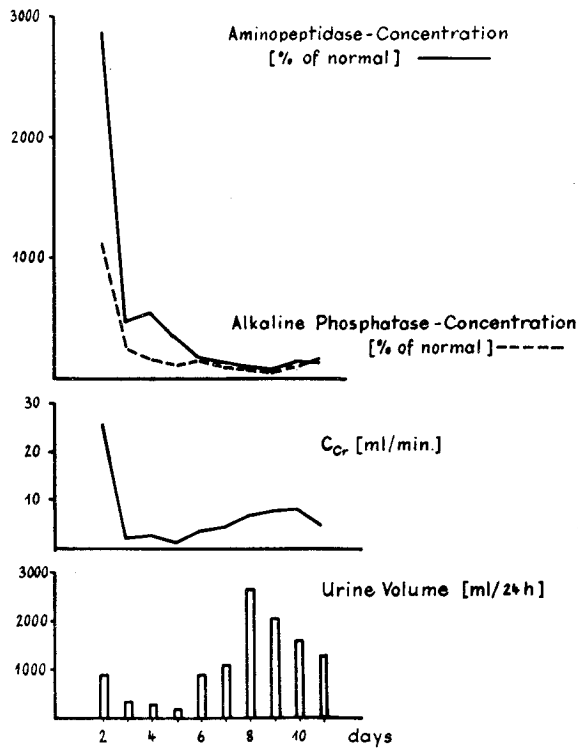


Figure 1. A single injury by injection of a contrast substance in a patient with diminished cardiac output produced acute renal failure. Marked elevation of enzyme activity in urine only at the beginning.

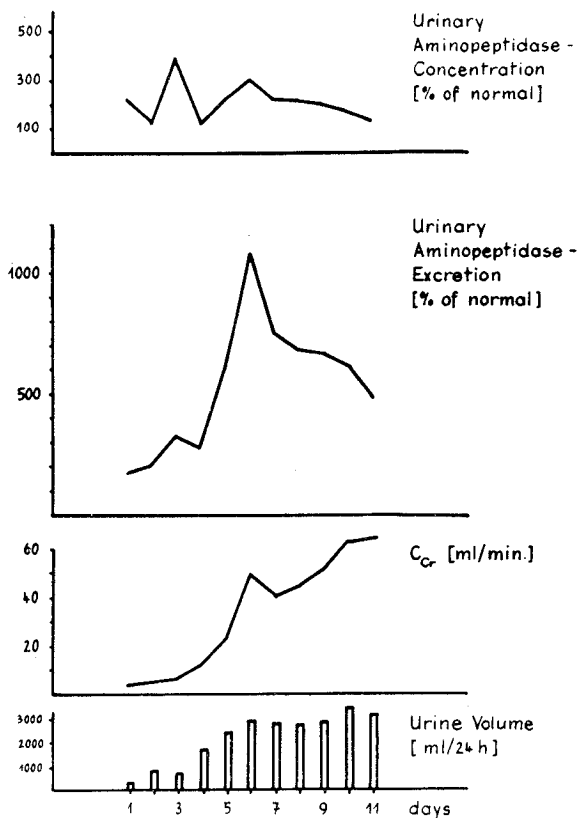


Figure 2. Only small increase of urinary aminopeptidase activity in acute renal failure induced by postoperative circulatory shock. Increase of enzyme excretion with the beginning of polyuric phase and increase of the endogenous Creatinine-Clearance.

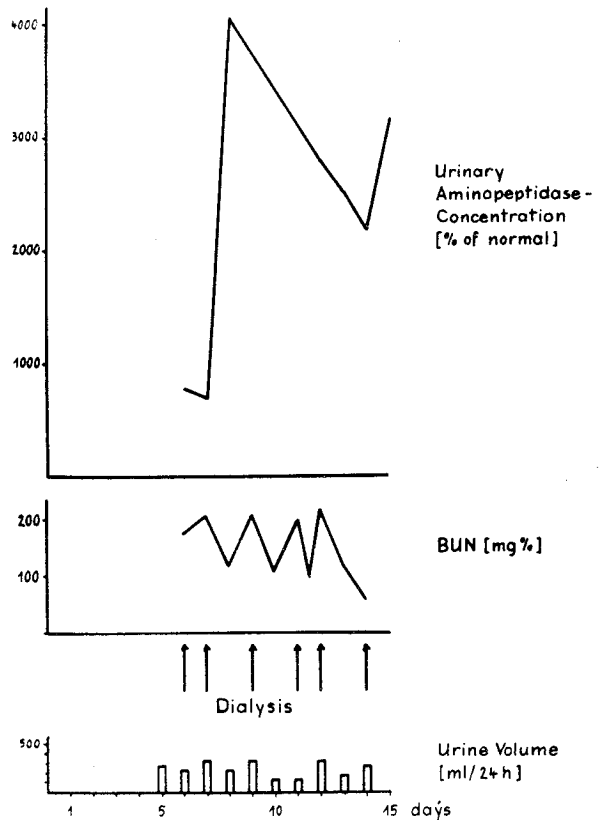


Figure 3. High aminopeptidase concentration in a case of severe postoperative acute renal failure with necrosis of the liver.

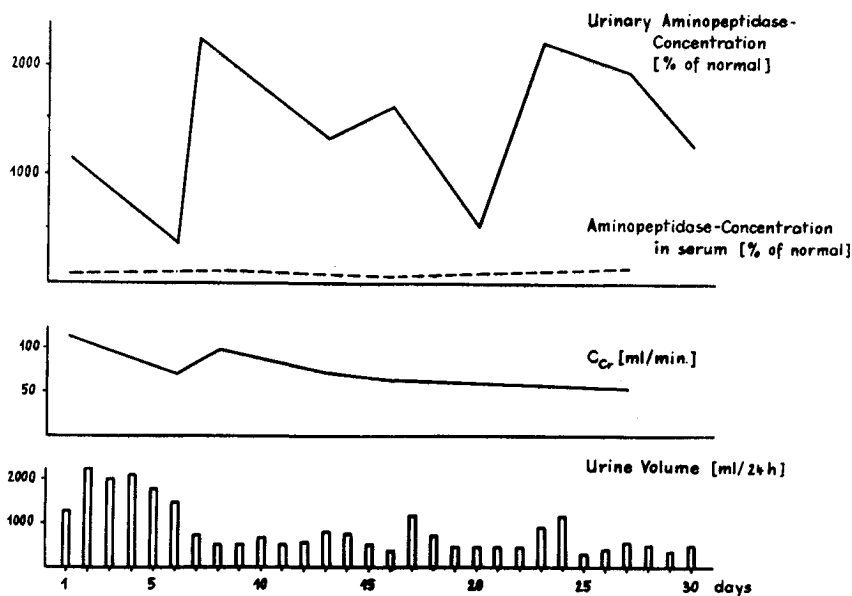


Figure 4. High urinary aminopeptidase concentration in the beginning of subacute glomerulonephritis. Serum-aminopeptidase-activity is untouched.

Number of cases	max. BUN (mg %) ×	oliguric days ×	Number of Dialysis for each pat. ×	±	max. Urinary Aminopeptidase Conc. (% of normal) ×
16	232	12,3	2,5	10	1210
9	185	4,2	0	0	415

× Values are means

Table I. Urinary aminopeptidase activity in acute renal failure.

	Number of patients	Number of determinations	Activity of Aminopeptidase (% of normal)
chronic Glomerulonephritis	13	88	82
chronic Pyelonephritis	17	138	60
subacute Glomerulonephritis	4	62	1320

Table II.