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Effect of Cortin on High Blood Non-Protein Nitrogen of Partially Nephrectomized Rabbits.*

MARVIN H. KUIZENGA. (Introduced by S. Tashiro.)

From the Department of Biochemistry, University of Cincinnati.

By limitation of the kidney tissue to a minimum compatible with life, blood non-protein nitrogen levels considerably higher than normal can be maintained for periods of several weeks or even months. The purpose of this paper is to report the effect of cortin, made by the method of Swingle and Piffner, on the blood non-protein nitrogen of partial renal insufficiency. Adult rabbits of both sexes were used in these experiments. The diet consisted of alfalfa hay plus vegetable greens twice weekly. The rabbits were fasted 12 to 16 hours before the beginning of an experiment. The cortin was administered intraperitoneally and the blood samples withdrawn from the marginal ear vein. The technique for partial nephrectomy described by Bradford¹ was used. A wedge shaped piece of kidney tissue was first removed from one kidney and after recovery from this operation the other kidney was entirely removed. The percentage of kidney tissue removed was calculated upon the basis that the total kidney tissue was twice that of the kidney removed at the second operation.

In a series of 22 rabbits it was found that when the kidney tissue was limited to 30%, the initial increase in the non-protein nitrogen of the blood was followed by several weeks of lower values, still higher than normal, and finally by increases up to 400 mg. per 100 cc. before death. These results confirm those of Anderson.²

In Table I are given the blood non-protein nitrogen levels before and after the cortin injections. Rabbit No. 775, from which 72% of kidney had been removed, was allowed to become pregnant and 2 weeks before parturition, the non-protein nitrogen began a steady climb. This was twice interrupted and appreciably lowered by injection of cortin. Before parturition the NPN rose to 95 to 100 mg. per 100 cc. blood, which after delivery of a normal litter of 5, dropped back to 75, where it remained until an injection of 15 cc. of

* The results here reported were taken from a thesis submitted to a committee of the graduate school of the University of Cincinnati in partial fulfillment of the requirements for the degree of Doctor of Philosophy in June, 1933.

¹ Bradford, J. R., *J. Physiol.*, 1897-1899, **22** and **23**.

² Anderson, H., *J. Exp. Med.*, 1924, **39**, 707.

TABLE I.

Rabbit No.	Injections of cortin	Blood non-protein nitrogen per 100 cc. at time of inj., mg.	Lowest non-protein nitrogen within 24 hr. after inj.
439	5 cc. twice. 2nd inj. one hour after 1st	266	250
443	3 cc. twice. 2nd inj. 1½ hr. after 1st	233	162
434	2 cc. three times at 2 hr. intervals	131	111
432	3 cc. twice. 2nd inj. 2 hr. after 1st	88	70
593	6 cc.	163	149
775	6 cc.	74	59
767	10 cc. twice. 2nd inj. 2 hr. after 1st	336	248
758	10 cc.	138	126
757	10 cc. at 10:30 A.M. 5 cc. at 1:00 P.M.	98	59
753	10 cc.	216	188
753	10 cc.	260	183
775	5 cc.	70	55
775	10 cc. at 10:00 A.M. 5 cc. at 1:00 P.M.	75	54

"cortin" preparation lowered it temporarily to 50. Four of the litter of 5 survived and remained healthy.

Controls were made with 0.9% NaCl, the solvent in which the cortin was injected. Two rabbits with blood non-protein nitrogen of 140 and 75 were each given 10 cc. of 0.9% NaCl solution. Samples were taken, as in the cortin injected group, at regular 2-hour intervals and again 24 hours after injection. In both cases no decrease in the non-protein nitrogen values was observed. The former increased to 160 and the latter to 86 mg. %.

The extracts used were tested in young bilaterally adrenalectomized white rats, and were found to be effective both in reviving these animals from adrenal insufficiency and in maintaining their lives.

Anderson² reported that pregnancy in the 6th week after nephrectomy in a rabbit which had only 63% of kidney removed resulted in death with blood urea nitrogen of 400 mg. %. He reports that none of the nephrectomized rabbits were successful in raising their litters even though the reduction of kidney was in no case greater than 65%.

It is probable that the lowering of the high blood non-protein nitrogen in partial renal insufficiency by injection of cortin is a result of an effect of the cortical hormone on the remnant of kidney remaining. A relationship of the adrenals to kidney function has been suggested. Marshal and Davis³ postulated a decreased kidney function after adrenalectomy, since urea and creatinine injected into the blood were excreted very slowly. Banting and Gairns⁴ de-

³ Marshal and Davis, *J. Pharm. Exp. Therap.*, 1916, **8**, 525.

⁴ Banting and Gairns, *Am. J. Physiol.*, 1926, **77**, 108.

scribed hyperemia of the kidney with swelling of the tubules, and found albuminous casts and blood cells in the tubules. Swingle⁵ found albumin in the urine of animals showing marked symptoms of adrenal insufficiency and reported congestion and hemorrhage in the kidneys. Hartman, *et al.*,⁶ reported an accumulation of large quantities of lipid substance in the *tubuli contorti* of the kidney.

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The Blood Picture of the Normal Dog.

H. D. BRUNER AND G. E. WAKERLIN.

From the Department of Physiology and Pharmacology, University of Louisville School of Medicine.

Since Wintrobe, *et al.*,¹ have pointed out the relative paucity of information in the literature concerning normal blood values for the dog, we are briefly recording additional data obtained during certain experimental studies.

Adult mongrel dogs weighing from 6 to 25 kg. were used. They were housed in individual cages and fed a commercial dog food supplemented with bones. Blood was drawn from the saphenous vein at approximately the same hour of the morning and collected into heparin. The blood values determined were the red blood cell count, hemoglobin, volume of packed red cells, reticulocyte percentage, and leucocyte count. Each red cell count was the average of 2 counts from separate pipettes differing by less than 200,000 cells per cmm.* Hemoglobins were determined by the Newcomer method. The volume of packed erythrocytes was the average of readings from 2 Wintrobe hematocrit tubes.² Reticulocytes were recorded from a count of 1000 red cells by the wet mount technique.³ Each leucocyte count was obtained from the average of 8 sq. mm.* Mean corpuscular volume, mean corpuscular hemoglobin, and mean cor-

⁵ Swingle, W. W., *Am. J. Physiol.*, 1928, **86**, 450.

⁶ Hartman, F. A., MacArthur, C. G., Gunn, F. D., Hartman, W. E., and MacDonald, J. J., *Am. J. Physiol.*, 1927, **81**, 244.

¹ Wintrobe, M. M., Shumacker, H. B., and Schmidt, W. J., *Am. J. Physiol.*, 1935, **114**, 502.

* The hemacytometers and red and white cell pipettes were certified by the United States Bureau of Standards.

² Wintrobe, M. M., *Am. J. Med. Sci.*, 1933, **185**, 58.

³ Wakerlin, G. E., Bruner, H. D., and Kinsman, J. M., *J. Pharm. and Exp. Therap.*, 1936, **58**, 1.