

Effect of Protein Depletion on Response to Water, Sodium Chloride and Pituitrin. (18677)

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The following study was undertaken to demonstrate the effect of protein depletion in otherwise healthy animals upon the excretion of water and sodium chloride. Progressive depletion of serum proteins was accomplished by dietary restriction combined with plasmapheresis. The responses of the normal and depleted animals to water, sodium chloride and pituitrin were studied. A brief account of these experiments follows.

Methods. Water balance and metabolic studies were accomplished during an experimental period lasting 90 days, equally divided into the control period and the period of protein depletion, each of 6 weeks duration.

Four healthy, episiotomized female dogs were placed on a purified diet containing 25% casein and providing 40 calories per lb. body weight (Table I). During the depletion period the casein content was reduced to 4% in the diet of 3 dogs, the fourth remaining as a control. In addition plasmapheresis was performed 3 to 5 times per week on the 3 dogs undergoing depletion. Twelve to 15 cc of blood per kg were withdrawn each time, the heparinized plasma was discarded and the washed red cells resuspended in 0.85% NaCl and injected into a vein. Plasma proteins (albumin and globulin) were determined by the micro-Kjeldahl procedure twice a week using 27% sodium sulfate for their separation.[†] The glomerular filtration rate as measured by the clearance of creatinine (0.2 g/kg subcutaneously)(1) and extracellular fluid volume by the sodium thiocyanate method(2) were determined weekly. A 5-hour period for

TABLE I. Composition of Diets.

	Control 25% protein diet	Low 4% protein diet
Casein	25%	4%
Sugar	40	61
Lard	20	20
Yeast	5	5
Salt mixture U.S.P.	5	5
No. 1 Cellurex	5	5
Percomorph	5 drops/lb	5 drops/lb

Dogs were fed 40 calories per lb body wt. Weight was maintained at approximately the same level throughout this experiment.

the study of water excretion appeared most suitable for these experiments. Following the administration of 50 cc of water per kilo by stomach tube, the time period to excrete 50% of the water load was measured before and after 0.01, 0.025, and 0.05 units/kg of pituitrin administered subcutaneously. (All pituitrin used in these experiments was from the same lot).[‡] Chloride excretion was(7) measured before and after administration of 50 cc of 0.85% NaCl per kg by stomach tube by following the 24-hour excretion for 3 subsequent days. Chloride excretion and response to water and pituitrin were studied on alternate weeks. The chloride content of diet remained constant. Dog A served as a control, dogs B, C, and D were placed on a protein deficient diet and subjected to plasmapheresis 3 to 5 times weekly after completion of 6 weeks of control observations.

Experimental results. 1. During the 6-week period of protein depletion, total serum proteins declined from control values ranging from 7.00-5.50 g % to 4.5-3.3 g % (Fig. 1). Serum albumin showed the greatest depression during the first 4 weeks; however, the globulin levels gradually became lower over the 6-week

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[†] Electrophoretic studies carried out on samples of normal and protein depleted animals indicated that 27% sodium sulfate gave only slightly higher albumin values than were obtained by electrophoresis.

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2. Crandall, L. A., and Anderson, M. X., *Am. J. Digest. Dis. and Nutr.*, 1934, v1, 126.

[‡] The authors wish to acknowledge their indebtedness to Sharp and Dohme, Philadelphia, Pa., for the Pituitrin used in these studies.

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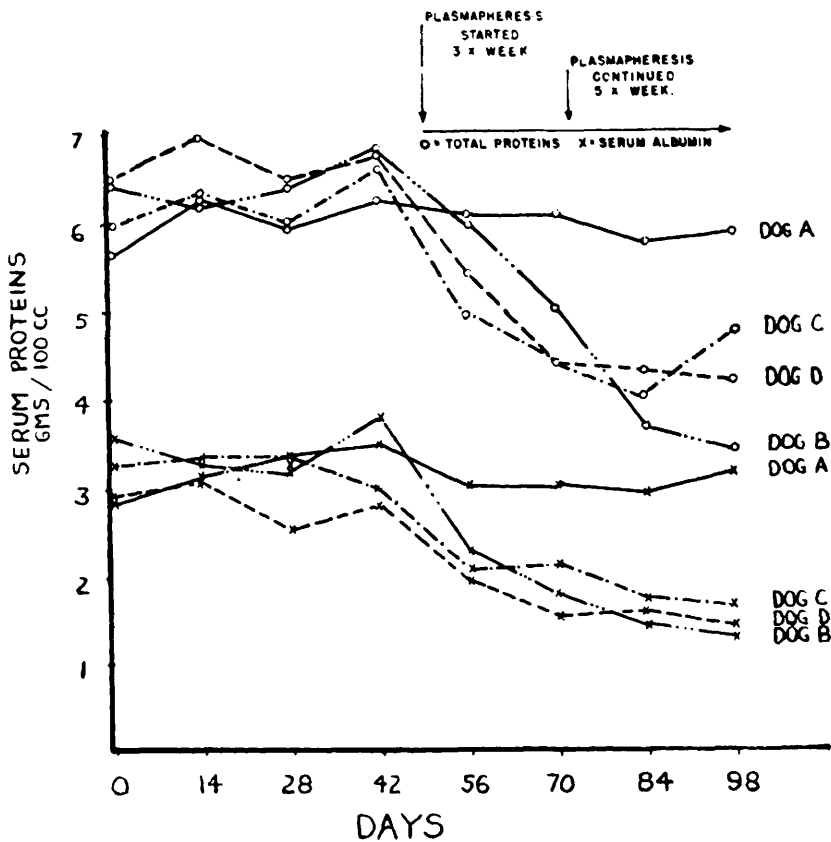


FIG. 1.

Effect of protein depletion upon the total serum proteins and serum albumin fraction.

period. Albumin values declined from a control range of 3.9-2.7 g % to 1.92-1.31 g %.

2. The time required to excrete 50% of a water load of 50 cc/kg increased slightly in all dogs. The results, however, are not statistically significant except for dog B (Table II).

3. Sixty to 70% of the test dose of sodium chloride was excreted within the first 24 hours. No significant change was noted in the rate of chloride excretion by the protein depleted dogs following ingestion of 50 cc/kg of 0.85% NaCl.

4. As serum proteins progressively decreased, the extracellular fluid volume in terms of per cent body weight increased, although the differences in values are not statistically significant. In all dogs the thio-cyanate space attained its highest level when the serum proteins were lowest (Table III).

5. As can be seen in Table III, the glomerular filtration rate decreased in all dogs maintained on a low protein diet. Lowest values were recorded when the serum proteins reached their maximum depression.

6. The degree of urinary suppression produced by the administration of a dose of pitu-

TABLE II. Effect of Serum Protein Depletion on Time Required to Excrete 50% of Water Load.

	Before protein depletion time in hr (mean)	After protein depletion* time in hr (mean)	t-ratio
Dog A (control)	2.48	2.36	0.53
B	1.51	10.93	3.55
C	2.50	4.61	2.04
D	2.21	3.10	1.05

* 5-6 wk of protein depletion.

TABLE III. Effect of Serum Protein Depletion on Extracellular Fluid Volume and Glomerular Filtration Rate.

	Extracellular fluid volume* Thiocyanate space as % body wt		Glomerular filtration rate Creatinine clearance cc/min.	
	Control period	Protein depletion*	Control period	Protein depletion†
Dog A (control)	28.7	27.6	54.6	51.2
B	29.5	33.9	79.7	39.8
C	29.4	29.9	53.6	35.3
D	36.1	38.3	57.5	28.4

* Mean of 3 determinations.

† 5-6 wk of protein depletion.

TABLE IV. Effect of Serum Protein Depletion on Pituitrin Sensitivity in Terms of Relative Potency Units.

	Protein before depletion	After depletion	t-ratio
Dog A (control)	52	54	0.106
B	65	369	5.24
C	142	168	0.50
D	121	146	1.04

itritin is expressed in terms of relative potency units derived from a dose-response curve of mean values obtained during the control period (Table IV).

Analysis of the data obtained from a series of experiments varying the dose of pituitrin from 0.01 to 0.05 unit per kilo body weight revealed considerable variations in degree of urinary suppression between dogs. The control animal, dog A, responded to pituitrin in a fairly consistent manner. Dog B exhibited a marked increase in sensitivity to pituitrin as the serum proteins declined. The other two dogs likewise showed increasing sensitivity to pituitrin but to a lesser degree. The change was only statistically significant for dog B.

Discussion. These results show that hypo-proteinemic dogs require a slightly longer period to excrete a water load than during the control period of study. Although the extracellular fluid volume increased slightly in all protein deficient dogs, gross edema was not observed. Ingestion of excess sodium chloride did not lead to edema formation and, according to the test employed, no gross impairment in chloride excretion was demonstrated in the hypoproteinemic animal.

Protein deficient dogs showed an increased suppression of urine to a given dose of pituitrin as compared to observations during the control period. Some reduction in glomerular filtration in dogs maintained on a diet low in protein has been demonstrated previously by Shannon(3). The increased sensitivity to pituitrin may be related to the reduction in glomerular filtration although the animal that was most sensitive to pituitrin did not have a lower plasma albumin or glomerular filtration rate than the other depleted animals. Wakim *et al.*(4) have stated that pituitrin decreased the renal blood flow and the rate of urine formation. Leslie and Ralli(5) have observed that the urine of rats on a high fat low protein diet exhibited marked antidiuretic properties. Impaired hepatic function produced by the protein deficient diet(6) may reduce pituitrin inactivation by this organ.

Summary. 1. The time required to excrete 50% of an ingested water load was increased in 3 protein-depleted dogs. 2. The glomerular filtration rate was reduced in all protein-depleted dogs. 3. The urinary suppression produced by pituitrin was increased in the protein-depleted dogs.

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