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Plasma Protein Concentrations and Organ Weights of Rats as Related to a High Protein Diet.*

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Adrenal hypertrophy resulting in an increased functional level of the cortex has been observed in rats fed a high protein diet and may be related to an increased rate of protein catabolism[1] but not all investigators have observed an increase in adrenal weight in either rats[2,3] or mice[4] eating a diet high in protein content. Furthermore, no change in plasma protein concentrations was observed in rats fed a 78% casein diet.[3] It was presumed that a change in functional activity of the adrenal cortex would be reflected in plasma protein levels since an important relationship between the adrenal cortex and plasma protein concentrations is known to exist.[5,6]

Ingle[7] reinvestigated the high protein diet-adrenal weight problem in both young and adult rats fed a diet of 67% protein and found the adrenals to be unchanged, but did observe a modest adrenal weight increase when dietary protein was increased to 80%. The primary protein sources used by Ingle were casein (Labco) and lactalbumin. Since a difference in the protein source itself can influence the experimental results as has been effectively demonstrated in adrenalectomized rats given 2 types of casein,[8] the current investigation involving a restudy of the adrenals in rats fed a high protein diet was undertaken and plasma protein levels were again used as a possible means of detecting an increased functional activity of the adrenal cortex.

Adult male rats 130 to 157 days of age were used. The diets fed were Purina fox chow as the control diet (22.8% protein) and the high protein diets which were composed of 78% casein (Merck) or lactalbumin (Borden, lot No. 15-42), 10% brewers yeast (Mead-Johnson), 5% Wesson's salt mixture, 5% Mazola and 2% cod liver oil (Squibb). The diet including casein simulated the Casein A diet of Tepperman *et al.*[1] Lactalbumin was chosen as another primary protein source because the nitrogen balance index for this protein is higher than that of casein.[9]

The experimental period was 20-27 days in duration and during the first 20 days food intake ranged between 280-291 g total per rat fed the high protein diets as compared with a 336 g total per rat fed fox chow. The rats were bled by cardiac puncture under light anesthesia at the conclusion of the experiment and the plasma analyzed for NPN, total protein, albumin and globulin by methods reported previously.[10] Each rat was autopsied and fresh weight of the carefully dissected pituitary, adrenal, thyroid, testis, seminal vesicle, kidney and liver was recorded.

Adult rats fed a high casein diet gained an average of 16 g in body weight as compared with a 28 g gain by rats eating fox chow. When lactalbumin was substituted for casein an average gain of only 4 g in body weight was recorded whereas the littermate controls

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TABLE I.
Influence of Diet on Organ Weight of Adult Male Rats.

Diet (No. of rats)	Casein 78% (14)	Fox chow (14)	Lactalbumin 78% (12)	Fox chow (12)
	Avg organ weight—mg.			
Adrenal	34.8 ± 2.2*	28.4 ± 1.4	34.8 ± 2.2	28.6 ± 2.0
Thyroid	23.6 ± 0.7	23.0 ± 0.5	22.8 ± 0.9	22.6 ± 0.4
Kidney	3248.0 ± 49	2652.0 ± 47	2962.0 ± 123	2811.0 ± 157
Liver	13579.0 ± 289	12303.0 ± 302	12595.0 ± 655	12649.0 ± 341
	Avg organ weight—mg/100 g body weight.			
Adrenal	10.7 ± 0.7	8.7 ± 0.5	11.2 ± 0.7	8.8 ± 0.6
Thyroid	7.3 ± 0.2	7.0 ± 0.2	7.4 ± 0.3	7.3 ± 0.1
Kidney	1008.0± 15	818.0 ± 14	959.0 ± 42	787.0 ± 57
Liver	4192.0 ± 83	3786.0 ± 94	4009.0 ± 220	3870.0 ± 97

$$^{*}\epsilon = \sqrt{\frac{\Sigma d^2}{n(n-1)}}$$

TABLE II.
Influence of Dietary Protein on the Plasma Protein Levels of Male Rats.

No. of rats	Diet	Body wt start-end, g	Hemato-crit, %	Non-protein N, mg/100 cc	Total protein, g/100 cc	Albumin, g/100 cc	Globulin, g/100 cc
			Rats 130-157 days old.				
14	Casein 78%	307-323	48.5 ± 0.7	76 ± 1.8	6.08 ± 0.15	3.06 ± 0.9	3.02 ± 0.08
14	Fox chow	296-324	47.6 ± 0.6	64 ± 2.0	6.13 ± 0.11	3.16 ± 0.10	2.96 ± 0.10
12	Lactalbumin 78%	309-313	47.5 ± 0.7	73 ± 2.1	6.01 ± 0.14	3.06 ± 0.14	2.95 ± 0.16
12	Fox chow	307-326	47.4 ± 0.3	60 ± 1.1	6.23 ± 0.12	3.29 ± 0.10	2.97 ± 0.16
			Rats 45-49 days old.				
8	Lactalbumin 78%	142-204	43.3 ± 0.5	80 ± 2.0	5.40 ± 0.19	3.20 ± 0.10	2.20 ± 0.17
8	Fox chow	144-227	44.4 ± 0.4	51 ± 1.2	5.87 ± 0.18	3.45 ± 0.09	2.42 ± 0.20

TABLE III.
Influence of Diet on Organ Weight of Young Male Rats.

Diet (No. of rats)	Lactalbumin 78% (8)	Fox chow (8)	Lactalbumin 78% (8)	Fox chow (8)
	Avg organ wt, mg		Avg organ wt, mg/100 g B.W.	
Adrenal	33.9 ± 3.2	27.2 ± 2.3	15.8 ± 0.9	12.1 ± 0.8
Thyroid	17.2 ± 2.1	16.4 ± 1.4	8.3 ± 0.7	7.5 ± 0.6
Kidney	2412.0 ± 161	1987.0 ± 63	1161.0 ± 74	875.0 ± 30
Liver	10595.0 ± 663	9770.0 ± 538	5127.0 ± 340	4315.0 ± 261

on stock diet gained 19 g during the same 20-day period.

It is apparent from the data in Table I that the adrenals from rats fed a high protein diet of either casein or lactalbumin had a tendency to be somewhat heavier than the adrenals from rats fed fox chow but the differences are not striking. Kidney and liver weights too were greater in rats fed 78% casein but not in those fed 78% lactalbumin. This seeming difference in results between the 2 high protein diets and kidney weight is shown to be due to body weight differences (Table I). Although it has been reported that thyroid hypertrophy can be induced by excess dietary protein, no indication of a change in thyroid weight was observed. Weights of the pituitary, testis and seminal vesicles were not influenced by diet.

Plasma protein concentrations failed to reveal any evidence that the functional level of the adrenal cortex was altered by a diet containing 78% casein or lactalbumin. The data in Table II reveal that albumin and globulin concentrations and consequently total plasma protein levels were not significantly influenced by the diet. Non-protein-nitrogen, however, was elevated when excess

protein was fed.

The possibility that young rats might exhibit a more pronounced response to a diet containing 78% lactalbumin than did the adults prompted an investigation of this point. Eight rats, 45-49 days old, were fed the 78% lactalbumin diet for an average of 23 days and the data were compared with littermate controls fed fox chow. Despite *ad libitum* feeding, the rats consuming the high protein diet gained an average of only 62 g as compared to the average 83 gain exhibited by rats eating fox chow (Table II). Despite the retardation in body weight gain, the adrenal, kidney and liver weights from rats fed a 78% lactalbumin diet exceeded those from rats fed stock diet. These organ weight differences are more apparent when organ weight is considered in terms of 100 g body weight (Table III). The weight of the thyroid, testis, seminal vesicles and pituitary was not influenced.

Examination of the plasma protein concentrations for total protein, albumin and globulin suggested that rats fed fox chow had the higher plasma protein levels but the differences are not clearly significant. NPN, however, was significantly higher in rats fed the high protein diet.

Since liver protein can be readily influenced by a dietary deficiency in protein it was of interest to examine the livers from some of these young rats under the opposite conditions or that of protein excess. The livers from 4 pairs of rats were dried to constant weight at 95° C and analyzed for total protein. Water content of the livers from rats fed 78% lactalbumin was 69.9% and from rats fed fox chow was 70.0%. Liver protein was found to be greater in the lactalbumin-fed rats than in stock-diet animals. Following the feeding of the high protein diet the livers contained an average 1.15 (0.98-1.26) g protein/100 g body weight as compared with an average 0.83 (0.76-0.89) g protein/100 g body weight. Furthermore, the percentage protein of the dry liver increased from 64.0% in rats fed fox chow to 72.3% in rats fed the high lactalbumin diet and therefore the increased liver protein was not alone due to increase in liver size.

Summary. The effect of a high protein diet (78% casein or lactalbumin) was studied in male rats. The rate of body weight increase was retarded over a 3-week period by a 78% lactalbumin diet in young and adult rats. A modest increase in adrenal weight was observed but no indication of increased functional activity was suggested by alterations in plasma albumin or globulin concentrations since the plasma protein levels remained unchanged. Non-protein nitrogen was elevated by the excess dietary protein. Thyroid, pituitary, testis and seminal vesicle weights remained normal but kidney and liver weights were increased. Liver protein was increased in young rats fed the high lactalbumin diet.

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Pyribenzamine Aerosol Inhalation and its Influence on Histamine Poisoning and Anaphylaxis.

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The lethal dose of histamine for guinea pigs by intravenous injection is 0.3 to 0.4 mg/kg body weight,[1] but the amounts required to kill guinea pigs when introduced into the lungs by aerosol inhalation are fractions of these doses.[2,3] Indeed, many guinea pigs breathing air containing less than 0.1 γ his-

[1] Guggenheim, M., *Die Biogenen Amine*, Basle, 1940.

[2] Halpern, B. N., *Arch. internat. de pharmacodyn. et de Therap.*, 1942, **68**, 339.

[3] Mayer, R. L., *J. Allergy*, 1946, **17**, 153.