No. of rabbits		Wt of livers	Niacin, µg per g	% protein	Tryptophane % in protein
		Group 1.	No treatment	given.	
$\overline{5}$	Avg	54	116	14.2	1.60
		Group 2. T	reated with try	ptophane.	
6	,,	82	177	15.0	1.56
		Group 3.	Treated with 1	niacin.	
5	,,	78	159	13.4	1.57
		roup 4. Treated	l with tryptoph:	ane and niacin.	
6	"	102	187	14.6	1.81
No. of rabbits		Niac ug pe	. /	% protein	Tryptophane % in protein
No. of rabbits		μg pe	er g	% protein	Tryptophane % in protein
		μg pe Group 1.	er g No treatment	given.	in protein
No. of rabbits	Avg	μg pe Group 1. 8	er g No treatment 88	given. 18.5	
5		μg pe Group 1. 8 Group 2. Τ	er g No treatment 38 reated with tryp	given. 18.5 otophane.	in protein 1.43
	Avg	μg pe Group 1. 8 Group 2. Τ 9	er g No treatment 38 reated with tryp 33	given. 18.5 otophane. 19.2	in protein
5 6	,,	μg pe Group 1. 6 Group 2. T 9 Group 3.	er g No treatment 38 reated with tryp 93 Treated with 1	given. 18.5 otophane. 19.2 niacin.	in protein 1.43 1.43
5	,, ,,	μg pe Group 1. 8 Group 2. Τ Group 3. 13	r g No treatment 88 reated with tryp 89 Treated with 1 30	given. 18.5 otophane. 19.2 niacin. 19.1	in protein 1.43
5 6	,, ,,	μg pe Group 1. 6 Group 2. T 9 Group 3.	r g No treatment 88 reated with tryp 89 Treated with 1 30	given. 18.5 otophane. 19.2 niacin. 19.1	in protein 1.43 1.43

TABLE III.

gain, hemoglobin, red and white blood cells were about equal when either of the substances were fed. The addition of both compounds to the ration resulted in greater responses. The niacin content of the livers of the rabbits that received either tryptophane or niacin supplements was approximately normal. The niacin in the muscles of the rabbits that were supplemented with niacin was found to be high, while the tryptophane animals had a niacin level similar to the concentration found in the muscles of the deficient rabbits.

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## Effect of Hypophyseal Growth Hormone Upon Rats Fed Low Protein Diets.\*

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In a current study<sup>1</sup> the degree of nitrogen retention produced by the hypophyseal growth hormone has been shown to depend on the dietary protein content. With diets containing 12, 18, 24 and 48% casein growth hormone produces prompt nitrogen retention and proportionate gain of weight. In this study adult female rats of the Long-Evans strain, aged 7 to 10 months, were each fed 12 g daily of a synthetic diet complete in all known dietary requirements with a protein content restricted to 6% alcohol-washed casein. This diet contains 0.1% choline

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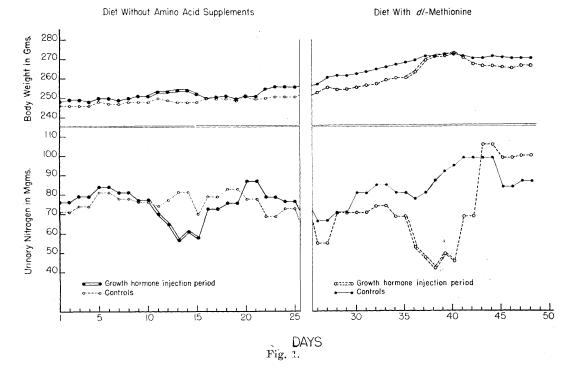
<sup>&</sup>lt;sup>1</sup>Gordan, G. S., Bennett, L. L., Li, C. H., and Evans, H. M., to be published.

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Effects of Growth Hormone on Body Weight and Urinary Nitrogen Excretion of Rats on 6%

	10 days preinj. period	5 days inj. periođ	Increment	10 days postinj. period
Controls				
$\mathbf{Wt}$	249 g	248 g	-1 g	$251\mathrm{g}$
N	$76 \pm 1.4 \text{ mg}$	$77 \pm 1.6 \text{ mg}$	0	$76\pm1.9$ mg
Growth horm	ione	8		0
injected				
Wt	251 g	252 g	$+1 \mathrm{g}$	$256~{ m g}$
N	$79\pm2.4$ mg	$62\pm3.2~{ m mg}$	15  mg	$78\pm2.1~{ m mg}$
	- 0	- 0	$p^* \equiv < 0.01$	_ 0

\* Fisher's<sup>3</sup> probability value.



Effect of Growth Hormone in Rats on Low Protein Diet

chloride. Animals have been fed this diet for 12 weeks without losing weight or developing hyperazoturia. The only sign observed which was considered evidence of a deficiency condition was loss of fur, especially that of white animals, most marked on the lower belly and flanks.

After a 7-week adaptation period on this diet rats were placed in individual screenbottomed cages. Urines were collected through acid-moistened ribbed glass funnels in which feces and hair were separated upon perforated porcelain discs. The funnels were washed down and urines collected at 48-hour intervals during control periods and at 24hour intervals during experimental periods. Urines were analyzed for nitrogen content by the micro-Kjeldahl method. Animals were weighed at the same time daily immediately before feeding.

After a 10-day control period 5 experimental animals were injected intraperitoneal-

## HYPOPHYSEAL GROWTH HORMONE AND LOW PROTEIN DIETS

	10 days preinj, period	5 days inj. period	Increment	8 days postinj. period
Controls				
Wt	269 g	$273  ext{ g}$	$+4 \mathrm{g}$	$271~{ m g}$
Ν	$77\pm2.3$ mg	$87\pm2.4$ mg		$92\pm2.0~{ m mg}$
Growth horn	none	- 0		
njected				
Wt	$261~{ m g}$	274  g	+13 g	$267~{ m g}$
$\mathbf{N}$	$60\pm2.3$ mg	$48\pm2.6$ mg	$39 \mathrm{mg}$	$92\pm3.9~\mathrm{mg}$
	9	_ 0	p = < 0.01	Ū.

TABLE II.

Effect of Growth Hormone on Body Weight and Urinary Nitrogen Excretion of Rats on 6%

ly with 0.5 mg of growth hormone<sup>2</sup> twice daily for 5 days while 5 control animals were similarly injected with an equal amount of serum albumen. Following injection the animals were observed for a second 10-day control period. The results of this experiment are presented in Table I and Fig. 1.

It will be noted that the growth hormoneinjected rats retained nitrogen but showed no significant weight gain. This experiment has been repeated in 2 further series with similar results.

Following the second control period all animals received a dietary supplement of dlmethionine 66 mg per animal per day. By reference to Fig. 1, it will be noted that there was an immediate but transient retention of nitrogen and the animals gained weight. During this period the loss of hair also ceased and fur began to grow again in thinned out areas.

Following a 10-day control period the animals which had formerly acted as controls were injected intraperitoneally with 0.5 mg of growth hormone twice daily while the former experimental group served as controls.

By reference to Table II and Fig. 1 it will be noted that on the methionine-supplemented diet the growth hormone-treated rats retained nitrogen and gained weight. This experiment has been repeated in a further series fed the methionine-supplemented diet with similar results (nitrogen retention 32 mg; weight gain 7 g). Another series in which the diet was supplemented with *dl*methionine 66 mg and *l*-tryptophane 22 mg per rat per day showed similar nitrogen retention (39 mg) and weight gain (7 g). In one series *l*-tryptophane 22 mg per day alone was used as the dietary supplement. When this group of rats was injected with growth hormone, there was an average nitrogen retention of 33 mg per day but no change of weight.

It thus appears that the addition of *dl*methionine specifically supports the 6% casein diet to render it capable of supporting the rapid growth induced by growth hormone. The action of methionine is probably related to the amino acid requirement for building new tissue rather than the repair of hepatic damage produced by the low protein diet, for no histological difference is noted between the livers of rats on the unsupplemented diet and those of rats on the methionine-supplemented diet.

Conclusions. (1) The injection of growth hormone into rats fed a 6% casein diet results in nitrogen retention without significant gain in weight. (2) The addition of *dl*-methionine renders the 6% casein diet capable of supporting the rapid growth induced by the growth hormone.

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<sup>&</sup>lt;sup>2</sup> Li, C. H., and Evans, H. M., Science, 1944, 99, 183.

<sup>&</sup>lt;sup>3</sup> Fisher, R. A., *Statistical Methods for Research Workers*, 10th edition, Edinburgh, London, Oliver and Boyd, 1946.