

0.025 and 0.050%, made greater gains and required less feed per gram of gain than did the controls. Those fed diets with 0.1 and 0.2% thyroactive iodocasein gained more than the controls and were more fully feathered than either the controls or those receiving the lower levels. The thyroactive iodocasein-fed chicks utilized their feed more efficiently than the controls only during the periods when

they were gaining at a more rapid rate.

Statistical analysis showed the difference in rate of gain to be of doubtful significance although the data indicate that at the proper dosage level growth rate was above normal. The differences in the rate of feathering in favor of the treated birds on higher dosage levels were highly significant.

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Influence on Growth of Thyroactive Iodocasein.*

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We have shown recently that small amounts of synthetic thyroxine injected over a period of 5 weeks will cause an acceleration in the growth rate of immature mice.¹ With the discovery that a highly potent thyroactive iodoprotein[†] could be formed by combination of iodine with tyrosine-containing proteins under controlled conditions,^{2,3} it was decided to test the effect of some of these products on the growth rate of mice and determine whether responses similar to these secured by giving small amounts of thyroxine would be obtained.

Materials and Methods. Virgin female mice weighing from 13 to 15 g at the beginning of

the trials were used as experimental animals. Three different trials were conducted over a period of 35 days each, different lots of thyroactive iodocasein being used for each trial. Suitable controls were kept for each experiment. The animals were numbered individually and their lengths determined under anesthesia at the beginning and at the end of the experimental period. Body weights were taken weekly. The dosages and methods of administration of the thyroactive iodocaseins as well as the grouping of animals in the experiments are indicated in Table I.

The thyroactive proteins used were prepared by iodination of casein at the optimal level as described in previous reports.^{2,3}

The material used in Experiment 1 was a highly potent preparation containing 7.14% iodine. It possessed 10.3% of the potency of synthetic thyroxine-sodium (BDH) on a weight basis when injected into tadpoles, and 4% of the activity of thyroxine when assayed on guinea pigs, by oral administration of the test substance. The material was injected subcutaneously at the rate of 0.55 mg every 2 days. This dosage was calculated purposely to contain the same amount of iodine as 0.06 mg synthetic thyroxine—an amount of thyroxine that has proven to cause acceleration of growth rate in young mice.¹

The material used in Experiment 2 was a less potent lot containing 1.8% the activity

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† The term thyroactive iodocasein is used to designate products formed by iodination of proteins in such a manner as to produce a substance with high thyroidal activity. It is necessary to distinguish between these preparations and compounds such as iodocasein and iodoalbumin which are used merely as carriers of organic iodine, and have little or no thyroidal effect.

¹ Koger, Marvin, Hurst, Victor, and Turner, C. W., *Endocrinology*, 1941, **29**, 667.

² Reineke, E. P., Williamson, M. B., and Turner, C. W., *J. Biol. Chem.*, 1942, **143**, 285; 1943, **147**, 115.

³ Reineke, E. P., and Turner, C. W., *Mo. Agri. Exp. Sta. Bull.* 355, 1942.

TABLE I.
Effect of Thyroactive Iodocasein on Body Weight Gain and Gain in Skeletal Length During a 5-Week Period.

Exp. No.	Treatment	No. animals	Body wt				Nose-tail length			
			Mean gain, g	Diff. in gain (treated above controls)		P value,* %	Mean gain, %	Diff. (treated above controls)		P value,* %
				g	%			mm	%	
1	Controls	7	6.4				17.3			
	0.548 mg inj. alternate days	7	7.9	1.5	23	>5	25.3	8.0	46.2	<5
2	Controls	11	7.7				25.8			
	0.3 to 0.5% of ration	16	8.9	1.2	16	>5	30.9	5.1	19.8	<5
3	Controls	22	6.4				16.4			
	.04% of ration	24	7.5	1.1	17	5	20.6	4.2	25.6	<5
	.08% " "	22	7.4	1.0	16	5	20.7	4.3	26.2	<5
	.16% " "	20	7.6	1.2	19	5	21.8	5.4	32.9	<5
	.32% " "	11	7.9	1.5	23	5	20.9	4.5	27.4	5
Total	Controls	40								
	Treated	100		1.2	18	<1		4.9	27.9	<1

*Probability that the differences observed are due to random fluctuation.

of thyroxine when injected into tadpoles. The preparation was not assayed with guinea pigs. It was given in the feed at the level of 0.3% to 0.6% of the ration.

In Experiment 3 a potent preparation containing 7.24% iodine was used and fed the different groups of animals, in graded amounts of 0.04, 0.08, 0.16 and 0.32% of the ration. The material had 9.3% the potency of thyroxine as assayed by injection into tadpoles.

Results. A summary of the growth data obtained from the different trials is presented in Table I. Without exception, the treated animals gained more in body weight and length than their corresponding controls. The thyroactive iodocasein-fed animals gained from 16 to 23% more in weight and an average of 28% more in length than the untreated controls. In Experiment 3 where graded amounts of the thyroactive iodocasein were fed, there was a tendency for the gains to be greater in the groups receiving 0.16% and 0.32% than in the groups receiving 0.04% and 0.08% in the ration.

Analysis of variance⁴ showed the difference

in gains in body weight and in length in favor of the treated animals to be significant for the larger groups of animals in Experiment 3 ($P = 5\%$ or less). In the smaller groups in Experiment 1 and 2 the differences in body weight gain were not significant for the numbers of animals included. The differences were in favor of the treated animals, however, and the differences in gain in body length were significant. When the data were summated (see totals in Table I), the differences in gain in both weight and in skeletal growth (length) in favor of the treated animals were highly significant (probability value of less than 1%).

The differences in gain in skeletal growth (length) are somewhat more marked and are significant even when only small groups are compared.

Summary. Immature virgin female mice were treated with thyroactive iodocasein by both oral and subcutaneous administration and their growth compared to that of controls. The treated animals gained significantly more in body weight and in total length than the non-treated controls.

⁴ Snedecor, George W., *Statistical Methods*, Iowa State College Press, 1940.