valid for young infants.

On theoretical grounds, one would expect the isotopic dilution values to be somewhat less than those obtained by carcass analysis since bromide^{82} equilibration in brain and cerebrospinal fluid is not complete at the end of 24 hours(12), yet precise data with which to evaluate the error involved are lacking. On the other hand, total body chloride progressively decreases as body weight increases during growth(13) and since the average weight of our subjects is approximately 480 g less than that of the subjects quoted above the 2 groups are not strictly comparable. According to equations developed by one of us (G.B.F.) from published data on carcass analysis it can be predicted that the average total body chloride for our group of subjects should have been 53.2 meq/kg. or 2.1 meq/kg more than the values observed.

Conclusion. 1.) Values for total body chloride, as determined by radiobromine^{83} dilution, averaged 51.1 meq/kg body weight for a series of normal newly born infants. Total body chloride, on a per kilogram basis is far higher in young infants than adults. 2.) Values obtained by this method show excellent agreement with those obtained by earlier workers employing direct chemical analysis. Therefore, the bromide dilution method would appear to be valid for the measurement of total body chloride in young infants.

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Effects of Cortisone on Thiamine-Deficient Young Rats.* (20519)

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Large doses of cortisone may increase requirements for vit. B_{12} and other factors in the young rat(1-3) and baby pig(4). Preexistent deficiencies of vit. B_{12} in these species were aggravated by cortisone injections, resulting in reduced body growth and survival rate. These detrimental actions of cortisone were largely counteracted in young rats by increasing vit. B_{12} intake at least 10 times above normal requirements (to 200 μg per kilo of diet). Addition of small amounts of aureomycin to the diet further enhanced the beneficial effects of vit. B_{12}, and both supplements were accompanied by increases in food intake and greater efficiency in converting food into body weight gains. It was the purpose of the present study to determine the effects of large doses of cortisone on requirements for thiamine by the young rat.

Methods and results. Exp. 1. Fifty-three young male Carworth rats were divided into

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TABLE I. Effects of Cortisone and/or Thiamine on Body Weight, Food Intake and Efficiency of Food Utilization.

Group and No. of rats	Treatment	Avg body wt, g		Avg food intake, g	
		Initial*	Final	Total	Per g gain body wt
	1st exp.—18 days duration				
1 (13)	1 mg thiamine	101.7 ± 2.3 †	151.5 ± 4.1†	153	3.0
2 (10)	No thiamine, no cortisone	105.6 ± 2.07	80.8 ± 3.1	65	—
3 (10)	Cortisone, no thiamine	105.2 ± 2.3	64.8 ± 2.9	62	—
4 (10)	" + 1 mg thiamine	102 ± 2.7	110.8 ± 5.1	135	15.3
5 (10)	" + 10 mg "	101.8 ± 2.8	137.6 ± 4.9	170	4.7
	2nd exp.—12 days duration				
1 (9)	1 mg thiamine	77.3 ± 1.1	107.3 ± 3.8	82	2.73
2 (9)	No thiamine, no cortisone	74.8 ± 1.8	62.0 ± 2.4	30	—
3 (10)	1 mg cortisone, no thiamine	73.0 ± 1.2	—	—	—
4 (10)	1 mg cortisone + 20 mg thiamine, pair-fed to group 3	73.8 ± 1.7	63.0 ± 1.4	30	—
5 (10)	1 mg cortisone + 1 mg thiamine	72.0 ± 1.7	71.2 ± 1.6	61	—
6 (9)	1 " " + 5 " "	75.5 ± 1.6	99.0 ± 6.3	96	4.1
7 (9)	1 " " +10 " "	73.1 ± 2.03	94.0 ± 3.6	93	4.4
8 (9)	1 " " +20 " "	71.3 ± 1.5	97.7 ± 2.1	105	4.0

* Represents avg body wt after thiamine-depletion period.
† Stand. error of mean.

5 uniform groups by weight and were fed the following semi-synthetic ration from which thiamine was omitted: alcohol washed casein, 25 g;‡ glucose (Cerelose), 62 g;§ corn oil (Mazola), 10 g; salt mixture, 4 g.‖ To each kilo of the above the following vitamins were added: riboflavin, 5.0 mg; pyridoxine, 2.0 mg; Ca pantothenate, 28.0 mg; niacin, 10.0 mg; choline, 1 g; 2-Me-1, 4 Naphthoquinone, 0.4 mg; vit. A, 100,000 I.U.; vit. D, 125,000 I.U.¶ After a depletion period of 10 days on this diet, each of the 5 groups was treated as shown in the upper part of Table I for a period of 18 days. Thiamine was incorporated into the ration and cortisone acetate was injected subcutaneously in 1 mg doses once daily. Measurements of individual body weight and average food consumption were made every 2 days. All rats were housed in metal cages with raised screen bottoms at a temperature of 78 ± 1.0°F.

The pertinent data are summarized in Table I, and the character of body growth and food intake are shown in Fig. 1. It can be seen that growth and appetite were reduced in all rats by the end of the 10-day depletion period. After this period, the rats fed 1 mg of thiamine per kilo of diet (Group 1) increased in average body weight from 101.7 ± 2.3 g to 151.5 ± 4.1 g and ate more food. The thiamine-deficient rats (Group 2) lost an average of about 25 g in body weight and ate less than half the food consumed by the rats in Group 1. An even greater loss in body weight occurred in the thiamine-deficient rats given cortisone (Group 3), although appetite was not depressed below that of the rats in Group 2. These rats were in the poorest state of any in the experiment and it is believed they would have died if cortisone treatment had been continued. In addition to extreme emaciation, they exhibited typical symptoms of thiamine deficiency such as hunched posture, paralysis and spinning when picked up by the tail. Eight of the 10 rats in this group showed pronounced priapism, a phenomenon not seen in any of the other rats. The addition of 1 mg of thiamine per kilo of diet enabled cortisone-treated rats (Group 4) to overcome partially the depression of body growth and eliminated other gross symptoms of thiamine deficiency. When 10 mg

‡ "Vitamin Test" casein, Nutritional Biochemical Corp., Cleveland, O.

§ Corn Products Refining Co., Chicago, Ill.

‖ Salt mixture No. 2, Nutritional Biochemical Corp., Cleveland, O.

¶ The B vitamins and cortisone acetate (Cortone) were supplied through the kindness of Dr. L. Michaud of Merck and Co., Rahway, N. J.

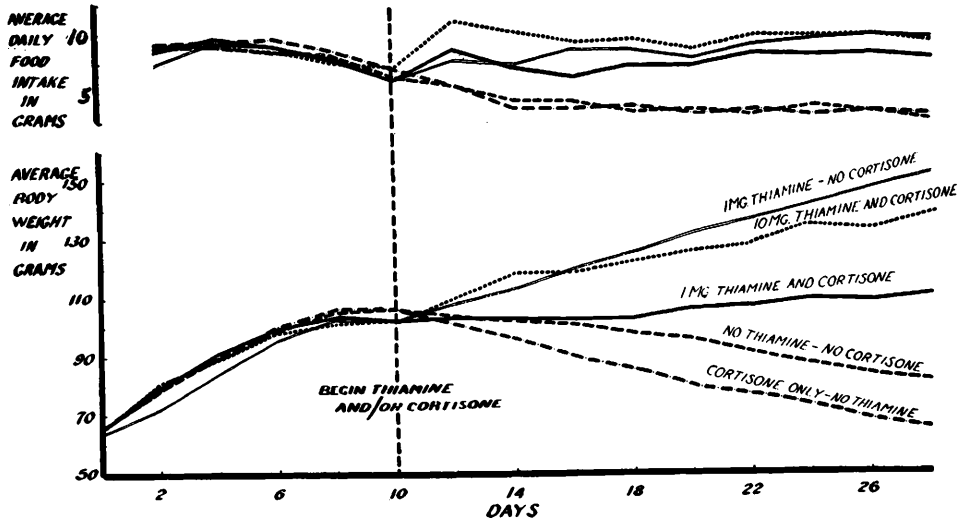

FIG. 1. Graph showing avg body wt and food intake of rats during 10-day, thiamine-depletion period and after treatment with cortisone and/or thiamine.

of thiamine per kilo were fed to cortisone-injected rats (Group 5), there was an almost complete counteraction of growth inhibition.

Exp. 2. A total of 75 young male Carworth rats were divided into 8 uniform groups by weight, and fed the thiamine-free ration for 18 days. At the end of this period each group was treated with thiamine and/or cortisone for 12 days as indicated on the bottom-half of Table I. The pertinent results are also given in this table.

The initial body weights of all rats averaged 46.7 $\pm$ 0.8 g, and at the end of the 18-day depletion period, 73.8 $\pm$ 1.6 g. The group which subsequently received 1 mg of thiamine per kilo of diet (Group 1) gained approximately 30 g each in body weight, while the animals which continued on the deficient diet (Group 2) lost about 12 g each in body weight. When cortisone was given to the thiamine-deficient rats (Group 3), a severe cannibalism developed which resulted in the death of 8 out of 9 rats by the end of 12 days. Priapism also appeared in most of these rats. The rats in Group 4 received cortisone and 20 mg of thiamine per kilo of diet, but were allowed only as much food as consumed daily by the rats in Group 3. Although these rats were reduced in body weight, they all survived and showed no gross symptoms of thiamine deficiency. When 1 mg of thiamine was fed to cortisone-treated rats (Group 5), there was no change in body weight but gross symptoms of thiamine deficiency were less marked than in Group 2. Groups 6, 7 and 8, received 5, 10 and 20 mg of thiamine per kilo of diet, respectively, and all levels were equally effective in counteracting the cortisone-induced inhibition of body growth and appetite. In this as well as in the first experiment, cortisone reduced the efficiency of transforming food into body weight gains.

Discussion. These data are believed to demonstrate that injections of large doses of cortisone can aggravate a pre-existent deficiency of thiamine in young rats, as shown by reduced body growth and survival rate and earlier manifestation of other extreme deficiency symptoms. The priapism, seen only in the cortisone-treated, thiamine-deficient rats, had previously been observed in young rats given huge doses of cortisone(5). The "toxic" effects of cortisone were more marked in rats of the 2nd than in those of the first experiment, presumably because they were younger and were initially made more deficient in thiamine prior to cortisone administration. Since 1 mg of thiamine per kilo of diet represents normal requirements for growth in young rats(6), the present data suggest that at least a 5-fold increase in thiamine is

necessary to counteract growth-inhibition induced by injections of 1 mg of cortisone daily. These data also suggest that large amounts of thiamine have beneficial effects on cortisone-treated rats, apart from any effect on appetite. Rats given cortisone and thiamine, but limited in food intake to that of cortisone-injected, thiamine-deficient rats, at least survived and failed to show typical deficiency symptoms. Data reported by Schultz *et al.*(7) suggest that large doses of cortisone may also aggravate a pre-existent deficiency of pantothenic acid in rats.

Summary. (1) A total of 128 young male albino rats were used in 2 experiments to determine the effects of large doses of cortisone on thiamine requirements. They were fed a semi-synthetic ration from which thiamine was omitted for preliminary periods of either 10 or 18 days, followed by injections of 1 mg of cortisone daily with or without several levels of thiamine for another 18 or 12 days. (2) Pre-existent deficiency symptoms were aggravated by cortisone, resulting in decreased body growth and survival rate, priapism, cannibalism and loss of muscular coordination. The rats which were initially deficient in thiamine for the longer period, showed the most severe reactions to cortisone administration. Cortisone decreased the efficiency of converting food into body weight gains in all cases. (3) When 1 mg of thiamine per kilo of ration was fed, representing normal requirements for growing rats, there was little or no increase in body weight although most deficiency symptoms disappeared. When 5, 10 or 20 mg of thiamine per kilo of ration were fed, each level was equally effective in counteracting growth inhibition by cortisone.

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Calorigenic and Antigoitrogenic Actions of L-Triiodothyronine and L-Thyroxine in Thyroidectomized and Intact Rats.* (20520)

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3:5:3′-L-triiodothyronine has been reported to be 3 to 4 times as effective as L-thyroxine in preventing goitre development in thiouracil-treated rats(1). Also, in the treatment of 2 myxedematous patients, it appeared to be effective at doses lower than those required with thyroxine administration(2). On the contrary, Gemmill(3), using a small number of intact rats, has recently reported that the two agents produce quite similar calorigenic responses. This latter apparent discrepancy might possibly be the result of variability in the individual animal or strain, differences in experimental approach or in the type of animal preparation (intact or thyroidectomized) used. To further an understanding of these dissimilarities of response, a comparison has been made in intact and thyroidectomized rats with reference to calorigenic and antigoitrogenic potencies of these two agents.

Experimental. Male rats (Albino Farms), weighing between 125 and 175 g at the beginning of the experiment, were used. Purina Dog Chow Checkers and tap water were given *ad libitum* unless otherwise indicated. Both the triiodothyronine (3:5:3′-L-triiodothyronine) and thyroxine (L-thyroxine sodium pentahydrate) were given by subcutaneous injec-

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