TABLE I. % of Administered Dose of Labelled Substance per g of Fresh Wt of Rat Tissues ± σm (Stand. Deviation of the Mean).

Tissue	Iodoacetate	I^{131}
Thyroid	8.304 ± .777	152.448 ± 10.542
Blood	1.201 ± .162	.698 ± .112
Saliva	.948 ± .265	——
Adrenals	.648 ± .159	.226 ± .057
Molars	.505 ± .109	.211 ± .031
Liver	.467 ± .078	.255 ± .033
Kidney	.402 ± .131	.266 ± .034
Incisors	.397 ± .138	.184 ± .017
Salivary glands	.358 ± .078	.250 ± .013
Skeleton	.285 ± .085	.187 ± .015
Striated muscle	.159 ± .065	.111 ± .031

uptake of I^{131}. This is probably due to the higher concentration of iodoacetate in the blood, almost double that of blood iodide, which is rapidly lowered by the thyroid. This fact, together with the rapid decrease in concentration with time seen in the oral tissues (Fig. 1) indicates that there is probably no selective uptake of iodoacetate. A diffusion into and out of the organs is indicated, a behavior characteristic also of iodine, where the thyroid is not involved.

Summary. (1) The distribution of iodoacetate and of potassium iodide, both labelled with I^{131}, has been determined in rats three hours after intraperitoneal injection. (2) The thyroid gland does not show a high selective uptake of iodoacetate. (3) Uptake of iodoacetate by tissues other than the thyroid is about twice that of iodide. There is no evidence of selective absorption by any tissue studied.

The authors wish to extend grateful thanks to Dr. Henry Elliott of the Department of Pharmacology, University of California Medical School for his valuable advice during this work, and for permitting the use of his Geiger-Muller Counter.

Received June 18, 1951. P.S.E.B.M., 1951, v77.

Response of Castrated Male and Female Hyperthyroid Rats to Vitamin B_{12}.* (18869)

A. B. WATTS, O. B. ROSS, C. K. WHITEHAIR, AND ROBERT MACVICAR.

From Departments of Animal Husbandry and Agricultural Chemistry Research, Oklahoma Agricultural Experiment Station, Stillwater, Okla.

Recent studies in this laboratory(1) indicated that the addition of vit. B_{12} to a purified ration containing toxic levels of iodinated casein effected a greater growth response in male than in female rats. Carrick(2) observed a sex difference in the response of chicks to fish solubles added to a ration presumably deficient in vit. B_{12}. An assay method for the determination of vit. B_{12} employing the hyperthyroid rat was developed by Frost *et al.*(3). These workers reported no sex difference in growth response to supplementation. Male and female offspring of vit. B_{12}-depleted rats showed a decided difference in growth response in studies reported by McCollum and Chow(4). Male rats grew more rapidly in the absence of vit. B_{12} supplementation than did their litter-mate females, suggesting a lower need for or more storage of this nutrient in the male rat. These results seemed to warrant further investigation of the influence of sex on the growth-promoting effect of vit. B_{12} in the hyperthyroid rat. Studies involving normal and castrate rats of both sexes were therefore initiated.

Materials and methods. Weanling rats of the Sprague-Dawley strain were used in this study. Thirty male and 18 female rats were

* Published with the approval of the Director, Oklahoma Agricultural Experiment Station.

1. Bolene, C., Ross, O. B., and MacVicar, R., PROC. SOC. EXP. BIOL. AND MED., 1950, v75, 610.

2. Carrick, C. W., Proc., 3rd Conference on Feeds of the Beverage Distillers, 1948, p. 10.

3. Frost, D. V., Fricke, H. W., and Spruth, H. C., PROC. SOC. EXP. BIOL. AND MED., 1949, v72, 102.

4. McCollum, E. H., and Chow, B. F., PROC. SOC. EXP. BIOL. AND MED., 1950, v75, 20.

TABLE I. Composition of Rations.

Ingredient	Ration* 1 (%)	Ration* 2 (%)	Ration* 3 (%)
Corn starch	68.80	68.80	68.80
Soybean protein†	21.75	21.75	19.75
Corn oil	5.00	5.00	5.00
Mineral mixture‡	4.00	4.00	4.00
DL-methionine	.20	.20	.20
Iodinated casein§	.25	.25	.25
Liver concentrate powder, 1:20	—	—	2.00
Vit. B_{12}, .25 mg/kg	—	+	—

* Vitamin mixture was fed to supply the following amounts of water soluble vitamins per kg of ration: thiamin 6 mg, riboflavin 12 mg, niacin 40 mg, calcium pantothenate 60 mg, pyridoxine 6 mg, para-amino benzoic acid 100 mg, folic acid 5.0 mg, inositol 1 g, choline chloride 2 g. During standardization period only one-half of above amounts of various vitamins were fed. In addition to water soluble vitamins the rats received twice weekly 2 drops of mixture of cod liver oil and alpha tocopherol.

† Sodium proteinate, Archer-Daniels-Midland, Minneapolis, Minn.

‡ Hegsted, D. M. *et al., J. Biol. Chem.*, 1941, v 138, 460.

§ "Protamone," Cerophyl Laboratories, Kansas City, Mo.

anesthetized with light ether anesthesia and the testicles and ovaries respectively removed. Thirty normal rats of each sex were retained as positive controls. All rats were fed ration 1 (Table I) without the addition of the thyroid-active material for a recovery and adjustment period of 10 days. At the end of this period, the rats were allotted into groups according to sex, weight, and gain during the standardization period. The rations shown in Table I were fed during the ensuing 2-week period; food and water were available *ad lib.* The rats were housed in individual cages and weighed at weekly intervals. Further details regarding the procedures employed will be found in a prevous communication(1).

Discussion. The results of this study are summarized in Table II. Examination of these data shows that the addition of either vit. B_{12} or 1:20 liver powder to the basal ration containing toxic levels of iodinated casein resulted in an increase of growth for all treatments. Analysis of variance of the data(5) showed that the differences were significant at the 1% level of probability. Normal males fed 1:20 liver powder showed an enhanced rate of growth compared with similar animals receiving crystalline vit. B_{12}. This difference was significant at the 5% level of probability. Liver also produced slightly better gains in castrate males than did vit. B_{12}. Normal females responded to either supplement, but significant differences between supplements were not found. Oophorectomized females responded in a similar manner as did normal males, but the differences in growth between supplements, although of nearly the same magnitude as in the normal males, did not achieve statistical significance.

It appears from these data that the male sex hormone may act synergistically in the hyperthyroid rat with some factor present in liver and not identical with vit. B_{12} or that the female sex hormone is antagonistic to such a factor. Thus, normal males and castrate females responded in a similar manner as did castrate males and normal females. The suggestion that factors other than B_{12} are necessary to cause a reversal of the growth-depressant effect of thyroid toxicity is in agreement with some of the findings of Ershoff(6). This worker, however, did not observe the growth stimulus with vit. B_{12} found in these experiments. The results of this study also suggest that the use of hyperthyroid animals for assay purposes without regard to sex, as recommended by Frost *et al.*(3), requires further investigation.

Summary. The growth response of normal and castrate hyperthyroid rats to supplementation with vit. B_{12} and liver concentrate powder has been investigated. Both supplements were effective in partially counteracting the growth depression induced by feeding toxic levels of iodinated casein to normal and castrate rats of both sexes. Vit. B_{12} was less effective than 1:20 liver powder for normal males and oophorectomized females. There were little difference in response to these supplements in normal females and castrate males. A sex difference in the growth response of the hyperthyroid rat to a factor

5. Snedecor, G. W., Statistical Methods, (Iowa State College Press, Ames), 1946.

6. Ershoff, B. H., PROC. SOC. EXP. BIOL. AND MED., 1950, v73, 459.

TABLE II. Response of Male, Female, and Castrated Rats to Rations Deficient in Vit. B_{12}.

Ration	2 weeks' gain			
	Uncastrated males, g	Castrated males, g	Uncastrated females, g	Castrated females, g
Ration 1 (basal ration)	46.7 (10)*	47 (10)	43.8 (10)	42 (6)
Ration 2 (ration 1 + 25 μg vit. B_{12} per kilo ration)	57.7 (10)†	60 (10)†	63 (10)†	64.4 (6)†
Ration 3 (ration 1 + 2% 1:20 liver concentrate powder)	69.2 (10)†‡	64.4 (10)†	62.2 (10)†	71.3 (6)†

* Numbers in parentheses are number of rats fed that ration.
† Indicates differences compared to basal ration were significant at 1% level of probability.
‡ Difference between gains of uncastrated males fed ration 3 and those fed ration 2 was significant at 5% level of probability.

present in liver concentrate and not identical with vit. B_{12} is suggested.

Appreciation is expressed to Merck and Co., Rahway, N. J., for the crystalline vitamins and vit. B_{12}, to Lederle Laboratories Division, American Cyanamid Corp., Pearl River, N. Y., for folic acid, to Wilson and Co., Chicago, Ill., for liver concentrate, and to the Cerophyl Laboratories, Kansas City, Mo., for iodinated casein (Protamone).

Received June 18, 1951. P.S.E.B.M., 1951, v77.

Metabolism of Plasma Substitute I. Dextran (Macrodex). (18870)

IRVING GRAY, PENTII K. SIITERI, AND EDWIN J. PULASKI.

From the Surgical Research Unit, Brooke Army Hospital, Brooke Army Medical Center, Fort Sam Houston, Texas.

The fate of dextran, unexcreted after intravenous infusion, is still undetermined. Bull and coworkers(1) report that it is not broken down by various animal tissues *in vitro*. Engstrand and Arberg(2) also have stated that dextran is not affected by tissue extracts, but is destroyed upon incubation with feces. They were able to recover 28% of infused dextran from the alimentary canal of the cat and 9% in the rabbit. We have attempted to confirm their results in 3 anesthetized dogs prepared as follows: (a) cannulae were placed in the bile duct and pyloric sphincter; (b) the upper end of the duodenum was tied off and a cannula placed in the lower end; (c) the upper end of the jejunum was tied off and a cannula placed in the ileo-caecal junction. The fluid from these areas was aspirated every 2 hours for 24 hours and each 2-hour sample was analyzed for dextran by the method of Hint and Thorsen(3). Less than 0.1% of 200 ml of 6% solution in physiologic saline infused, was found in any one of the regions cannulated. Failure to account for unexcreted dextran in the gastrointestinal tract led to study of the fate of this substance in the phlorizinized starved dog(4) to determine possible *in vivo* breakdown to dextrose.

Method. Mongrel dogs of both sexes were starved except for water. After 3 days, daily subcutaneous injections of 1 g of phlorizin suspended in 10 ml of olive oil, were begun and continued for the duration of the experiment (13-15 days). The animals were kept in metabolism cages and the urine collected every 24 hours. Complete collection was assured by catheterization. Dextrose in urine

1. Bull, J. P., Ricketts, C., Squire, J. R., Maycock, W. A., Spooner, S., Mollijon, J. C., and Patterson, J. C. S., *Lancet*, 1949, v256, 134.

2. Engstrand, L., and Arberg, B., *Lancet*, 1950, v258, 1071.

3. Hint, H. C., and Thorsen, G., *Acta Chem. Scand.*, 1947, v1, 808.

4. Lusk, G., The Elements of the Science of Nutrition, 4th ed., Philadelphia, W. B. Saunders, 1928.