

variation, and on the average is less than average values of 2.4 ml and 2.7 ml/g reported previously (10,11).

Summary. Changes in liver glycogen, water and potassium were compared in normal and potassium-deficient rats following administration of glucose, fructose and alpha-alanine, with and without potassium. Potassium-deficient rats deposited liver glycogen equally as well as normal rats. The simultaneous increases in liver water and potassium were likewise similar in the 2 groups of animals. No significant differences in changes in liver glycogen, water or potassium were noted with simultaneous administration of potassium.

1. Fenn, W. O., *Physiol. Rev.*, 1940, v20, 377.
2. Hastings, A. B., Renold, A. E., Teng, C. T., *Rec. Prog. Hormone Res.*, 1955, v11, 381.

3. Fenn, W. O., *J. Biol. Chem.*, 1939, v128, 297.
4. Gardner, L. I., Talbot, N. B., Cook, C. D., Berman, H., Uribe, R. C., *J. Lab. and Clin. Med.*, 1950, v35, 592.
5. Fuhrman, F. A., *Am. J. Physiol.*, 1951, v167, 314.
6. Silvette, H., Britton, S. W., Kline, R., *ibid.*, 1938, v122, 524.
7. Muntwyler, E., Griffin, G. E., Samuelsen, G. S., Griffith, L. G., *J. Biol. Chem.*, 1950, v185, 525.
8. Muntwyler, E., Griffin, G. E., *Proc. Soc. Exp. Biol. and Med.*, 1955, v89, 349.
9. Seifter, S., Dayton, S., Novic, B., Muntwyler, E., *Arch. Biochem.*, 1950, v25, 191.
10. Puckett, H. L., Wiley, F. H., *J. Biol. Chem.*, 1932, v96, 367.
11. MacKay, E. M., Bergman, H. C., *ibid.*, 1932, v96, 373.

Received April 18, 1958. P.S.E.B.M., 1958, v98.

Serum Calcium Levels in Thyroid-Ablated Rats.* (24058)

MARSHALL W. PARROTT, PATRICIA W. DURBIN, AND JUSTINE J. BURG
(Introduced by C. Willet Asling)

University of California Radiation Laboratory and Division of Medical Physics, Berkeley

Radioiodine is used extensively to destroy the thyroid gland. Complete and permanent thyroid ablation can be achieved in rats with an I^{131} dosage of 3 to 4 $\mu\text{C/g}$ body weight (1). Microscopic examination of peritracheal remnants from rats injected with I^{131} at this dosage revealed only superficial alteration of the intimately associated parathyroid glands, and for this reason the parathyroids have been presumed to be functional. At very high levels of I^{131} administration, however, enough of energetic beta radiation penetrates the parathyroid glands to effect an almost complete destruction (2). In a study of comparative reproductive capacities of female rats, whose thyroid glands had been destroyed with 5 $\mu\text{C/g}$ of I^{131} , and rats whose thyroid and parathyroid glands had been removed surgically (3), it was brought to our attention that parathyroid deficiency might seriously affect experimental results (4,5). McLean and

Urist (6) point out that parathyroid glands are of major importance in maintenance of normal blood calcium level. In the absence of parathyroid glands, the plasma calcium may fall 30% or more below normal. The calcium level in plasma should therefore be a good measure of the functional status of parathyroid glands. These studies compare the serum calcium levels of rats whose thyroids had been destroyed by low and high dosages of I^{131} beta radiation, with those in surgically thyro-parathyroidectomized rats.

Methods. The animals used were female Sprague-Dawley rats obtained from the original colony. They were housed in metal cages on wood shavings and were fed Purina Laboratory Chow and tap water *ad lib*. When the animals were 60 to 80 days old, 12 were surgically thyro-parathyroidectomized, 6 were given I^{131} † intramuscularly 5 μC I^{131} /gram body weight (1,3), 16 rats were given I^{131} in-

* This work was performed under auspices of U. S. Atomic Energy Com.

† I^{131} was obtained from Oak Ridge Nat. Lab. and was administered in basic solution of Na_2SO_3 .

travenously 50 to 90 $\mu\text{C/g}$, and 12 normal rats of varying ages served as controls. Sixty or more days after treatment (see Table I for exact age at sacrifice) the animals were anesthetized with ether, and 6-ml blood sample was drawn into a heparinized syringe from the inferior vena cava. The red cells were separated from plasma by centrifugation, and plasma calcium was measured in duplicate 1-ml samples by the method of Rehell(7). When present, thyroid and (or) parathyroid remnants were dissected and fixed in Bouin's fluid. Paraffin embedded sections were cut at 6 μ and stained with hematoxylin and eosin.

TABLE I. Serum Calcium Levels of I^{131} Thyroid-Ablated Rats and Surgically Thyro-parathyroidectomized Rats.

Treatment group	Rats			Serum Ca^{++} (mg/100 ml $\pm$ S.E.)	
	No.	Age (days)	Wt (g)		
Control	12	143 to 443	292	9.84	.11
Surgery	12	472	259	7.86	.21
I^{131} , 5 $\mu\text{C/g}$	6	143	278	9.30	.02
" , >50 $\mu\text{C/g}$	16	300 to 400	185	7.91	.29

Underlined means were compared to the control mean by the t-test of Fisher(8) and P-value was beyond the 1% level of confidence.

Results. Serum calcium levels of various groups are shown in Table I. No significant difference was found between 8 control rats 143 days old and 4 controls 443 days old; therefore data for these groups have been combined. Rats that received I^{131} 50 $\mu\text{C/g}$ had serum calcium levels identical to those given 90 $\mu\text{C/g}$ of I^{131} ; therefore these groups also have been combined. As shown in the Table, animals whose thyroid and parathyroid glands had been removed surgically or destroyed by very large amount of I^{131} had plasma calcium levels 22% below the normal mean. On the other hand, the low-level I^{131} -treated rats whose thyroid glands had been completely ablated, as shown in Fig. 1 (see also ref. 1), had a mean serum calcium level that differed only slightly from that of intact rats. For comparison the extent of parathyroid destruction following a massive dose of I^{131} is shown in Fig. 2.

Discussion. These measurements indicate that at relatively low dosages, 5 to 10 $\mu\text{C/g}$

body weight, I^{131} can be used to effect complete destruction of thyroid gland of the rat

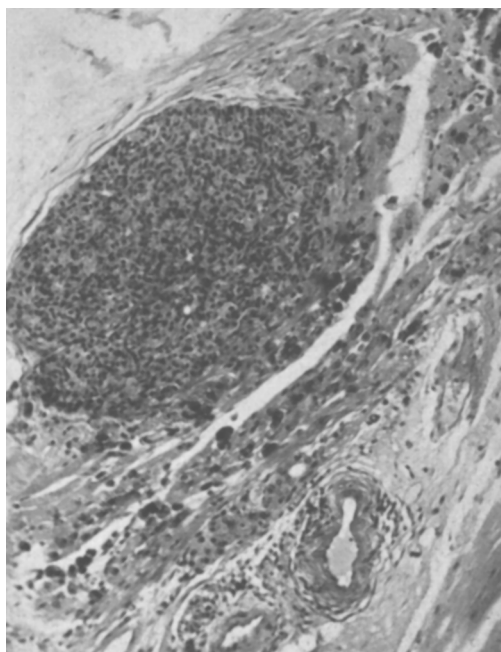


FIG. 1. Tracheal remnant from a rat 10 mo after receiving 10 $\mu\text{C/g}$ of I^{131} . Note absence of any thyroid tissue and almost intact parathyroid gland. H and E, $\times 50$.

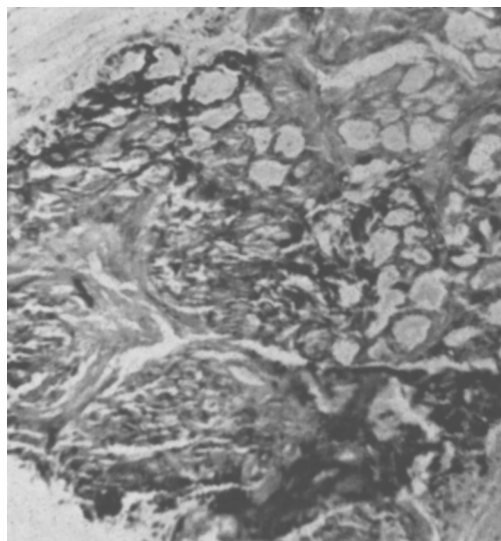


FIG. 2. Tracheal remnants from a rat 12 mo after receiving 50 $\mu\text{C/g}$ of I^{131} . Note "burned-out" appearance of thyroid tissue and marked fibrous replacement of parathyroid tissue. (Peritracheal tissue uptake of a tracer dose of I^{131} 24 hr before sacrifice of this animal was 0.02%.) H and E, $\times 60$.

without serious impairment of the capacity of parathyroid glands to maintain a normal plasma calcium level. At higher I^{131} dosages, however, the parathyroid glands are severely damaged, and the plasma Ca^{++} falls to the same level as that observed in surgically thyroparathyroidectomized animals.

Summary. Serum calcium levels have been measured in adult female Sprague-Dawley rats whose thyroid glands had been removed either with I^{131} or by surgery. The mean serum Ca^{++} level of rats whose thyroids had been completely ablated with $5 \mu C/g$ body weight of I^{131} was within normal limits, 9.3 ± 0.02 mg. 100 ml. Complete destruction of the parathyroids, as well as the thyroid gland, was effected by a dosage of $50 \mu C/g$ I^{131} .

1. Goldberg, R. C., Chaikoff, I. L., *Endocrinology*, 1949, v45, 64.
2. Durbin, P. W., Asling, C. W., Johnston, M. E., Hamilton, J. G., *Am. J. Roentgenol. Rad. Therapy Nuc. Med.*
3. Parrott, M. W., Durbin, P. W., Hamilton, J. G., *Univ. Calif. Radiation Lab.*, 1957, UCRL-8042.
4. Mazur, H. M., Univ. Calif. (Berkeley), Thesis, 1935.
5. Bodansky, M., Cooke, W. R., *Proc. Soc. Exp. Biol. and Med.*, 1937, v36, 188.
6. McLean, F. C., Urist, M. R., *Bone*, Univ. Chicago Press, Chicago, 1955, Chapter 10.
7. Rehell, B., *Scand. J. Clin. Lab. Invest.*, 1954, v6, 335.
8. Fisher, R. A., *Statistical Methods for Research Workers*, Hafner Publishing Co., N. Y., 1954, 12th Edition.

Received April 21, 1958. P.S.E.B.M., 1958, v98.

Role of Adrenaline and Nor-Adrenaline on Response of Cold-Acclimatized Animals to Chlorpromazine. (24059)

J. A. LEBLANC*

Directorate of Medical Research, U. S. Army Chemical Warfare Laboratories, Army Chemical Center, Md.

Adrenaline has proved important in increased potential for chemical regulations observed in cold-acclimatized animals(1-7). Recently Hart(8) and Sellers(9) summarized present knowledge on acclimatization to cold in homeotherms. In terms of survival, acclimatization may be defined as an acquired increase in resistance to hypothermic effect of cold environment. Recently we reported that acclimatized animals are not only resistant to hypothermia caused by cold temperatures but also to that induced by chlorpromazine(10). The present study was designed to find out if decreased hypothermic effect observed in acclimatized animals after chlorpromazine injection was related in some way to adrenaline or nor-adrenaline action.

Methods. White male rats weighing 200 g were used. Thirty rats, acclimatized to cold for 4 weeks at $40^{\circ}F$ were divided into 5 groups

which were treated respectively with: (1) chlorpromazine (CPZ) (10 mg/kg); (2) CPZ (10 mg/kg) + adrenaline bitartrate (0.2 mg/kg of base); (3) CPZ (10 mg/kg) + nor-adrenaline bitartrate (0.2 mg/kg of base); (4) CPZ (10 mg/kg) + dibenamine (20 mg/kg) and (5) CPZ (10 mg/kg) + pyribenzamine (10 mg/kg). Five groups of control animals, non-acclimatized to cold, were treated in the same manner. All drugs were injected intraperitoneally. Rectal temperatures were measured with a thermocouple inserted at a depth of 40 mm. The cold-acclimatized animals after being in the cold for 4 weeks were kept for 24 hours at $72^{\circ}F$ prior to drug injection. The experiment was performed in room maintained at $72^{\circ}F$.

Results. Fig. 1 illustrates the typical CPZ hypothermia which is not, however, significantly affected by injections of either adrenaline or nor-adrenaline. The potentiation of CPZ hypothermia by dibenamine and pyri-

* Present address: Dept. de Physiol., Ecole de Medecine, Univ. Laval, Quebec, Canada.