Of considerable interest, however, is the pronounced increase in weight shown by the uterus under the influence of this extract. These weights are out of all proportion to the ovarian response and show a progressive increase according to the amount of extract administered. This is also marked even with small doses when the preparation is given over a prolonged length of time. In the appended table are a few examples illustrating the effects obtained with one of the extracts, and for comparison are listed the findings in 3 immature rats each of which received one rabbit anterior pituitary gland implant daily for 3 days. However, as pointed out by Smith and Engle,[4] the uterine weights do not represent the absolute tissue gain as they were almost all done at a stage of uterine engorgement when the vaginal smear showed cornified or nucleated epithelial cells. The factors concerned in this phenomenon are not clear, but it is believed that the uterine growth is not due to ovarian hormones present in the extracts since these were ineffective in immature spayed rats.

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Observations on Mørch's Method for Standardization of Thyroid Gland Preparations.

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Mørch[1] devised a method for the standardization of thyroid preparations based on the percentage increase of the carbon dioxide output of white mice after administration of thyroid preparations. Gaddum and Hetherington[2] compared the physiological activity of thyroid preparations with the thyroxine content as determined by Harington and Randall.[3] It seemed desirable to investigate the question whether the thyroid glands of patients with exophthalmic goiter contained some substance other than thyroxine itself which might cause an increase in the basal metabolic rate. An answer seemed possible by feeding animals equi-thyroxine doses of dif-

[1] Mørch, J. R., *J. Physiol.*, 1929, **67**, 221.

[2] Gaddum, J. H., and Hetherington, M., *Quart. J. Pharm. and Pharmacol.*, 1931, **4**, 183.

[3] Harington, C. R., and Randall, S. S., *Quart. J. Pharm. and Pharmacol.*, 1929, **2**, 501.

ferent gland preparations obtained from patients with Graves' disease and from normal individuals. If the physiological activity of the 2 types of preparations proved to be the same, this might be considered evidence that the increase in basal metabolism characteristic of Graves' disease could be accounted for by the thyroxine content alone. It would then be unnecessary to postulate the presence of any other toxic substance. The method developed by Mørch was chosen since it has the necessary feature that small amounts of material can be employed.

Normal thyroid preparations from the series of Leland and Foster[4] and exophthalmic goiter preparations from the series of Gutman, Benedict, Baxter and Palmer[5] were used. All glands were analyzed by the method of Leland and Foster. The optimal experimental conditions worked out by Mørch were closely adhered to and it was found that the carbon dioxide output of the mice could be determined with the degree of precision which he claims (Table I).

TABLE I.
Normal Mice.

No	Wt. in gm.	Production of CO_2 in 24 hours on consecutive days in gm. 1st	2nd	3rd	4th	5th	Average
11	18.0	3.14	2.90	2.99	3.13	3.13	3.06
12	17.0	3.10	3.20	3.24	3.10	2.94	3.12
17	17.5	3.36	3.45	3.47	3.44	3.34	3.41
29	17.5	3.44	3.60	3.43	3.35	3.39	3.44
20	17.0	3.14	3.13	3.23	3.20	3.25	3.19
25	17.0	3.55	3.58	3.74	3.74	3.63	3.65
31	18.5	3.27	3.35	3.38	3.44	3.34	3.36

The commercial thyroid preparation used as a standard (Burroughs Wellcome & Co.) was first administered by mixing dry with the food as directed by Mørch. Later it was given in the form of a uniform suspension in 0.9% NaCl. A sufficient amount of the thyroid preparation was weighed out so that 2 cc. contained the correct dosage for a 20 gm. mouse. Daily variation of the dosage with change in weight was thus made easy. The suspension was shaken well and delivered directly onto the dry food, followed by 3 cc. of milk. The food intake was cut to a minimum for weight maintenance, so that every morsel was eaten. This method of administration seemed more satisfactory than mixing a very small amount of gland material with a large quantity of food. No other variations were made from Mørch's technique.

[4] Leland, J. P., and Foster, G. L., *J. Biol. Chem.*, 1932, **95**, 165.

[5] Gutman, A. B., Benedict, E., Baxter, B., and Palmer, W. W., in press.

The results are shown in Table II.

TABLE II.

Mouse No.	Thyroid Preparation	Type Gland	Total Iodine	Thyroxine Iodine	CO_2 Increase Av. 5 days	Daily Dosage per 20 gm. Mouse Thyroid	Daily Dosage per 20 gm. Mouse Thyroxine Iodine	Control Response to Standard Preparation (2)
			mg. per gm.	mg. per gm.	%	mg.	γ (1)	
1	B. W. & Co.	Hog	2.54	0.592	—1.2	0.12	0.071	
2	"	"	2.54	0.592	6.7	0.12	0.071	
3	"	"	2.54	0.592	7.4	0.12	0.071	
4	"	"	2.54	0.592	8.0	0.15	0.089	
5	"	"	2.54	0.592	—1.8	0.15	0.089	
6	"	"	2.54	0.592	9.9(3)	0.20	0.118	
7	"	"	2.54	0.592	25.5	0.20	0.118	
8	"	"	2.54	0.592	22.6(3)	0.20	0.118	
9	"	"	2.54	0.592	8.6	0.25	0.148	
10	"	"	2.54	0.592	29.6	0.25	0.148	
11	"	"	2.54	0.592	22.3	0.25	0.148	
12	N. J.	Graves'	2.80	0.540	21.3	0.274	0.148	
13	"	"	2.80	0.540	1.2	0.274	0.148	2.3
14	No. 40	Normal	1.43	0.352	—3.3	0.420	0.148	1.1
15	"	"	1.43	0.352	4.0	0.420	0.148	10.3
16	"	"	1.43	0.352	3.6	0.420	0.148	9.9
17	"	"	1.43	0.352	2.6	0.420	0.148	
19	P. S.	Graves'	3.90	1.10	18.7	0.134	0.148	
20	"	"	3.90	1.10	8.1	0.134	0.148	
21	A. S.	"	3.18	0.468	0.8	0.316	0.148	—5.2
22	"	"	3.18	0.468	1.9	0.316	0.148	7.4
23	C. W.	"	1.54	0.16	—3.4	0.92	0.148	—2.4
24	"	"	1.54	0.16	—10.0	0.92	0.148	1.3
25	"	"	1.54	0.16	7.1	0.92	0.148	4.7
26	"	"	1.54	0.16	1.6	0.92	0.148	14.6
27	"	"	1.54	0.16	8.7	0.92	0.148	10.7
28	"	"	1.54	0.16	—2.4	0.92	0.148	7.9
29	A. H.	"	2.14	0.535	—7.9	0.277	0.148	0.4
30	"	"	2.14	0.535	—15.3	0.277	0.148	—14.2
31	"	"	2.14	0.535	2.1	0.369	0.148	12.4
32	A. M.	"	3.88	0.69	15.0	0.213	0.148	
33	"	"	3.88	0.69	14.9	0.213	0.148	
34	No. 27	Normal	1.21	0.272	—0.3	1.09	0.296	
35	"	"	1.21	0.272	7.9	1.09	0.296	
36	"	"	1.21	0.272	17.2	1.09	0.296	
37	"	"	1.21	0.272	16.5	1.09	0.296	
38	"	"	1.21	0.272	13.1	2.18	0.592(4)	

(1) $1\gamma = 0.000001$ gm.

(2) Animals failing to show a significant increase in CO_2 production after treatment with human thyroid preparations were rested from 10 to 15 days and then treated with the same dose of standard preparation.

(3) Accidental death after 2 days in the respiratory chamber.

(4) Two animals (not reported) died after 3 weeks' treatment with this dosage.

Although Gaddum and Hetherington found it necessary to use large amounts of thyroid in order to obtain significant increases in CO_2 production, positive responses were obtained in this laboratory in some cases at the low levels of dosage recommended by Mørch.

Gaddum and Hetherington attribute this difference in dosage to the possibility that their animals were less sensitive than those of Mørch. From Table II it may be seen that no valid conclusions can be drawn as to the comparative activity of different thyroid preparations since different mice vary markedly in their response to the same dose of a given thyroid preparation, even though administered in an identical manner to animals kept under similar conditions. For example, a given dose of gland No. 27 produced changes in CO_2 output ranging from —0.3 to +17.2, while preparation marked N. J. produced in one case +21.3% and in another case +1.2%.

Our experience with the method of Mørch is disappointing. Possibly observations sufficiently great in number to afford a comparison of the means rather than of individual values might yield intelligible results. The method is long and tedious. Its reliability, even with a large series, is doubtful.

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Assay of Thyroid by Chemical Estimation of the Thyroxine Content.

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To investigate the variation in the thyroxine content of commercial thyroid preparations, thyroid tablets from 15 representative pharmaceutical firms were obtained in the open market and analyzed for total iodine, inorganic iodine and thyroxine. Harington and Randall[1] made a similar survey, and found in tablets "each equivalent to 5 grains of fresh thyroid gland", a variation of about 600% in the thyroxine content, as estimated by the total iodine in the acid-insoluble fraction. However, recent work[2, 3, 4] suggests that abso-

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[1] Harington, C. R., and Randall, S. S., *Quart. J. Pharm. and Pharmacol.*, 1929, **2**, 501.

[2] Kendall, E. C., and Simonsen, D. G., *J. Biol. Chem.*, 1928, **80**, 357.

[3] Leland, J. P., and Foster, G. L., *J. Biol. Chem.*, 1932, **95**, 165.

[4] Gutman, A. B., Benedict, E. M., Baxter, B., and Palmer, W. W., *J. Biol. Chem.*, in press.