blood). Such a theory is reinforced by the observation that 2 of the normal subjects given 5 mg of folic acid daily for a week showed more prolonged high levels and a later peak in the 1 mg tolerance test after this "saturating dose" than before.

From these limited observations, the oral folic acid tolerance test appears to be a useful tool in the study of folic acid metabolism. Additional studies of the level and duration of serum folic acid increases should provide evidence concerning the rate of folic acid absorption as well as the rate of its removal from the blood in suspected deficiency states.

Summary. An oral folic acid tolerance test is described and its limitations discussed. Evidence is presented that the test is useful in assessing the absorption of folic acid. No defect in the gastrointestinal absorption of folic acid in patients with pernicious anemia has been demonstrated.

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Thyroid Function in Hypophysectomized Mice Bearing Intraocular Pituitary Implants. (20012)

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(Introduced by Roy Hertz.)

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There are conflicting reports(1-8) on the degree of secretory activity of the mammalian pituitary transplanted from its normal site. Most investigations were conducted with animals of unspecified genetic constitution. Since genetic heterogeneity may have affected the viability of the transplants, it was felt that a reinvestigation of the problem utilizing a genetically homogeneous group of animals might be of value. In the present experiments, intraocular pituitary transplants maintained a level of thyroidal radioiodine metabolism much higher than that of hypophysectomized controls but had no significant effect on body weight or on the weight of the thyroid, adrenals, ovaries, or uterus.

Materials and methods. BALB/c x C_3H mice were used in all experiments. As F_1 derivatives of 2 closely inbred lines, transplantation among them produces no incompatibility reaction and implants persist indefinitely. Two-month-old females were used as hosts except in Exp. VII, where 4-week-old females were implanted. In one experiment, not included in Table I, males were used as hosts. There was no indication of a sex difference in the response. Donors were embryos at the 14th or 15th day of gestation (Exp. I, II, VI, VII) or 1-2 day old newborn mice (Exp. III, IV, V) irrespective of sex. A single pituitary was transplanted into each animal except in Exp. IV, in which 4 pituitaries were implanted, 2 into each eye. The pituitaries were placed into the anterior chamber by a method previously described(9). Exp. VIII was designed to test the potency of adult pituitaries. Here 3-month-old females were donors and 1/3 pituitary was placed in each

TABLE I. Effect of Pituitary Implants on Thyroid Function and Target Organ Weight.

Exp. # and group*		No. of animals	Age at autopsy, wk	Terminal body wt	Ovaries wt, mg	Uterus wt, mg	Adrenal wt, mg	Thyroid wt, mg	T/S ratio of I^{131}	Total thyroidal I^{131} uptake, %‡
I	C	4	14	22.5± .8†	12 ±1.3	119.5±19.1	6 ±.4	2.4±.1		100 ± 9.3
	H	5		18.2± .5	3.2± .2	22.2± 1.2	2.6±.2	1.5±.1		.9± .2
	I	6		18.6± .9	3.4± .5	22.7± 1.8	2.8±.2	1.6±.1		33.6± 2.5
II	C	6	13					2.1±.1		100 ±13.3
	I	5						1.4±.1		27.3± 2.8
III	C	13	14	23 ± .3				2.4±.1		100 ± 6.3
	H	11		18.6± .6				1.6±.1		2.1± .2
	I	13		20.4± .5				1.7±.1		47 ± 4.1
IV	C	4	18	25.5± .6	15 ± .6	154.1±18	6.5±.1	2.6±.1		100 ±15.4
	H	5		16.7±1.1	1.8± .1	15.1± 2.2	2.1±.2	1.1±.1		1.9± .9
	I	2		19 ±1	1.8± .3	17.1± 1.8	2.3±.1	1.5±.2		41.1± 3.2
V	C	6	15	22.7± .3		120.4±15.5		2.5±.1	265±20.2	
	H	6		16.2± .3		18.6± .3		1.4±.1	29± 4.6	
	I	11		17.3± .3		18.6± .6		1.5±.1	175±18.1	
VI	C	6	13	23.2±1			5.6±.2			
	H	6		18.5± .6			2.7±.2			
	I	4		19.1± .6			2.5±.2			
VII	C	4	9	19.1± .8	7.2± .8	56.7±10	4.7±.1	1.8±.1		
	H	3		12.9± .3	1.6± .2	8.8± 1.7	1.7±.1	.9±.1		
	I	4		14.6± .6	1.6± .1	9.1± .9	2.1±.1	1.2±.2		
VIII	C	6	15	23.8± .5		156 ±15.2		2.5±.1		100 ± 5.4
	H	11		21.5± .3		21.3± .3		1.9±.1		2.5± .2
	I	8		19.4± .3		21.8± .4		2 ±.1		32.2± 2.9

* C = intact controls, H = hypophysectomized controls, I = hypophysectomized-implanted mice.
† Stand. error.
‡ Thyroidal I^{131} uptake is expressed as total uptake for entire thyroid gland. For comparison the uptake of intact controls in each exp. is given as 100% and other figures are relative to this standard. The absolute thyroidal accumulation of intact controls averaged 10-15% of administered dose at end of 4 hr.

eye of the host. In all experiments the animals were hypophysectomized by the parapharyngeal approach one week after implantation. Control groups consisted of unoperated and hypophysectomized mice of the same age. Three weeks after hypophysectomy the animals were utilized in the definitive experiments.* To determine *total accumulation* of *radioiodine,* each animal was injected with a small tracer dose of I^{131}, ranging from 0.05 to 1 μc in the individual experiments. All animals in a given group were killed by exsanguination at the same interval after radioiodine injection—either 3½ or 4 hours. After weighing, the thyroid was placed on a filter-paper-covered flat copper planchet, the whole enclosed in Scotch tape, and the thyroid smashed flat by drawing a heavy weight over it. Radioactivity of the sample was determined by beta-counting with a mica end-window G-M tube. The *thyroid/serum iodide ratio,* comparing the concentration of I^{131} as iodide in the thyroid with that of the serum, was determined by a method similar to that previously described for the rat(10). Each mouse received a subcutaneous injection of 2.5 mg propylthiouracil 30 minutes before the administration of a tracer dose of radioiodine. The animals were killed by exsanguination 2 hours after the I^{131} injection. Radioactivity per unit weight of thyroid was then compared to that of the serum. The uteri were weighed on a 0-200 mg Roller-Smith torsion balance. All other organs were weighed on a 0-15 mg Roller-Smith balance.

Results. No significant anterior lobe func-

* The animals were fed the following pellet diet: skim milk powder, 22.75; ground whole wheat, 61.52; brewer's yeast (dried), 4.00; cod-liver oil, 2.00; sodium chloride, 1.40; ferric citrate, 0.13; corn oil, 8.20.

tion could be detected from the weight of the various target endocrine organs or from body weight. As seen in Table I, thyroid, adrenals, ovaries, and uterus were equally atrophic in the hypophysectomized control and hypophysectomized-implanted animals. In marked contrast to this was the ability of the thyroid of the implanted animals to accumulate I^{131}. Intraocular pituitary tissue enabled the thyroid to accumulate radioiodine to levels 20-30 times that of hypophysectomized controls and 2/3 that of intact controls per unit thyroid weight. Similarly, the implanted animals had a much higher thyroid/serum iodide ratio than their hypophysectomized controls, but again this was only 2/3 that of the intact controls.

No difference resulted when either embryonic, newborn, or adult donors were used, or when two-thirds, one, or 4 pituitaries were implanted.

Discussion. These results indicate that thyroidal concentration and uptake of iodine can vary independently of thyroid weight. Apparently an intraocular pituitary implant in the mouse is able to maintain approximately normal iodine metabolism by the thyroid gland, as measured by the thyroid/serum iodide ratio and by total thyroidal accumulation of I^{131} at the end of 4 hours. It is not, however, able to maintain thyroid weight significantly above the values of hypophysectomized controls.

Experiments in the rat have previously indicated that thyroid weight and follicle cell height vary independently of the thyroid/serum ratio(10). Anterior hypothalamic lesions in this animal prevent any increase in thyroid size due to chronic thiouracil administration but do not prevent the usual 10-fold increase in thyroid/serum iodide concentration(11). This indicates that integrity of the anterior hypothalamus may be necessary for the pituitary to maintain the weight and cell height of the thyroid. The present data indicate further that the pituitary of the mouse may maintain thyroidal iodine metabolism in the absence of direct hypothalamic connections.

Summary. Intraocular hypophysial transplants in hypophysectomized mice did not maintain body weight or the weights of thyroid, ovaries, adrenals, or uterus significantly above those of hypophysectomized controls. Nevertheless, the implants were able to maintain a radioiodine uptake per unit thyroid weight and a thyroid/serum iodide ratio at 2/3 the level of the intact controls. This indicates that thyroid function and thyroid size are not necessarily correlated in the mouse and that the former can be maintained to considerable degree in the absence of the normal hypophysial anatomical relationship.

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