LITERATURE CITED

- 1. V. P. Evdakov, A. N. Gvozdetskii, A. A. Gorokhov, et al.. Dokl. Akad. Nauk SSSR, <u>214</u>, 970 (1974).
- 2. A. G. Konoplyannikov, O. A. Konoplyannikova, O. V. Semina, et al., Radiobiologiya, No. 1, 49 (1974).
- 3. R. V. Petrov, A. N. Gvozdetskii, V. P. Evdakov, et al., Zh. Mikrobiol., No. 11, 37 (1974).
- 4. R. V. Petrov, R. M. Khaitov, E. V. Kozhinova, et al., Tsitologiya, No. 3, 321 (1975).
- 5. O. V. Semina, A. G. Konoplyannikov, and A. M. Poverennyi, Radiobiologiya, No. 5, 686 (1974).
- 6. M. Degre, Proc. Soc. Exp. Biol. (N. Y.), <u>142</u>, 1087 (1973).
- 7. P. Dukor, G. Schumann, R. H. Gisler, et al., J. Exp. Med., 139, 337 (1974).
- 8. A. K. Field, A. A. Tytell, G. P. Lampson, et al., Proc. Nat. Acad. Sci. USA, <u>58</u>, 1004 (1967).
- 9. T. A. McNeill, W. A. Fleming, and D. J. McCance, Immunology, <u>22</u>, 711 (1972).
- 10. T. A. McNeill and J. Gresser, Nature New Biol., 244, 173 (1973).
- 11. P. J. Quesenberry, A. Morley, M. Ryan, et al., J. Cell Physiol., 82, 239 (1973).
- 12. G. Rita, F. Dianzani, and S. Gagnoni, Coll. Inst. Nat. Sante Rech. Med. (L. Interferon), 6, 193 (1970).
- 13. L. Siminovitch, E. A. McCulloch, and J. E. Till, J. Cell. Comp. Physiol., 62, 327 (1963).
- 14. J. E. Till and E. A. McCulloch, Radiat. Res., 14, 213 (1961).

STATE OF THE PITUITARY—THYROID SYSTEM IN PREGNANT RABBITS, FETUSES, AND NEWBORN RABBITS

Academician Ya. Kh. Turakulov,*
N. S. Salakhova, and T. P. Tashkhodzhaeva

UDC 612.63+612.64]:612.433'441

The functional state of the pituitary—thyroid system was studied in pregnant rabbits and in their fetuses during the last third of pregnancy. Between the 23rd and 27th day of pregnancy the uptake of ¹³¹I and the intensity of hormone synthesis in the thyroid glands of mother and fetus were increased; this, together with changes in the histological structure of the gland, was evidently connected with an increase in the thyroxine requirement at this period in the mother + fetus system. The above-mentioned changes in the mother were preceded by increased thyrotropic function of the pituitary, but no such correlation was found in the fetus. The results are evidence that the functional activity of the maternal pituitary—thyroid system changes rapidly in accordance with the body's requirements of thyroid hormone.

KEY WORDS: pregnancy; fetus; thyroid gland; pituitary gland.

This investigation consists of an analysis of the function of the pituitary—thyroid gland system of the mother and fetus in rabbits.

*Academy of Sciences of the Uzbek SSR.

Laboratory of Hormone Biochemistry, Institute of Biochemistry, Academy of Sciences of the Uzbek SSR, Tashkent. Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 83, No. 4, pp. 476-479, April, 1977. Original article submitted October 26, 1976.

This material is protected by copyright registered in the name of Plenum Publishing Corporation, 227 West 17th Street, New York, N.Y. 10011. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, microfilming, recording or otherwise, without written permission of the publisher. A copy of this article is available from the publisher for \$7.50.

TABLE 1. Content of Iodinated Components in Thyroid Gland and Uptake of ^{131}I by It in Fetuses and Newborn Rabbits (M \pm m)

Days of develop- ment	· · · · · · · · · · · · · · · · · · ·	131I, counts/											
	MIT	DIT	IOD	Т3	T4	X com- ponent	iodothyro- nines/iodo- tyrosines	made: 1					
Fetuses													
20 (3)* 21 (3) 22 (2) 23 (3) 24 (4) 25 (4) 26 (3) 27 (4) 28 (3) 29 (4) 30 (4)	30,9±1,5 21,6±1,2 18,0±0,8 13,2±1,0 12,8±1,6 15,2±1,2 11,0±2,0 10,5±3,1 14,2±4,4 17,2±0,8 13,6±1,7	21,9±1,8 17,6±2,4 23,9±2,1 17,5±0,7 16,1±0,8 11,6±1,8 18,7±2,3 16,7±1,1 12,4±2,2 19,1±4,1 18,2±2,9	$4,8\pm0,8$ $13,2\pm0,9$ $14,0\pm1,1$ $16,5\pm2,4$ $9,0\pm0,98$ $12,8\pm1,1$ $17,4\pm1,8$ $21,0\pm3,1$ $18,5\pm5,2$ $13,8\pm0,9$ $11,9\pm2,3$	15,4±1,0 15,0±0,8 13,5±1,0 14,5±0,2 14,9±0,5 10,2±0,6 11,0±1,5 10,2±1,5 8,5±0,58 7,8±1,45 8,5±2,3	9,6±0,94 12,4±1,0 17,7±0,5 22,6±1,2 27,2±1,0 31,5±2,2 29,5±4,2 27,5±1,8 26,3±3,1 30,0±11,5 28,7±2,0	17,2±1,2 19,5±0,7 12,9±1,2 18,8±0,7 13,7±1,0 18,5±3,0 12,1±2,0 13,8±2,2 19,9±3,3 12,0±2,0 18,5±4,2	0,47 0,70 0,74 1,21 1,47 1,56 1,36 1,38 1,31 1,02 1,17	$5,6\pm1,32$ $14,7\pm3,0$ $20,1\pm3,8$ $52,9\pm1,1$ $468,3\pm23,4$ $183,3\pm45,2$ $114,8\pm38,1$ $255,3\pm83,5$ $132,4\pm46,7$ $159,6\pm41,5$ $329,3\pm105,3$					
Newborn rabbits													
1 (3) 7 (5) 10 (3) 24 (3) 30 (4)	13,1±3,1 13,1±2,8 12,8±4,1 16,6±4,0 18,6±3,5	21,6±6,1 22,1±4,1 19,5±3,6 25,1±3,1 26,2±2,9	19,1±3,3 16,3±5,1 21,6±4,2 15,1±2,6 14,1±3,8	6,0±1,2 10,3±1,5 6,1±0,80 5,8±0,90 19,5±4,4	19,0±3,5 18,0±2,6 13,5±2,1 18,2±3,2 6,2±2,81	21,1±3,6 19,7±2,1 24,8±4,0 19,2±3,7 15,7±1,21	0,70 0,79 0,60 0,56 0,57	220,5±34,0 364,0±80,0 172,8±24, 83,4±9,4 93,0±10,5					

*Here and in Table 2, number of litters (for fetuses) and number of rabbits (newborn) shown in parentheses.

EXPERIMENTAL METHOD

Experiments were carried out on 100 rabbits during the last third of pregnancy on their fetuses, and on 25 newborn rabbits aged from 1 day old to 1 month old. The adult animals, on the day before the analysis, were given ^{131}I in a dose of 10 μCi , and the newborn rabbits received ^{131}I intravenously in doses of between 0.5 and 5 μCi . The iodine uptake of the thyroid gland was measured with an MST counter and the composition and content of iodine-containing components in the gland were investigated radiochromatographically. For morphological analysis the thyroid glands were processed by the usual histological methods and stained with hematoxylin-eosin. The pituitary gland was stained in accordance with the scheme: potassium permanganate—alcian blue—PAS—orange G [3].

EXPERIMENTAL RESULTS

Incorporation of ¹³¹I by the fetal thyroid gland was found on the 15th-16th day of development. In increased until the 24th day, remained at a high level until birth, and gradually returned to normal in the postnatal period.

On the 20th day of development, a complete quota of iodinated amino acids was present in the fetal thyroid gland, the iodothyronines/iodotyrosines ratio at first showed a shift toward the iodotyrosines, but by the 23rd day it was close to the value for the adult gland; and it remained at a high level until birth (Table 1).

Morphological analysis of the fetal thyroid gland showed a very high level of functional activity between the 24th and 26th days of development; many follicles contained a high thyroid epithelium and vacuolated colloid of very small diameter. Later the height of the thyroid epithelium was reduced, colloid accumulated, and the follicles enlarged to reach the characteristic size of the gland in animals aged 1 month.

Thyrotrophs could be distinguished in the fetal adenohypophysis as early as on the 21st-22nd day of development: Their number rose steadily to reach a fairly high level at birth. However, their intensity of staining was low, indicating a low content of secretion. On the 24th day, large numbers of somatotropic cells began to appear in the pituitary.

The ability of the maternal thyroid gland to assimilate ¹³¹I, which increased until the 24th day of pregnancy, fell sharply toward its end.

The intensity of hormone formation in the maternal thyroid gland rose sharply after the 22nd day of pregnancy and remained at a high level until the 27th day (Table 2).

TABLE 2. Content of Iodinated Components in Thyroid Gland and Uptake of 131 I by It in Rabbits during Last Third of Pregnancy (M \pm m)

	Iodinated components, %								
Days of pregnancy	MIT	DIT	IOD	T4	T4	ponents	iodothyro- nines /iodo- tyrosines	131 I, counts/ min/mg	
19 (n=4) P 20 (n=4) P 21 (n=3) P 22 (n=3) P 23 (n=3) P 24 (n=4) P 25 (n=4)	19,5±1,9 >0,1 20,0±1,3 >0,1 13,7±1,5 <0,01 11,2±3,2 <0,01 6,3±1,23 <0,001 8,9±1,34 <0,001 15,7±0,6 <0,01	21,4±1,6 >0,1 22,3±163 >0,1 18,9±1,8 <0,01 21,8±2,9 >0,1 23,4±0,6 >0,1 16,8±2,9 <0,01 14,8±0,7 <0,01	$ \begin{vmatrix} 9,6\pm 1,35 \\ >0,1 \\ 10,4\pm 0,72 \\ >0,1 \\ 8,5\pm 0,92 \\ >0,1 \\ 12,7\pm 1,0 \\ >0,1 \\ 7,2\pm 0,89 \\ <0,001 \\ 11,1\pm 1,8 \\ >0,1 \\ 9,3\pm 1,45 \\ >0,1 \end{vmatrix} $	7,0±1,25 >0,1 5,2±0,81 <0,01 12,2±0,1 <0,01 4,9±1,11 <0,01 21,7±0,9 <0,001 15,4±1,3 <0,01 9,2±0,85 >0,1	$\begin{array}{c} 27,2\pm2,1\\ <0,02\\ 28,8\pm1,0\\ <0,01\\ 29,3\pm2,5\\ <0,001\\ 36,2\pm10,0\\ <0,01\\ 25,9\pm2,1\\ <0,05\\ 27,7\pm2,5\\ <0,02\\ 36,5\pm3,1\\ <0,001\\ \end{array}$	14,3±3,4 <0,02 13,1±3,2 <0,02 17,1±2,2 <0,01 12,9±2,6 <0,02 15,2±1,1 <0,02 19,8±0,6 <0,05 14,6+1,2	0,84 0,80 1,28 1,25 1,61 1,69	$\begin{array}{c} 329,4\pm86,3\\ <0,001\\ 60,0\pm1,0\\ <0,001\\ 136,8\pm12,2\\ <0,001\\ 205,6\pm32,5\\ <0,001\\ 106,3\pm17,8\\ <0,001\\ 499,5\pm158,8\\ <0,001\\ 84,5\pm11,3\\ <0,001\\ \end{array}$	
26 (n=4) 27 (n=4) P 28 (n=4) P 29 (n=4) P 30 (n=4) P Not pregnant (n=6)	$\begin{array}{c} 13,2\pm1,0\\ < 0,01\\ 10,4\pm2.5\\ < 0,01\\ 11,9\pm2.6\\ < 0,01\\ 13,5\pm2.9\\ < 0,01\\ 23,1\pm1.9\\ > 0,1\\ 23,2\pm2,1\\ \end{array}$	$\begin{array}{c} <0,01\\ <0,01\\ 16,4\pm0,9\\ <0,01\\ 17,5\pm1,7\\ <0,02\\ 16,8\pm1,4\\ <0,01\\ 21,8\pm2,1\\ >0,1\\ 27,3\pm1,4\\ >0,1\\ 28,3\pm3,0\\ \end{array}$	7,8±1,15 <0,05 11,6±3,5 >0,1 9,3±0,75 >0,1 13,8±1,8 >0,1 11,9±0,8 >0,1 11,2±0,6	11,4±0,8 <0,001 10,8±0,7 >0,1 15,2±2,5 <0,02 9,2±2,70 >0,1 10,1±0,9 >0,1 9,4±1,0	41,0±2,1 <0,001 36,9±2,9 <0,001 27,7±1,4 <0,02 30,9±1,9 <0,001 17,9±1,5 >0,1 19,7±1,1	\(\sqrt{0,01}\) 10,2\pm 1,3 \(\sqrt{0,01}\) 12,4\pm 3,1 \(\sqrt{0,02}\) 18,8\pm 1,0 \(\sqrt{0,01}\) 10,7\pm 2,8 \(\sqrt{0,1}\) 8,9\pm 1,2 \(\sqrt{0,1}\) 8,1\pm 0,4	1,72 1,49	66,2±8,0 <0,001 137,8±37,4 <0,001 29,7±5,5 <0,001 31,0±1,6 <0,001 36,8±6,0 <0,001 321,4±38,5	

Legend. Criterion of significance (P) indicated relative to nonpregnant rabbits.

Changes in the histological structure of the maternal gland confirmed the biochemical observations: After the 21st day proliferation of the thyroid epithelium intensified, with the formation of young follicles which, on the 24th-26th day of pregnancy, formed the greater part of the parenchyma of the gland. However, the newly formed follicles quickly grew large, the height of the epithelium decreased, and at birth the structure of the maternal gland again consisted of large follicles with flattened epithelium and with stagnant colloid.

In the maternal adenohypophysis on the 20th-23rd day of pregnancy a sharp increase was observed in the number of thyrotrophs; this increase took place before the increase in functional activity of the maternal thyroid gland. The number of somatographic cells in the maternal pituitary increased after the 24th day of pregnancy.

The increase in the hormone content in the thyroid glands of mother and fetus in the period from the 23rd to the 27th day of pregnancy was evidently connected with an increase in the thyroxine requirement at that period. One of the manifestations of this increase was a sharp rise in the number of somatotropic cells in the pituitary glands of the mother and fetus on the 24th day of pregnancy, and thyroxine is known to be essential for their differentiation [2]. The absence of correlation between the thyrotropic activity of the fetal pituitary and changes in the fetal thyroid gland between the 23rd and 26th days of pregnancy can evidently be attributed to the fact that this is only the initial period of formation of the fetal hypothalamic-pituitary-thyroid system, which ends with activation of the regulatory influence of the hypothalamus, which does not arise until the 14th day after birth [4]. The maternal hypothalamic-pituitary-thyroid system, which responds rapidly to the thyroxine requirement in the period of pregnancy can thus change its biochemical, morphological, and functional characteristics.

LITERATURE CITED

- 1. M. S. Mitskevich, The Glands of Internal Secretion in the Embryonic Development of Birds and Mammals [in Russian], Moscow (1957).
- E. B. Pavlova, Current Problems in Endocrinology [in Russian], No. 1, Moscow (1960), p. 142.
- 3. M. Herlant and J. L. Pasteels, Exp. Pathol., 1, 250 (1967).
- 4. A. Slebodzinski, L. Mach, and M. Malinowska, J. Endocrinol., 49, 559 (1971).