the other methods (although more traumatizing and perhaps with side-effects) used to produce non-specific suppression of the normal immunological function in rabbits, and to repeat the present experiment.

Riassunto. Conigli immunologicamente tolleranti alla caseina trattati parenteralmente con la stessa proteina vanno soggetti ad amiloidosi in misura uguale a quella degli animali di controllo, dimostrando che la patogenesi della malattia non è riconducibile a schemi immunologici classici.

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Thyroid and Pituitary Gland Activity during Compensatory Renal Hypertrophy

Though there have been several investigations as to endocrine factors controlling renal compensatory hyperplasia and hypertrophy, the exact roles of the thyroid and pituitary glands are not fully understood. Despite its consequent low metabolism, thyroidectomy does not prevent compensatory renal enlargement[1,2]. On the other hand, thyroxine administration enhances kidney hypertrophy in uninephrectomized rats[3]. The effect of hypophysectomy is more controversial. Several investigators have reported failure of compensatory renal hypertrophy in the absence of the pituitary[1,4–6]. However, compensatory renal hypertrophy can be demonstrated if allowance is made for the rapid drop in weight or deoxyribonucleic acid (DNA) synthesis after hypophysectomy[7–9].

This investigation explored the cellular activity and morphologic changes of the thyroid and pituitary glands during renal compensatory hypertrophy in rats. Autoradiographic techniques with tritiated thymidine were used to measure deoxyribonucleic acid (DNA) synthesis and cell proliferation rates.

Materials and methods. Female albino rats of the Sprague-Dawley strain (Charles River Laboratories, Wilmington, Mass.)weighing between 135 and 150 g were kept in a room where the temperature was maintained between 65 and 80°F. They were housed two to a cage and fed Purina Laboratory Chow and water *ad libitum*. A left nephrectomy was performed on the experimental group through a lateral abdominal incision. The control animals were sham operated; the left kidney was manipulated and replaced. The animals were sacrificed on various days after the operation. An intraperitoneal injection of tritiated thymidine (1 μc/g body weight) was given 4 h prior to death. The tritiated thymidine had a specific activity of 2.0 c/m*M* and was purchased from New England Nuclear Corp., Boston (Mass.) All animals were sacrificed between 1 p.m. and 3 p.m. to avoid variations in diurnal mitotic activity[10,11]. After death, the thyroid and pituitary glands were removed, weighed, fixed in formalin, embedded in paraffin, cut at 5 μ, and mounted on glass slides for autoradiography according to the method of Messier and Leblond[12]. After 4 weeks' exposure, the autoradiographs were developed, fixed and stained with hematoxylin and eosin. The degree of labelling of the thyroid and anterior pituitary parenchymal cells was obtained by counting the number of labelled nuclei with 8 or more silver grains. At least 10,000 parenchymal cells were counted per gland. Sections were selected 25 μ apart to avoid recounting the same labelled cell. After initial examination, the slides were relabelled and renumbered, and counted as unknowns.

Results and discussion. Kidney hypertrophy began 24 h post nephrectomy and appeared to reach a plateau 20 days after operation (Table). The findings agree with reports by ADDIS and LEW[13], and ROLLASON[14].

The results of tritiated thymidine autoradiographic studies are also seen in the Table. The thyroid and pituitary glands of the uninephrectomized rats exhibited a marked increased incorporation of tritiated thymidine. A

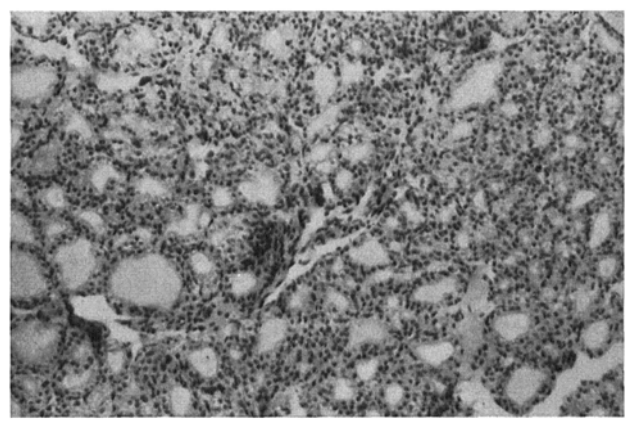

Fig. 1. Section of thyroid gland from 5th day uninephrectomized rat. The follicle lining cells are enlarged and many follicles show colloid depletion (125 × H & E stain).

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Uptake of tritiated thymidine in pituitary and thyroid glands of rats following left unilateral nephrectomy

Days after nephrectomy	Rat no.	Control group		Uninephrectomized group			
		Pituitary labelled cells/10,000	Thyroid labelled cells/10,000	Pituitary labelled cells/10,000	Thyroid labelled cells/10,000	% Hypertrophy[a] of right kidney	% Increase in body weight
Zero day	27B	0	0				0
	28B	0	0				0
	27A	0	0				0
1 day	23B	0	0				3.6
	32A	0	0				2.6
	20B			3	22	5.1	1.9
	22B			18	4	8.3	1.3
	21B			42	54	9.0	1.2
2 days	9A	0	0				1.9
	10B	0	1				4.1
				8	11	32.2	2.7
				2	4	42.5	1.4
				18	0	6.0	4.6
3 days	10B	1	0				6.2
	26A	0	0				6.4
	6B			6	54	28.3	5.3
	7B			16	4	20.6	6.9
	8B			5	1	21.6	4.1
4 days	19A	0	1				11.5
	23A	0	2				7.8
	22A			1	4	32.8	9.9
	25A			0	5	43.3	2.0
	25B			0	0	29.3	7.8
5 days	11A	0	0				11.1
	11B	0	0				15.6
	14B			22	24	41.0	10.7
	15A			66	43	26.5	13.7
	24A			0	3	46.0	13.6
6 days	12A	0	1				10.4
	12B	0	0				18.7
	13A			1	3	39.9	16.6
	13B			0	4	26.0	19.3
	18A			0	0	29.0	8.1
8 days	16A	58	17				21.9
	16B	3	5				16.9
	15B			26	11	45.7	17.1
	17A			2	3	24.4	12.2
	17B			18	0	37.1	17.5
14 days	1A	4	0				39.7
	4A	1	0				40.0
	2A			51	38	67.1	53.2
	3A			28	8	59.9	28.6
21 days	1B	1	3				60.0
	4B	3	0				53.0
	2B			13	7	85.3	52.0
	3B			11	9	47.4	42.1
	5B			3	3	44.9	45.0

[a] % Hypertrophy = (weight of right kidney— weight of left kidney/weight of left kidney) × 100.

definite peak period of thymidine incorporation was not evident. Direct correlation between the level of thymidine incorporation and degree of hypertrophy is not seen. Very slight uptake of tritiated thymidine was noted in the control group except on the 8th day. Although there are many factors controlling endocrine gland activity, there is no satisfactory explanation for the high labelling index recorded on the 8th day control animal. The elevated thymidine uptake strongly suggests increased DNA synthesis and cell proliferation in the thyroid and pituitary glands during renal compensatory hypertrophy. The amount of thymidine incorporation did not appear to follow a constant pattern. This may be a reflection of intermittent changes in endocrine activity.

The uninephrectomized rats revealed morphologic changes in the thyroid gland. These changes were definitely noted on the 4th post operative day and were present throughout the duration of the experiment. The thyroid glands showed enlarged columnar follicle cells. In many instances the lumens of the thyroid follicles were completely devoid of colloid material (Figure 1). The control animals showed mainly low cuboidal epithelium

with many follicles filled with colloid (Figure 2). No significant morphologic alteration was noted in the pituitary glands of either group.

Thus it appears the thyroid and pituitary glands may in a direct or indirect fashion influence the rate of compensatory renal hypertrophy. The changes reflected in the thyroid glands of uninephrectomized rats may be secondary to pituitary stimulation[15].

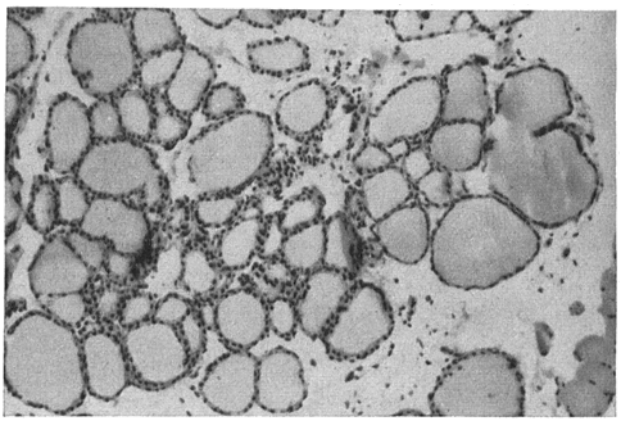

Fig. 2. Section of thyroid gland from typical control rat showing low cuboidal epithelium with follicles filled with colloid (125 × H & E stain).

Résumé. Des études autoradiographiques avec la thymidine tritiée ont mis en évidence l'augmentation de la synthèse de l'acide déribonucléïque et la prolifération cellulaire de la thyroïde et de la pituitaire pendant l'hypertrophie compensatoire rénale.

Les sections de la glande thyroïde de rats néphrectomisés unilatéralement montraient une plus grande activité des follicules columnaires et perte de colloïde.

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Thymectomized Rats, Treated with Thymic Homogenate, Reject Skin Homografts

Thymectomy, performed in laboratory animals within 24 h of birth, causes reduced body development, deterioration in physical conditions, diarrhoea, and death in a few months. A failure of small lymphocytes was terminally observed in blood and in lymphoid organs[1]; however, no alteration in the lymphocyte/granulocyte ratio, lymphatic structure or plasmocyte number was found in the first 4 to 5 weeks after thymectomizing mice neonatally[2].

Besides these modifications, it was observed that thymectomy strikingly impairs immunological response: a thymectomized animal does not reject skin homografts[1,3–5] or grafts of either normal or neoplastic foreign cells[6–9], and it is not able to produce antibodies to several antigens (sheep erythrocytes; Salmonella H antigen; bovine serum albumine)[8,10,11].

The data reported point out that the thymus gland has an important role in immunogenesis; most authors agree about this. However, the various hypotheses concerning the mechanism of this action are conflicting. MILLER[3], GOOD et al.[8], and BEAOUIEUX[12] believe the thymus may be the primitive site of lymphopoiesis, and its presence might establish the development of the lymphoid system; from it, immunologically competent cells (or progenitor elements) may originate, which migrate to the peripheral stations.

Such a theory, which we may define as 'histological', is in opposition to some observations of a humoral type of action supported by the thymus within immunogenesis. In 1959 METCALF[13] demonstrated a thymic factor stimulating a lymphopoiesis in lymphatic structures. More recently LEVEY et al.[14] observed that thymectomized mice, implanted with millipore chambers containing thymus from new-born mice, do not present any alteration of blood lymphocyte distribution or of lymphoid organ development. Animals so treated also regain the capacity to reject skin homografts[15]. The implantation of a thymus-containing millipore chamber, 3 to 4 weeks after birth and thymectomy, reinduces in mice the capacity to produce antibodies to several antigens, although they may sometimes show signs of 'wasting syndrome' and the troubles of lymphatic tissue trophism[16].

Therefore, the problem of the mechanism of thymus interference on immunogenesis is still open. We attempted to clarify it by performing the following experiments:

16 Sprague-Dawley strain rats were thymectomized 24 h after birth. 8 of the thymectomized animals were

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