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].

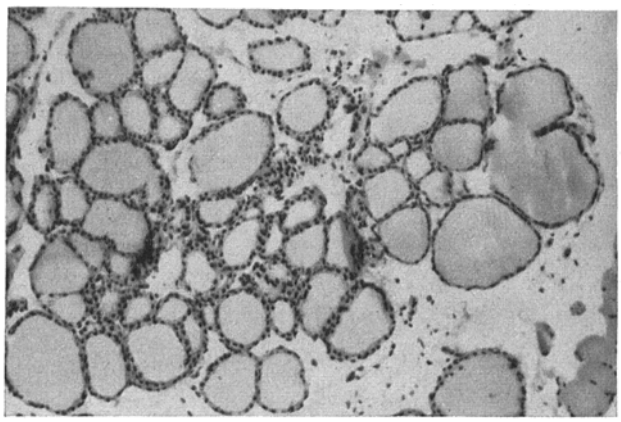

Fig. 2. Section of thyroid gland from typical control rat showing low cuboidal epithelium with follicles filled with colloid (125 × H & E stain).

Résumé. Des études autoradiographiques avec la thymidine tritiée ont mis en évidence l'augmentation de la synthèse de l'acide déribonucléique 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].

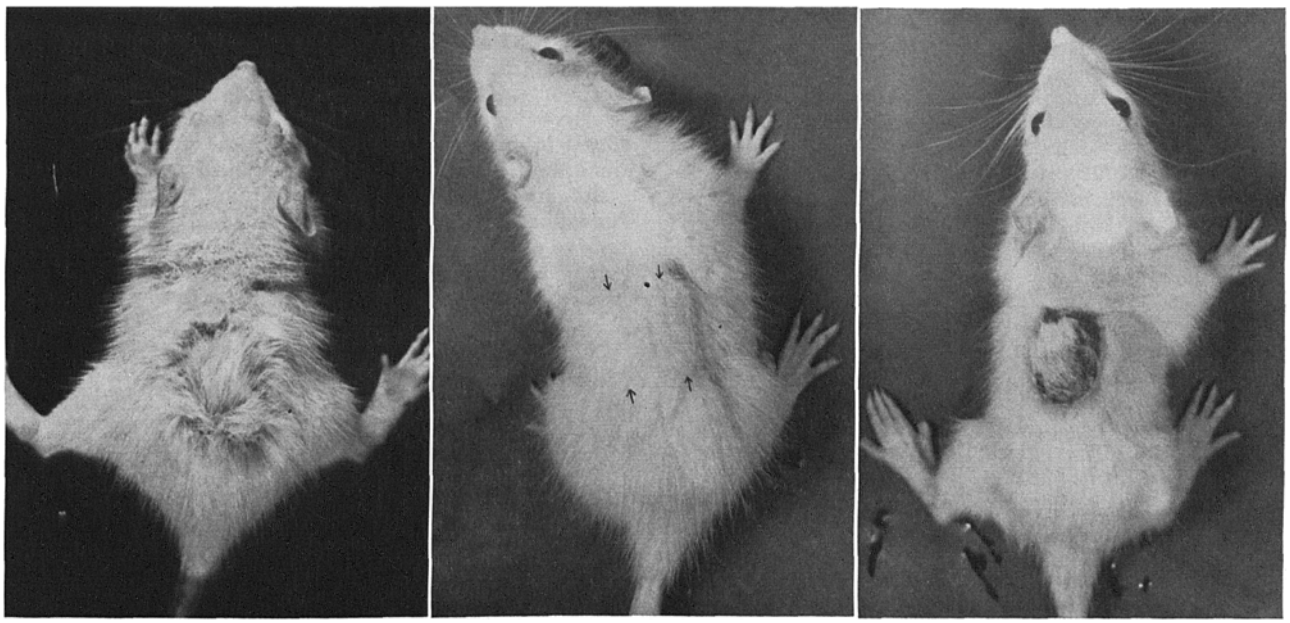
The data reported point out that the thymus gland has an important role in immunogenesis; most authors agree about this. However, the various hypotheses concerning the mechanism of this action are conflicting. MILLER[3], GOOD et al.[8], and BEAOUIEUX[12] believe the thymus may be the primitive site of 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

[1] J. F. A. P. MILLER, Lancet *1961 ii*, 748.
[2] G. BEDARIDA, L. BUSCARINI, and P. MARANDOLA, Omnia Med. Ther., in press.
[3] J. F. A. P. MILLER, Ann. N.Y. Acad. Sci. *99*, 340 (1962).
[4] A. P. DALMASSO, C. MARTINEZ, and R. A. GOOD, Proc. Soc. exp. Biol. Med. *111*, 143 (1962).
[5] B. D. JANKOVIC, B. H. WAKSMAN, and B. G. ARNASON, J. exp. Med. *116*, 159 (1962).
[6] D. M. V. PARROTT, Transplant. Bull. *29*, 102 (1962).
[7] D. M. V. PARROTT and J. EAST, Nature *195*, 347 (1962).
[8] R. A. GOOD, A. P. DALMASSO, C. MARTINEZ, O. K. ARCHER, S. C. PIERCE, and B. W. PAPERMASTER, J. exp. Med. *116*, 773 (1962).
[9] C. MARTINEZ, J. KERSEY, B. W. PAPERMASTER, and R. A. GOOD, Proc. Soc. exp. Biol. Med. *109*, 193 (1962).
[10] J. F. A. P. MILLER, Proc. Roy. Soc. London *156*, 415 (1962).
[11] J. F. A. P. MILLER, A. H. E. MARSHALL, and R. G. WHITE, Adv. Immunol. *2*, 111 (1962).
[12] Y. J. BEAOUIEUX, Presse Méd. *71*, 1367 (1963).
[13] D. METCALF, Ann. N.Y. Acad. Sci. *73*, 113 (1959).
[14] R. H. LEVEY, L. TRAININ, and L. W. LAW, J. Nat. Cancer Inst. *31*, 199 (1963).
[15] D. OSOBA and J. F. A. P. MILLER, Nature *199*, 653 (1963).
[16] L. W. LAW, L. TRAININ, R. H. LEVEY, and W. F. BARTH, Science *143*, 1049 (1964).



1 2 3

Fig. 1 and 2. 25 days after transplantation the skin-homograft persists in the thymectomized rats. Fig. 3. The thymectomized rat, treated with thymic homogenate, rejects the skin-homograft within 12 days.

injected intraperitoneally with 0.5 ml of thymus homogenates. Each time the thymic glands were immediately removed from normal new-born rats of the same strain, and they were homogenized immediately by an apparatus type Terzano (50,000 RPM at 4°C for 30 min). Distilled water was employed as a diluent, using 1 ml for each thymus. At the end of the preparation, the absence of cellular structure was controlled microscopically. On the 18th day, each animal of the two groups (thymectomized non-treated and thymectomized injected) was grafted with heterologous skin from new-born Wistar strain rats. The graft, of 1 by 1 cm, was placed in the dorsal region. Thymectomized rats did not reject it, but the rats which had been thymectomized and treated with thymic homogenate did (Table).

The data we and others have obtained permit the following conclusions:

(1) Thymus action within immunogenesis is not likely to be represented by the hypothesis ascribing to it the production of immunologically competent cells; in fact such an action is present even if the organ is replaced by a thymic tissue closed in a diffusion chamber preventing the passage of cells.

(2) The injection of a thymus homogenate from a new-born animal into a thymectomized rat (repeated three times in our experiment) is likely to be equivalent, for the immunological development, to the implantation of a thymus-containing diffusion chamber.

If the thymus action is a humoral one, it must be emphasized that the thymic factor works even if it is not introduced into the organism in a continuous way (experiment of the diffusion chamber) but at intervals and only a very restricted number of times, as in our experiment. On the other hand, we think our research suggests that, within the generic limits of a humoral type action, it may be supported by some cellular component instead of by a thymic factor.

We emphasize that, at present, the results we have obtained are valid within the strict limits of the experimental scheme we have chosen. It will be interesting to establish, by further research, what the limits to their repetition are (time of thymectomy; interval between thymectomy and homogenate injection; age of the thymus donor animal). It will also be interesting to establish if the action of thymic homogenate is merely limited to the immunogenesis or if, on the contrary, it affects the other symptoms of thymectomy too.

Group 1 (8 rats)	Group 2 (8 rats)
Thymectomy 24 h after birth	Thymectomy 24 h after birth
10th day	Injection of thymus homogenate
14th day	Injection of thymus homogenate
18th day: skin homograft	Injection of thymus homogenate; skin homograft
Non-rejection of the graft and persistence for more than two months	*Rejection* of the graft in each animal within 12 days; necroscopy shows the absence of thymic remnants

Riassunto. La introduzione, nel ratto timectomizzato alla nascita, di omogenati di timo prelevato a neonati dello stesso ceppo, pur se ripetuta un numero molto limitato di volte, appare atta ad influenzare lo sviluppo immunologico dell'animale che riacquista la capacità di rigettare gli innesti di cute.

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