

Lymphocytes and, sometimes, plasma cells are the main cellular types of the infiltrates. In severe cases lymphoid germinal centers appear within the affected areas (Figure 1), and disorganized follicular epithelial cells exhibit oxyphilic alteration of their cytoplasm with large nuclei (Figure 2). The gland was usually affected bilaterally. Both sexes were affected but the incidence in females was higher than that in males. Thymectomy at 7 days of age was usually less, but, in the present animals, not effective in inducing the disease. The course of this disease is till far from clear, but it will occur insidiously a few months after thymectomy and may last for a considerable period of time.

The pathological process of this thyroiditis appears also to be dependent on the genetic background of the mice used. (C3H $\times$ 129) hybrid mice are so far most susceptible to neonatal thymectomy, but the incidence does not exceed 30%. (C57BL $\times$ C3H) combination is highly refractory to the treatment (0%) and (BALB/c $\times$ 129) is intermediate (less than 10%).

In the next experiment, neonatally thymectomized mice were reconstituted by the subcutaneous grafting of a neonatal whole thymus or by the i.p. injection of 7-day thymus cells ( $10^7$ ) at 7 days of age, and killed at 4 months of age. Such treatments prevented not only infertility with ovarian dysgenesis but also lymphocytic thyroiditis. No direct connection, however, was observed between thyroiditis and ovarian dysgenesis (Table).

Since no serological examinations were carried out in the present experiments, it is impossible to answer whether

this murine thyroiditis is based strictly on an autoimmune process or any other unknown causes. The assumption, however, can be made that the onset and the perpetuity of the disease may be dependent on the sustained unbalance between T and B cells and that the presence of an intact thymus, or of a sufficiently large number of T cells, would prevent the disease.

Together with the other 2 types of thyroiditis, EAT and SAT, the present thyroiditis may provide a unique approach to the study of human Hashimoto's thyroiditis. Further studies are now under way<sup>9</sup>.

*Zusammenfassung.* Nachweis einer Thyroiditis bei hybriden Mäusen, die bei der Geburt thymektomiert wurden. Die Entzündung der Thyroidea wurde durch Implantation von Thymus bzw. Injektion von Thymuszellen verhindert.

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## Hyperthyroidism and Gonadotropin Secretion in Male and Female Rats

Short-term hyperthyroidism has been reported to increase ovulation rate and litter size in rats<sup>1,2</sup>. Hyperthyroidism of long duration however has been found to have a detrimental effect on reproduction in female rats resulting in prolonged periods of diestrus<sup>3-5</sup>. In the male rat hyperthyroidism has been reported to cause a decrease in testicular and accessory sex gland weights<sup>6</sup>. Although reduced gonadal sensitivity to gonadotropins may be partially responsible for the adverse effects of hyperthyroidism on reproduction<sup>7,8</sup>, reduced secretion of gonadotropins may also be involved. The present study was conducted to obtain preliminary data on the effects of treatment with triiodothyronine on pituitary and serum gonadotropin levels in rats of both sexes.

*Materials and methods.* 15 male rats of the Long-Evans strain and 16 females of the Sprague-Dawley strain that were produced in our own colony were used in this study. All animals were 6-7 months of age. During the experiments the animals were individually caged in a light (12 h light, 12 h dark) and temperature (22-24°C) controlled room. The animals were injected each morning for 13 days with either 16  $\mu$ g triiodothyronine ( $T_3$ ) in 0.2 ml of alkaline saline or the alkaline saline alone. Body weight changes and the amount of feed consumed over the experimental period were measured. Approximately 24 h after the last injection the animals were lightly anesthetized with ether and blood samples were obtained by cardiac puncture. The animals were then killed with an overdose of ether. The anterior pituitary gland, gonads and seminal vesicles were removed and weighed. Anterior pituitary glands and serum samples were frozen and later assayed for follicle stimulating hormone (FSH) and luteinizing hormone (LH).

The concentrations of LH in the homogenates of individual pituitary glands and the serum samples were

measured by the ovine-ovine radioimmunoassay of NISWENDER et al.<sup>9</sup>. FSH concentrations were determined using the double antibody radioimmunoassay distributed by the National Institute of Arthritis and Metabolic Diseases (NIAMD), NIH. The standards used in the LH and FSH assays were NIAMD-rat-LH-RP-1 and NIAMD-rat-FSH-RP-1, respectively. All samples were assayed in duplicate. The data were analyzed by analysis of variance with sums of squares adjusted for unequal subclass numbers by use of the harmonic mean of  $N$  (SNEDECOR<sup>10</sup>).

*Results and discussion.* The results are summarized in the Table. Treatment with  $T_3$  resulted in a loss of body weight ( $P < 0.01$ ) but did not affect the amount of feed consumed. The male rats consumed more feed ( $P < 0.01$ ) than did the female rats. The pituitary glands of male rats were smaller ( $P < 0.01$ ) and contained higher concentrations ( $P < 0.01$ ) of FSH and LH than those of females. Treatment with  $T_3$  did not affect gonadal weight

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Body weight loss, feed intake, organ weights and gonadotropin levels in male and female rats treated with saline or T<sub>3</sub>

	Male		Female	
	Saline	T <sub>3</sub>	Saline	T <sub>3</sub>
Number of rats	7	8	8	8
Body weight loss (g) <sup>a</sup>	-0.6 ± 3.5 <sup>b</sup>	30.3 ± 5.7	2.6 ± 3.7	27.6 ± 6.9
Total feed consumed (g) <sup>c</sup>	404 ± 11	406 ± 24	251 ± 8	250 ± 10
Testes (g)	3.38 ± 0.02	3.50 ± 0.08	—	—
Ovaries (mg)	—	—	78 ± 6	86 ± 11
Seminal vesicles (mg)	329 ± 16	333 ± 9	—	—
Pituitary gland (mg) <sup>c</sup>	13.3 ± 0.6	12.8 ± 0.3	18.7 ± 1.8	19.5 ± 0.8
Pituitary FSH conc. (μg/mg) <sup>c</sup>	5.52 ± 0.62	5.74 ± 0.44	1.13 ± 0.05	1.23 ± 0.14
Pituitary LH conc. (μg/mg) <sup>c</sup>	8.2 ± 2.0	10.7 ± 1.7	6.5 ± 0.6	4.8 ± 1.0
Serum FSH conc. (ng/ml)	372 ± 25	316 ± 26	331 ± 30	320 ± 33
Serum LH conc. (ng/ml) <sup>d</sup>	15.7 ± 2.4	22.0 ± 3.1	22.8 ± 4.5	12.6 ± 2.3

<sup>a</sup>T<sub>3</sub> treatment  $P < 0.01$ . <sup>b</sup>Mean ± S.E. <sup>c</sup>Sex  $P < 0.01$ . <sup>d</sup>T<sub>3</sub> treatment  $\times$  sex  $P < 0.05$ .

in rats of either sex and did not alter the weight of seminal vesicles in males. The ovaries of female rats receiving T<sub>3</sub> contained numerous large corpora lutea. The prolonged maintenance of corpora lutea in hyperthyroid rats has been reported previously<sup>4</sup>. T<sub>3</sub> treatment had no effect on the concentration of gonadotropins in the pituitary gland or on the concentration of FSH in the serum. A significant ( $P < 0.05$ ) T<sub>3</sub> treatment  $\times$  sex (or strain) interaction was noted for serum LH concentration. This resulted from T<sub>3</sub> causing a reduction in LH concentration in females while in males it tended to elevate LH levels.

The dose of T<sub>3</sub> employed in this study was approximately 13-fold higher than the dose required to restore metabolic rate to normal in thyroidectomized rats<sup>11</sup>. The hyperthyroid state was confirmed by the body weight loss in treated animals. The reason for the lack of effect on food intake is unknown. HSIEH and TI<sup>12</sup> have reported increased feed consumption in rats treated with thyroxine.

The results obtained in this study provide no evidence that the hyperthyroid state adversely affects gonadotropin secretion or sex organ weights in male rats. In hyperthyroid female rats however, serum levels of LH appear to be reduced. Although ovarian weight was not affected by treatment, we have assumed that the maintenance of ovarian weight in treated rats was due to the presence of maintained corpora lutea and therefore was not indicative of normal function.

In this study we have assumed that the differences between the males and females represented sex differences

however the possibility that some of the apparent sex differences may have been the result of strain differences should not be overlooked.

*Résumé.* Chez des rats adultes, mâles et femelles, traités à la triiodothyronine (T<sub>3</sub>), on a remarqué une perte de poids qui n'est pas due à une diminution de consommation de nourriture. Les niveaux sériques de l'hormone lutéinisante semblent être réduits par le traitement au T<sub>3</sub> chez les rats femelles, mais non pas chez les rats mâles. Le niveau sérique de l'hormone stimulante de la follicule et le niveau pituitaire de gonadotropines ne sont pas affectés de façon significative par le traitement au T<sub>3</sub>.

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## Effect of Lactic Acid on the Aggregation of Human Platelets Induced by ADP, Adrenaline and Collagen

Intravascular coagulation is reported in connection with hypoxaemia and anoxaemia under various clinical and experimental situations<sup>1-4</sup>. As a consequence of tissue hypoxaemia and/or anoxia, lactate might be increased in tissues and blood<sup>5-7</sup>. In animal experiments, thrombosis was observed after i.v. injection of lactic acid<sup>8</sup>. Lactic acid has even been reported to increase platelet adhesiveness in vitro<sup>9</sup>. This suggests that under these conditions lactic acid plays an intermediary role between hypoxaemia and intravascular coagulation. Considering

this evidence, we have investigated in vitro the effect of hyperlactacidaemia on the human platelet aggregation, induced by ADP, adrenaline and collagen.

*Materials and methods.* Human blood was collected from the antecubital vein of healthy volunteers (who had not taken medication within the previous week) into 1/10 its volume of 3.1% trisodium citrate. Platelet rich plasma (PRP) was prepared by centrifugation of the blood at 180  $\times g$  for 15 min at room temperature, and the platelet count was determined using an automatic