Table II. Comparison of Delta and F antigens from rat liver

Property	Delta	F
Mol. weight (gel filtration)	around 58,000	around 65,000
pI (ion exchange chromatography)	lower than 7	around 7
Immuno-electrophoresis	mobility of α-globulin	mobility of β-globulin
Anion exchange chromatography	several molecular species	no detectable polymorphism
Temperature stability		
50 °C 10 min	inactivated[a]	little affected
−30 °C	decrease to $^1/_2$ of original activity within 15 h	unaffected by prolonged frozen storage
pH stability		
pH 5	inactivated	unaffected
pH 11	inactivated	little affected
Effect of enzymes		
DNAase	unaffected	unaffected
RNAase	unaffected	unaffected
α-Chymotrypsin	inactivated only when semipurified	crude extracts readily inactivated
Localization in liver cells	cytosol	cytosol
Distribution in various organs		
liver	large amount	large amount
kidney	small amount	small amount
other organs	not detectable	not detectable
Distribution of cross-reactive antigens in various species		
Mouse	yes	
Rat		yes
Cow	yes	yes
Man	yes	yes

[a] Inactivated = substance no longer precipitable by corresponding antisera in gel diffusion tests.

thus characteristics of a true autoantibody. This was further ascertained by showing that the serum from one animal precipitated an extract made from the liver of that same animal. The autoantigen involved will henceforth be called Delta. The exact immunological relationship between anti-Delta and the alloantibodies mentioned above (induced in Lewis rats by BN and DA extracts) has not yet been worked out.

Since the autoantibody-autoantigen system of rats was so strikingly similar to that found earlier in mice, it seemed important to compare the two antigens. Both were widely distributed in liver extracts of mammalian species, so that a meaningful comparison within the same species was possible. For instance, rat liver extracts, in addition to Delta, contained an antigen which strongly cross-reacted with F antigen from mouse liver[1], and mouse liver extracts, in addition to F, contained a Delta-like antigen. Immunologically, the 2 antigens appeared completely unrelated in all species tested (rat, mouse, cow and man), with undisturbed crossing of the precipitation lines in double diffusion studies. Nevertheless, physicochemical properties of the 2 antigens were grossly similar, as shown in Table II. (The data shown are similar to those of mouse liver F antigen[3,4].)

It therefore appears that autoantibodies to soluble liver antigens can be readily induced in 2 species, rat and mouse, provided allogeneic stimulation in the proper strain combination is arranged.

Zusammenfassung. Es werden einige Eigenschaften eines leberspezifischen Antigensystems der Ratte beschrieben. Es wird gezeigt, dass das entsprechende Antigen aus Lewis-Ratten in BN-Ratten einen universell kreuzreagierenden Autoantikörper induziert.

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Murine Thyroiditis Induced by Neonatal Thymectomy

Since WITEBSKY and ROSE[1] reported an experimental induction of thyroiditis in rabbits by an immunizing procedure, allergic thyroiditis has been induced by the same treatment in various laboratory animals, including mice. With the establishment of the thymic role in cellular immunity, it has now been generally accepted that experimental allergic thyroiditis (EAT) is also dependent on the presence of the thymus, especially of thymus-derived lymphoid cells (T-cells). In chickens[2] and rats[3], neonatal thymectomy made the animals less responsive to the induction of thyroiditis.

On the other hand, spontaneous autoimmune thyroiditis (SAT) has been reported in dogs, chickens and rats. WICK et al.[4,5] and recently ROSE et al.[6], using the Obese

Incidence of lymphocytic thyroiditis (LT) and its relation to ovarian dysgenesis (OD) in neonatally thymectomized (C3H/HeMs × 129)F_1 4-month-old mice and prevention by thymus grafting or thymus cell injection

Sex	Thymectomy	Treatment	No. of mice	No. of LT	(%)	No. of OD	(%)	No. of LT with OD
♀	—	—	50	0	(0)	0	(0)	0
♀	at 3 days	—	50	15	(30)	27	(54)	10
♀	at 3 days	thymus graft at 7 days	22	0	(0)	1	(5)	0
♀	at 3 days	thymus cell at 7 days	20	0	(0)	1	(5)	0
♀	at 7 days	—	20	0	(0)	0	(0)	0
♂	—	—	51	0	(0)	—	—	—
♂	at 3 days	—	34	3	(9)	—	—	—

strain of chicken, have found that neonatal thymectomy increased the severity of spontaneous thyroiditis in chickens, while neonatal or embryonal bursectomy resulted in a significant decrease of both the frequency and severity of the disease. They interpreted these findings as an indication that the Bursa-dependent lymphocytes, which are assumed to be equivalent to bone marrow derived lymphoid cells (B-cells) in mammals, play the major role in the development of spontaneous bird thyroiditis, and proposed that different pathological processes may be concerned in these 2 types of thyroiditis.

NISHIZUKA et al.[7,8] have investigated the long-term effects of neonatal thymectomy in mice and found that a complete removal of the thymus at neonatal age induces ovarian dysgenesis, and such dysgenetic ovaries are often infiltrated by lymphoid cells. Furthermore, the administration of human chorionic gonadotropin induces 'lymphocytic oophoritis' in pre-dysgenetic ovaries of neonatally thymectomized mice. In relation to the above, we now report another interesting finding that neonatal thymectomy, without any other treatment, induces lymphocytic thyroiditis in some hybrid mice.

Female and male mice of (C3H/HeMs × 129/J)F_1, /BALB/c × 129/J)F_1 and (C57BL/6J × C3H/HeMs)F_1 were used. All the mice were bred in our laboratory. The thymus was removed at 3 or 7 days of age as previously described[8]. Alternative littermates were used as controls. The mice were killed at 4 or 12 months of age and the thyroid glands, together with neighboring tissue, were sectioned at more than 4 different levels and stained with Hematoxylin and Eosin.

Macroscopically, normal thyroid glands or glands with mild thyroiditis were reddish and flat, while the glands with severe lesions were pale-grayish and bulged. In the section, early scattering lymphocytic infiltrations appear first at perivascular regions and with the progression of interfollicular infiltration by lymphoid cells, thyroid follicles show loss of colloid, increase in epithelial cell height and destruction of the follicular architecture.

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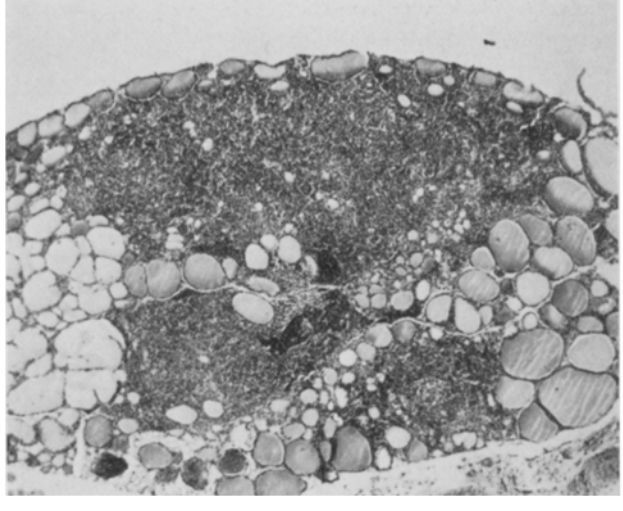

Fig. 1. Thyroid of a neonatally thymectomized (BALB/c × 129)F_1 mouse at 12 months of age, showing massive lymphoid infiltration with germinal centers. H. and E., × 70.

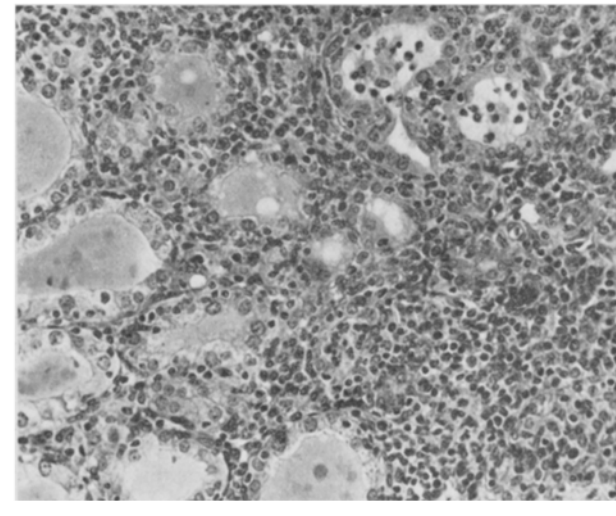

Fig. 2. Thyroiditis of a neonatally thymectomized (C3H/He × 129)F_1 mouse at 4 months of age. Diffuse lymphocytic infiltration, destruction of follicles and cuboidal epithelial cells with large nuclei. H. and E., × 350.

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[9].

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[1,2]. Hyperthyroidism of long duration however has been found to have a detrimental effect on reproduction in female rats resulting in prolonged periods of diestrus[3–5]. In the male rat hyperthyroidism has been reported to cause a decrease in testicular and accessory sex gland weights[6]. Although reduced gonadal sensitivity to gonadotropins may be partially responsible for the adverse effects of hyperthyroidism on reproduction[7,8], 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 µg triiodothyronine (T3) 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.[9]. 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[10]).

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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