Role of the Hormonal Status of the Father in Involution of the Thymus in the Progeny

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This study was aimed at assessing the consequences of the influence of exogenous androgens on the epididymal sperm of fathers for their progeny. A single injection of testosterone or dihydrotestosterone to adult rats caused a transient increase of the level of the corresponding androgen, later leading to augmentation of the androgen-dependent organs and loss of thymus weight. Hyperandrogeny and earlier age-associated involution of the thymus were observed in the male progeny of androgenized males of reproductive age.

Key Words: *androgens; males; progeny; thymus; ontogenesis*

It is still not known why the function of the thymus falls off sharply in early ontogenesis, although this problem no doubt merits attention. The few attempts made to account for thymomegaly in children with hereditary factors have been far from enlightening [1,2].

Sex hormones cause involution of the thymus. It is not clear, however, whether this phenomenon is reproducible in the fetus. Injection of estrogens to pregnant guinea pigs led to a reduction in the number of large cortical lymphoid cells in the fetal thymus [3]. There are virtually no data about the role of the father in the formation of the fetal immune system.

This experimental study was aimed at investigating the possibility of influencing the function of the thymus in the progeny by altering the hormonal status of the father. We are unaware of any experiments or clinical observations having been performed in this area.

MATERIALS AND METHODS

Experiments were carried out with Wistar rats. Testosterone (TS, 0.05% solution) or dihydrotestosterone (DHT, 0.01% solution) was injected intramuscularly in single doses of 1 and 0.2 mg/kg, respectively. Use of nonaromatized DHT permitted us to ascertain whether TS exerts the effect by itself or by metabolizing to estradiol [4].

Control animals were injected androgen solvent — kernel oil — under the same conditions. Two days after injection the males were mated with intact females in order to obtain progeny. The consequences of the effects of the studied androgens on the epididymal sperm of the father for the progeny were assessed. The parameters characterizing the activity of the thymus in various periods of ontogenesis were studied in the progeny. TS was radioimmunoassayed using a Steron-T-^{125}I kit (Minsk).

RESULTS

The level of TS in the peripheral blood rose after a single injection to males, the peak being observed 40 min after injection (72.76±4.24 nmol/liter, the initial level being 6.09±0.87 nmol/liter, $p<0.001$). Twenty-four hours after injection of the androgen, its concentration in the blood normalized. Injection of DHT under similar conditions was also associated with a transient rise of its concentration. Despite the brief duration of the "androgen attack," consequences were observed on both androgen-depend-

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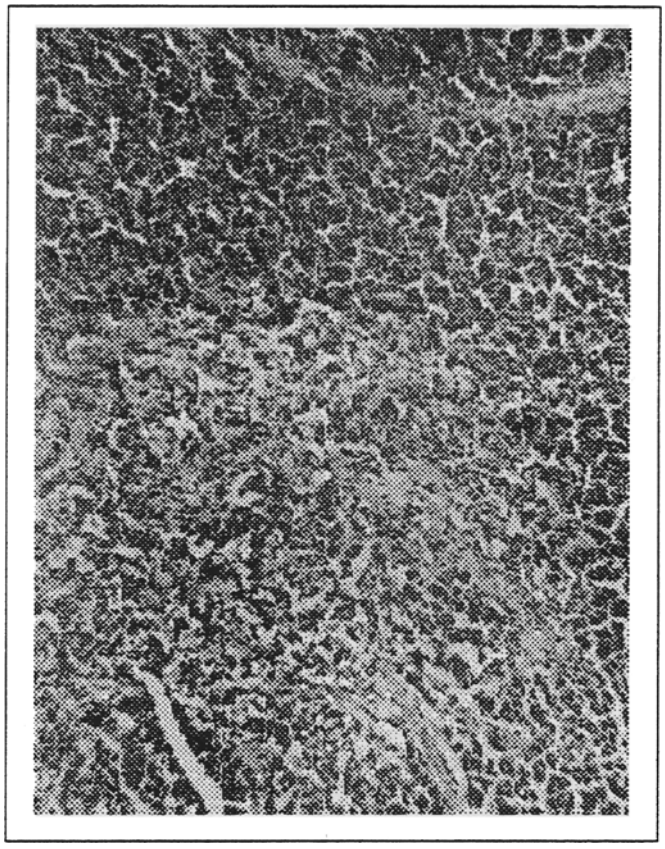

Fig. 1. Dense-cellular cortical matter and well-developed reticuloepithelial component of the medulla.

Control: rat aged 48 days. Hematoxylin-eosin staining, ×160.

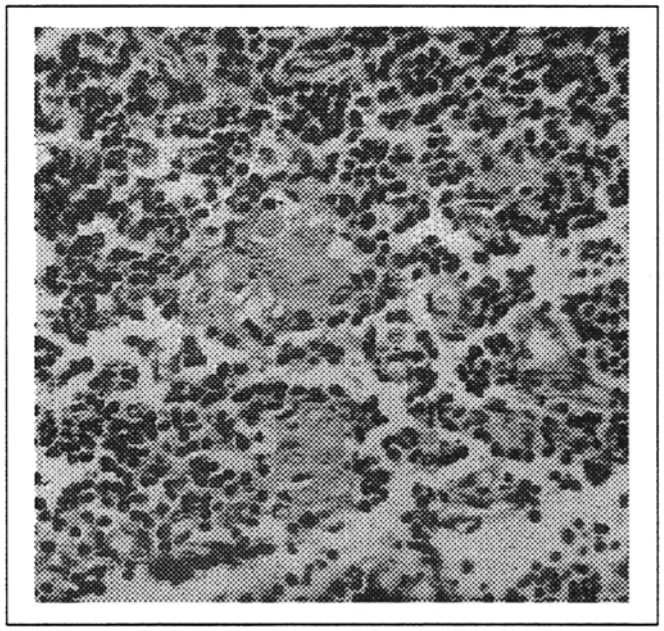

Fig. 2. Formation of large, actively functioning thymic corpuscles of the medulla.

Progeny of rats injected testosterone before mating, rat aged 48 days.

Here and in Fig. 3: hematoxylin-eosin staining, ×400.

ent organs (seminal vesicles and prostate) and the thymus. They were more pronounced from day 3 to day 6 postinjection, this indicating that it takes some time for the biological effects of androgens to make themselves felt in the studied systems. During this period after injection of TS the total weight of androgen-dependent organs increased by 63%, after DHT by 40%. A negative correlation was revealed between the weight of the thymus and of the androgen-dependent organs; this correlation was reliable only in the group of rats injected DHT (r=-0.9). However, there was no direct correlation between the weight of the thymus, seminal vesicles, and prostate, because a more expressed involution of the thymus was observed after DHT. The relative weight of the thymus 6 days after injection of TS was 0.832±0.125, and that after DHT 0.458±0.173, as against 1.121±0.133 in the control.

Hence, experiments on adult males demonstrated that TS transformation into estradiol is not necessary for the suppression of the thymus, which was even more sensitive to DHT.

By puberty an elevated level of TS was observed in the male progeny of androgenized males. The concentration of TS in the peripheral blood of offspring from TS-treated fathers was 7.58±0.61 nmol/liter, that in the progeny of DHT-treated fathers 14.92±2.91 nmol/liter versus 5.17±0.76 nmol/liter in the control. The weight of the thymus was 14% reduced in group 1 and 29% in group 2.

Histological examination of the thymus in the progeny of androgenized fathers showed a lesser density of thymocytes in the cortical layer and extension of the medullary layer. The medulla was characterized by a better developed ample reticuloepithelial component with a great number of cells with very large euchromatic nuclei; there were more active thymic corpuscles (Figs. 1 and 2). A tendency toward active functioning of the reticuloepithelial component was observed in the progeny at a very early age. In the progeny of fathers treated with DHT the thymus was characterized, among other things, by the presence of hyalinized thymic bodies, which made the gland look "older" (Fig. 3).

Hence, injection of androgens to males 2 days before mating boosted the development and functioning of the reticuloepithelial component of the thymus in the male progeny, with a certain hypoplasia of the cortical layer. This phenomenon may be interpreted as the need for an earlier and more active stimulation of the initially less intensive lymphopoiesis in the cortical matter of the thymus so as to develop an adequate response to the "foreign" matter.

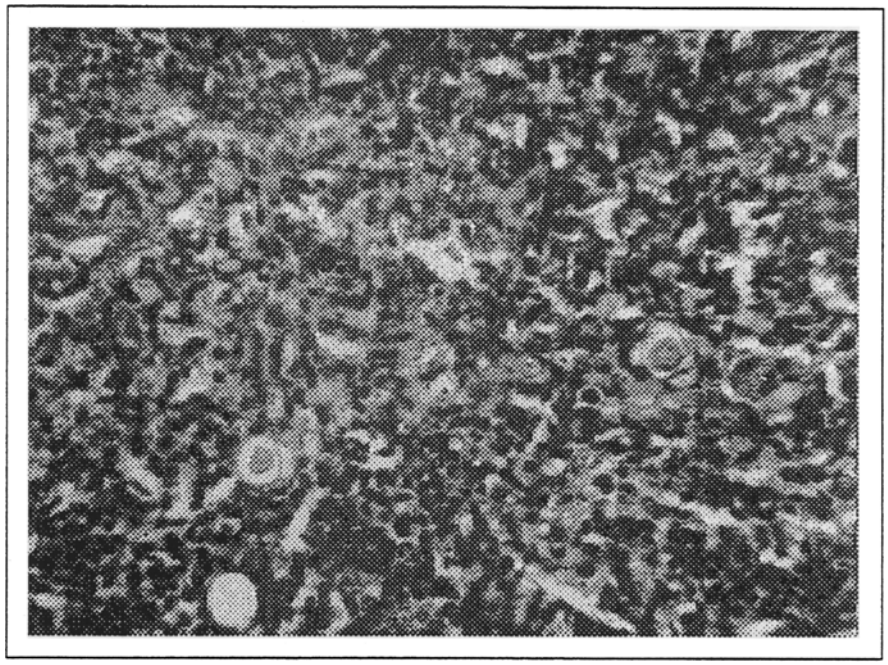

Fig. 3. Hyalinized Hassall's bodies in the medulla. Progeny of males injected DHT before mating, rat aged 61 days.

The results suggest that an initial rise of the level of androgens in the father not only leads to suppression of the function of the thymus in himself, but also accelerates the involution of this organ in the progeny. This implies that the parental hormonal status is one of the pathogenetic factors of thymic abnormalities.

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