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MECHANISM OF DISTURBANCE OF ANDROGEN PRODUCTION IN STRESS

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There is abundant clinical and experimental evidence [10-13] of weakening of reproductive function and lowering of fertility during stress. A fall in the plasma testosterone concentration and in the excretion of its metabolites with the urine, especially of the androsterone fraction, has been demonstrated in surgical or traumatic stress [2, 4, 8, 9]. Sexual function is known to be depressed in "hunger stress," and this also is connected with a fall in the plasma testosterone level and stimulation of the luteinizing function of the pituitary [6]. The absence of progeny of animals in captivity (in a state of alarm and fear) also is due to despression of spermatogenesis associated with depression of androgen activity. Data in the literature thus reveal depression of reproductive function and androgenic status in stress, but the mechanism of the inhibition of androgenic activity under these conditions still remains largely unstudied. In particular, it has not yet been settled whether testosterone production is blocked in the testes, whether the disturbances of androgen production are connected with structural changes, and specifically, whether the disturbances of androgen production are connected with structural changes in Leydig's interstitial cells or whether they are physiological in character.

The aim of the present investigation was to study functional and structural changes in the testes in stress.

EXPERIMENTAL METHOD

Experiments were carried out on 28 young sexually mature male rabbits. Stress was induced in the animals by daily immobilization for 1 h and simultaneous electrical stimulation (frequency 100 Hz, duration 1 msec) from an ÉI-1 pulse generator for 2 weeks. The strength of the current was chosen arbitrarily so as to produce contraction of the hind limb muscles. Testicular androgen activity was judged from the concentration of testosterone and androstenedione measured by a spectrofluorometric method [7] in blood from the spermatic vein [14]. Plasma sterods were identified on the Ultrachemiscope apparatus (UFS-1 filter) and determined quantitatively on the BIAN fluorometer at wavelengths of 436 and 510 nm. Changes in weight of the gonads and prostate gland and also the state of the spermatogenic epithelium and inter-

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TABLE 1. Effect of Long-Term Stress on Parameters of Androgen Function in Gonads of Young Sexually Mature Male Rabbits (M ± m)

Experimental conditions	Weight of testes, g	Androgen in gonads, nmoles/liter		Weight of prostate, g
		testosterone	androstenedione	
Control (intact rabbits)	3,320±170 (13)	1816,7±280,82 (10)	1033,17±488,85 (10)	2,760±0,130 (10)
Stress (2 weeks)	2,530±0,112* (13)	287,76±73,84* (20)	41,60±16,64* (10)	1,310±0,266* (10)

* $P < 0.001$.

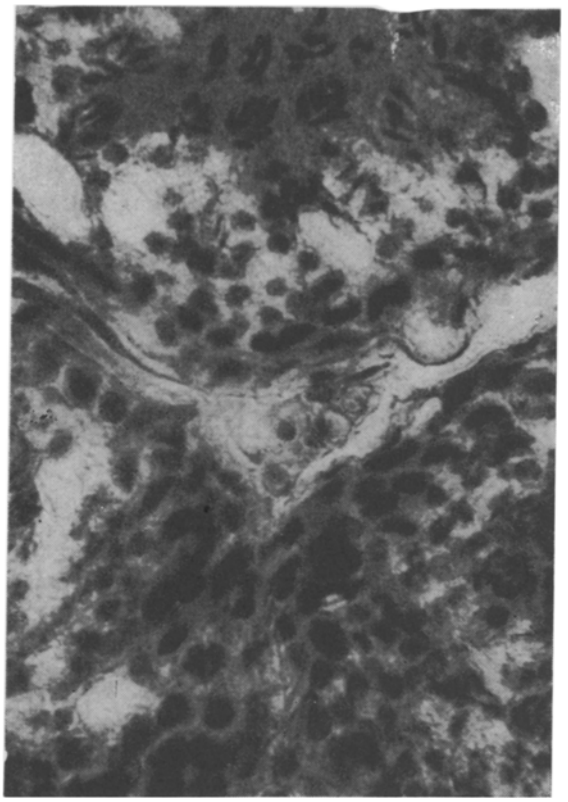

Fig. 1. Leydig's interstitial cells under the influence of stress.

stitial cells were analyzed, for which purpose the testes were fixed in Bouin's fluid and celloidinparaffin sections were stained with Mayer's acid hematoxylin and counterstained with eosin.

EXPERIMENTAL RESULTS

Prolonged exposure to the stressor agent led to marked inhibition of testicular androgen production (Table 1). For instance, 2 weeks after the beginning of exposure to electric shock stimulation testosterone secretion by the testes of the experimental animals was 16%, and androstenedione secretion only 4% of the levels of these hormones in intact rabbits. Weakening of testosterone production was confirmed demonstratively by the decrease in weight of the prostate ($P < 0.001$). It will be clear from Table 1 that inhibition of testicular androgen production takes place against the background of a marked decrease in weight of the gonads ($P < 0.001$). Meanwhile the number and size of the Leydig's interstitial cells were indistinguishable from normal, nor were any signs of weakening of activity observed (Fig. 1). Histological investigation of the seminiferous tubules showed loosening of the structure of the spermatogenic epithelium, slight but definite reduction of the formation of spermatozoa, and arrest of spermatogenesis mainly at the stage of primary spermatocytes.

It can be concluded from these results that inhibition of androgen activity in stress is due to weakening of male sex hormone production actually in the testes. One cause of weakening of biosynthesis and androgen secretion in stress may be the marked increase in production of pituitary prolactin [3, 5], large doses of which are known to sharply inhibit testicular androgen production. Considering the high level of gonadotrophins observed in the pituitary when their discharge into the blood stream is blocked in rats during hunger stress [6], it can be postulated that the cause of weakening of androgen production in the testes during stress is evidently a decrease in the supply of gonadotrophins (especially luteinizing hormone) from the pituitary into the circulation. Finally, the writers' previous investigations showed [1] that the ratio of the noradrenalin and serotonin concentrations in the hypothalamus in rabbits during stress is shifted toward considerable predominance of serotonin, an excess of which is known to inhibit the secretion of luteinizing hormone releasing factor, and thereby to reduce secretion of luteinizing hormone by the pituitary.

Preservation of the structural integrity of Leydig's interstitial cells suggests that during stress the pathway of androgen biosynthesis is shifted toward the formation of steroids that are not characteristic of the activity of the intact gonads.

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