Corticosterone Content of Adrenals in Gonadectomized Rats

Changes in adrenal weight of gonadectomized rats were reviewed in several publications[1-4]. Their authors agree that gland weights in ovariectomized females decrease. Adrenal weights of males either remain unchanged[4,5] or increase[2,3] after castration. In any case, the extent of changes depends on the age at gonadectomy, the duration of the condition[3], and probably also on the strain of the animals. On the other hand, circulating corticoids were found to be reduced about 20% in ovariectomized female rats and augmented in castrated males[6].

As hormone stores of the adrenal cortex reflect suitable the secretion rate of animals at the time of death[7], it was considered interesting to study the corticosterone content of adrenals on gonadectomized rats.

Material and Methods. Eighty Wistar rats, 8 weeks old, weighing between 150 g and 180 g were used. Gonadectomy was performed on 20 males and 20 females. One, two, four, and eight months after operation, 5 gonadectomized and 5 control rats were killed under resting conditions, with Nembutal (40 mg/kg) and their adrenals dissected. Completeness of gonadectomy was verified in all cases.

Analyses were performed immediately after removal of the glands, by the fluorometric method of SILBER, BUSCH, and OSLAPAS[8], adapted by GUILLEMIN to the Farrand, Model A fluorometer[9]. Slight modifications were introduced to this method.

Results and Discussion. According to Tables I and II the following results were obtained:

Males: (1) No significant differences were found between adrenal weights of the castrated males and their controls. However, as 8 months after castration the males began to weigh less than controls, the ratio adrenal weight/body weight was higher (31%) in the gonadectomized group, from this moment on. (2) The following parameters were found to be significantly decreased: corticosterone content per whole gland (31%–55%), per gland weight unit (25%–55%) and per body weight (52%–75%)[10]. The decrease in every case was found to be larger in recently castrated animals and lowered with the duration of gonadectomy.

Females: (1) Adrenal weight was slightly decreased in spayed rats (7%–25%). The ratio adrenal weight/body weight was also smaller in the ovariectomized group. (2) A striking reduction was found in corticosterone content per whole gland (47%–72%), per gland weight unit (34%–60%) and per body weight (52%–75%). Diminutions became larger with duration of ovariectomy.

The adrenal weight of male and female rats of this experiment, in which the animals were gonadectomized after puberty, are in accordance with the findings of ANDERSEN[4] and GOMPERTZ[5]: smaller adrenals were found in spayed females and no changes took place in castrate males. The authors' attention was specially drawn to the much higher diminution of adrenal corticosterone content, as compared to the decrease of adrenal weight, in spayed females. This diminution was still more surprising in castrated males, in which adrenal weight remained unchanged and in which an augmented hormone secretion after castration was expected[1].

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[10] Differences of adrenal corticosterone—both per adrenal weight and per body weight—at the 2 months level, were non-significant because of unusually high Standard errors of the means. This fact is thought not to be in contradiction with general results.

Tab. I. Body weight, adrenal weight and adrenal corticosterone content in *castrated male rats*, killed 1, 2, 4, and 8 months after gonadectomy

		1 month	2 months	4 months	8 months
Body weight (g)	C	262.9 ± 9.5[a]	349.6 ± 18.0	410.3 ± 16.4	456.6 ± 15.3
	G	255.3 ± 6.3	296.8 ± 17.8	346.0 ± 15.4	331.4 ± 11.6
ΔC%		−3 n.s.	−15 n.s.	−16[d]	−27[b]
Adrenal weight (mg)	C	17.1 ± 0.9	15.4 ± 0.5	17.4 ± 0.6	16.6 ± 0.5
	G	16.4 ± 0.4	15.0 ± 0.8	15.2 ± 0.5	15.6 ± 0.7
ΔC%		−4 n.s.	−3 n.s.	−13[d]	−6 n.s.
Adrenal weight (mg)/body weight (g)	C	65.2 ± 1.7	44.3 ± 1.9	42.7 ± 1.6	36.6 ± 0.9
	G	65.3 ± 2.0	51.1 ± 2.5	44.2 ± 1.2	47.6 ± 1.3
ΔC%		0 n.s.	+15 n.s.	+3 n.s.	+31[b]
Adrenal corticosterone per whole gland (μg)	C	0.94 ± 0.08	1.24 ± 0.19	1.38 ± 0.16	1.33 ± 0.035
	G	0.42 ± 0.03	0.64 ± 0.08	0.85 ± 0.09	0.93 ± 0.09
ΔC%		−55[b]	−48[d]	−39[d]	−31[c]
Adrenal corticosterone (μg)/adrenal weight (g)	C	56.8 ± 4.5	78.8 ± 13.3	78.4 ± 5.9	80.0 ± 2.35
	G	25.5 ± 1.8	47.2 ± 7.1	55.9 ± 5.7	60.5 ± 6.5
ΔC%		−55[b]	−40 n.s.	−29[d]	−25[d]
Adrenal corticosterone (μg)/body weight (kg)	C	3.6 ± 0.3	3.5 ± 0.5	3.4 ± 0.3	3.03 ± 0.07
	G	1.6 ± 0.2	2.3 ± 0.4	2.5 ± 0.2	2.7 ± 0.2
ΔC%		−55[b]	−34 n.s.	−26[d]	−10 n.s.

C Controls; G Gonadectomized; [a] Standard Error; ΔC% % difference between means; [b] $P < 0.001$; [c] $P < 0.01$; [d] $P < 0.05$; n.s. non significant ($P > 0.05$).

Tab. II. Body weight, adrenal weight and adrenal corticosterone content in *ovariectomized female rats*, killed 1, 2, 4, and 8 months after gonadectomy

		1 month	2 months	4 months	8 months
Body weight (g)	C	206 ± 4.5[a]	221 ± 5.5	226.6 ± 7.1	266.0 ± 9.4
	G	231.8 ± 8.5	268.8 ± 8.7	270.0 ± 12.0	319.0 ± 16.0
Δ C%		+ 13[d]	+ 22[c]	+ 19[d]	+ 20[d]
Adrenal weight (mg)	C	23.1 ± 0.9	17.3 ± 1.0	20.5 ± 0.7	20.3 ± 0.8
	G	19.6 ± 0.73	16.1 ± 0.27	15.4 ± 0.6	16.9 ± 0.4
Δ C%		− 15[d]	− 7 n.s.	− 25[b]	− 17[c]
Adrenal weight (mg)/body weight (g)	C	112.0 ± 3.2	78.0 ± 4.1	90.4 ± 2.4	76.6 ± 2.9
	G	84.0 ± 3.1	60.2 ± 1.7	56.8 ± 1.9	53.4 ± 1.3
Δ C%		− 25[b]	− 23[c]	− 37[b]	− 30[b]
Adrenal corticosterone per whole gland (μg)	C	1.35 ± 0.16	2.20 ± 0.20	2.16 ± 0.26	2.90 ± 0.30
	G	0.72 ± 0.09	0.86 ± 0.12	0.96 ± 0.16	0.82 ± 0.13
Δ C%		− 47[c]	− 61[b]	− 56[c]	− 72[b]
Adrenal corticosterone (μg)/adrenal weight (g)	C	59.5 ± 4.2	129.7 ± 11.4	103.5 ± 10.6	145.0 ± 13
	G	39.4 ± 6.2	52.5 ± 7.3	65.3 ± 7.3	48.0 ± 7.5
Δ C%		− 34[d]	− 59[c]	− 37[d]	− 60[b]
Adrenal corticosterone (μg)/body weight (kg)	C	6.5 ± 0.6	10.0 ± 0.8	9.5 ± 1.1	10.3 ± 1.3
	G	3.1 ± 0.3	3.2 ± 0.6	3.8 ± 0.3	2.6 ± 0.3
Δ C%		− 52[b]	− 68[b]	− 60[b]	− 75[b]

For explanation of symbols and abbreviations, see Table I.

HALBERG found decreased hormone storage in ovariectomized mice[11], this diminution being, however, far smaller than the one observed in Wistar rats of the present experiment.

According to the results obtained, there is some evidence for a dissociation between the weight-modifying and corticosterone-content-decreasing factors in adrenals of gonadectomized rats. Contrary to the results observed in chronic experiments under the influence of other different factors[7,12], gonadectomy modifies the corticosterone content to a much higher extent than the weight of the gland.

The authors' attention was drawn to the high corticosterone content of the adrenal in control animals. To outrule the possibility of an increased output due to stress previous to death, an additional experiment was performed, in which the effect of Nembutal *versus* decapitation was compared. Results obtained when Nembutal was used were significantly lower ($0.02 > P > 0.01$).

With the analytical method used, only corticosterone and cortisol were determined, the latter steroid giving readings 3 times lower than corticosterone[8]. The results obtained show, therefore, a clear decrease in corticosterone content, but do not rule out the possibility of the formation or increased production of other corticoids.

Even an augmented secretion of cortisol, at the expense of corticosterone, would give lower readings in the fluorometer, which this method would assign to a reduction in total corticoids. Further experiments, employing different analytical techniques, would be necessary and are being carried out to obtain better understanding of this aspect of the problem.

Zusammenfassung. Ein bedeutender Rückgang des Corticosterongehaltes in den Nebennieren wurde bei weiblichen und männlichen Wistar-Ratten nach Kastration beobachtet. Die Verminderung ist aber besonders bei den männlichen Kastraten überraschend, da sich bei diesen nach der Gonadektomie das Drüsengewicht nicht ändert. Bei den Weibchen hingegen ist die Hormongehaltverminderung bedeutend stärker als der entsprechende Rückgang des Drüsengewichts. Nach diesen Resultaten dürfte eine Dissoziation zwischen Gewichts- und Corticosterongehalt-vermindernden Faktoren bei kastrierten Ratten angenommen werden.

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The Comparative Enhancement of the Depressant Action of Alcohol by Eight Representative Ataractic and Analgesic Drugs[1]

The continued extensive use of tranquilizers emphasize the importance of a possible synergistic action of these drugs with alcoholic beverages. The enhancement of the effects of centrally depressant drugs including alcohol by tranquilizers has been reported[2–6]. In contrast, these drugs have been used successfully in the treatment of alcoholism[7,8]. The evaluation of a synergistic action in humans is difficult and time consuming. A rapid pharma-

[1] This study was supported (in part) by a P.H.S. research grant AC-20 from the Division of Accident Prevention, Bureau of State Services, Public Health Service.
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