XIV. THE INFLUENCE OF THE GONADS ON PROTEIN METABOLISM.

I. URINARY CREATININE AFTER CASTRATION.

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IN the first of a series of papers on the sex glands and metabolism, Korenchevsky [1925] summarises the results of castration and ovariectomy on obesity and on gaseous and nitrogen metabolisms obtained by various investigators since 1890. In regard to nitrogen metabolism some observers report no effect, some a decrease and others an increase after gonadectomy. Luthje [1902] for instance was unable to find any change in the nitrogen balance of a castrated dog. Korenchevsky's own work on dogs and rabbits showed that removal of the gonads leads to a decrease in the total daily urinary nitrogen in fed animals. This effect was more pronounced in fasting animals. The only reference to the influence of castration on creatine or creatinine metabolism is a paper by Tsun-Chee-Shen [1927] who reported an unchanged creatine metabolism after castration in dogs and albino rats. Werner [1929] found an increase in the blood-urea of castrated sheep. Most workers confined themselves to an investigation of the changes in nitrogen balance or nitrogen output. In the following research the effect on urinary creatine and creatinine was investigated because of the obvious fact that these end-products are much more accurate indices to changes in endogenous protein metabolism than the total nitrogen excretion.

The dates corresponding to the points on the graph refer to the final 24-hour period of each series. The arithmetical mean of the daily creatinine outputs of each series is plotted.

EXPERIMENTAL.

The experiments were performed on adult male rabbits. The animals were kept in metabolism cages, fed on cabbage leaves and carrots, and the urine was collected every 24 hours. From the Tables, it can be seen that the daily output of creatinine was very constant. This indicated that complete 24-hour urines had been collected and consequently catheterisation, *etc.* was considered unnecessary. At the end of each 24-hour period the sides and funnel-shaped bottom of the collecting portion of the cage were washed with water and the washings added to the urine. The clear filtrate from about 100 cc. of

the diluted urine was used for the estimations of creatine and creatinine by Folin's method. The colorimetric readings were usually checked independently by one or other of us.

The animals remained in the cages for 3-8 days; in some cases for a longer period. They were then put into a large cage which communicated with a large open run on the outside of the animal house and were fed on bran, oats and vegetables. After 1-4 weeks they were returned to the metabolism cages. Both when in the metabolism cages and when in the general run the animals got plenty of sunlight, and throughout the course of the experiment (several months) they were in a healthy condition.

Collection of urine from operated animals was usually begun about a fortnight after the operation. The testis for grafting was taken from a rabbit, divided into two, and each half inserted between the external and internal oblique muscles, one on either side just above and lateral to the symphysis pubis. In those cases in which the graft was subsequently removed it was found that the transplanted testis had become vascularised.

EXPERIMENTAL DATA.

In the following Tables the dates refer to the first of a number of 24-hour periods. The arithmetical mean and standard deviation of the daily creatinine output in milligrams are given for each series of 24-hour periods.

Table I.

Date		Daily urinary creatinine mg.	No. of 24-hr. periods	Weight kg.
A. Rabbit No. 1. Castrated 17. ix. 29. Grafted 2. v. 30.				
5. ix. 29	Pre-period	85 $\pm$ 5.0	12	2.03
8. x. 29	After castration	90 $\pm$ 1.4	3	2.25
30. x. 29	"	92 $\pm$ 2.3	5	2.33
20. xi. 29	"	97 $\pm$ 2.0	4	2.46
10. i. 30	"	105 $\pm$ 2.2	4	2.55
1. ii. 30	"	104 $\pm$ 4.5	5	2.55
17. ii. 30	"	108 $\pm$ 6.0	5	2.62
19. iii. 30	"	110 $\pm$ 7.2	5	2.63
14. iv. 30	"	109 $\pm$ 5.2	6	2.79
19. v. 30	After grafting	106 $\pm$ 6.1	3	2.68
2. vi. 30	"	101 $\pm$ 8.1	3	2.61
16. vi. 30	"	92 $\pm$ 7.0	3	2.66
B. Rabbit No. 2. Castrated 19. xii. 30. Grafted 23. ii. 31.				
10. xii. 30	Pre-period	61 $\pm$ 6.5	7	1.94
5. i. 31	After castration	57 $\pm$ 5.7	7	2.25
20. i. 31	"	80 $\pm$ 7.7	8	2.23
9. ii. 31	"	84 $\pm$ 6.7	8	2.27
2. iii. 31	After grafting	61 $\pm$ 5.0	4	2.30

These two preliminary experiments (Table I *A* and *B*) show that removal of the testes results in a definite increase in the daily output of creatinine. In the case of rabbit No. 2 the daily urinary creatinine had risen, a month after the operation, from 61 mg. to 80 mg., a month later this high level was still

maintained, the mean being 84 mg. A fortnight after grafting, the creatinine excretion had fallen to the normal pre-castration value of 61 mg. Similar results were obtained for rabbit No. 1. Seven months after castration the urinary creatinine was still 25 % above the value before the operation.

Table II.

		Daily urinary creatinine mg.		No. of 24-hr. periods	Weight kg.	
		Operated animal	Control animal		Operated	Control
Date						
Rabbit No. 3.	Castrated 23. ii. 31.	Grafted 22. vii. 31.	Rabbit No. 4 (Control).			
8. ii. 31	Pre-period	60 $\pm$ 1.9	58 $\pm$ 4.4	8	2.05	1.87
4. iii. 31	After castration	62 $\pm$ 6.0	61 $\pm$ 5.0	6	2.02	1.81
13. iv. 31	„	75 $\pm$ 5.3	61 $\pm$ 2.1	5	1.95	1.81
10. v. 31	„	79 $\pm$ 1.3	64 $\pm$ 0.4	5	2.0	1.77
13. vii. 31	„	89 $\pm$ 8.0	Died	6	1.94	—
27. vii. 31	After grafting	77 $\pm$ 6.2	—	3	1.84	—
10. viii. 31	„	63 $\pm$ 6.4	—	5	1.88	—
18. viii. 31	„	59 $\pm$ 3.7	—	5	1.88	—

Animal No. 3 (Table II) shows a 50 % increase five months after castration, the normal control having remained at a steady level during that period. About three weeks after grafting the creatinine excretion was again normal.

The experiment in the case of rabbit No. 5 was carried further and the graft removed after its effect had become fully established. This resulted, about a fortnight after removal, in the reappearance of the usual castration effect. The complete experiment is graphically represented in Fig. 1.

Fig. 1. The dates corresponding to the points on the graph refer to the final 24-hour period of each series. The arithmetical mean of the daily creatinine outputs of each series is plotted.

Read [1921] in a study of the metabolism of eunuchs found that castration before puberty induced a continuance into adult life of the pre-pubertal creatinuria, but castration after puberty did not result in excretion of creatine. Tsun-Chee-Shen and Hao Lin [1927] report that creatinuria was present in only one case out of nine eunuchs examined by them. No creatine was found in the urines of the above castrated adult rabbits, thus confirming the results in eunuchs.

SUMMARY.

1. Castration of adult male rabbits gives rise to a 25–50 % increase in the excretion of urinary creatinine.
2. Grafting of testes into castrated rabbits causes a fall in the high creatinine excretion to the normal pre-castration level.
3. Subsequent removal of the graft leads to the reappearance of the usual castration effect—increased creatinine output.

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