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Effect of Castration on Thyroid in Female Guinea Pigs.

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A study of the literature on the effect of castration on the thyroid gland has shown many contradictory results. Earlier work seems to indicate a reduced thyroid activity in castrate animals. A decreased metabolic rate after castration has been reported by Loewy and Richter¹ and by Savage, Sherwood and Hall.² Histological studies by Korenchevsky,³ Constantini⁴ and Chouke⁵ show a decreased activity of the gland and a decrease in the number of mitotic figures. A decrease in the weight of the thyroid and an atrophy of the gland have been reported by Anderson and Kennedy⁶ and Bokelman.⁷ Others have reported no marked change in the structure or weight of the gland, namely Leonard, Myer and Hisaw⁸ and Freudenberger and Billeter.⁹ More recent work by Biale-Laprida¹⁰ and Korenchevsky and Dennison¹¹ report a slight hypertrophy of the thyroid. Bates, Riddle and Lahr¹² in a quantitative assay of the occurrence of thyreotropic hormone in 7 types of cattle classified as to age, sex and stage of reproductive cycle, found a decreased amount of hormone in the pituitary gland of steers (adult, male castrates).

Contradictory results have been reported independently by Loeser and Aron. Loeser,¹³ who has studied the thyreotropic hormone extensively, claims that 18 days after castration the thyroid gland of female guinea pigs is markedly stimulated. Other work by Loeser¹⁴ indicates that the pituitary gland of a castrated animal when implanted into a normal animal will cause an increased activity of the

¹ Loewy, A., and Richter, P. F., *Zentralbl. f. Physiol.*, 1902, **16**, 449.

² Savage, Sherwood and Hall, *Am. J. Physiol.*, 1933, **105**, 741.

³ Korenchevsky, *Brit. J. Exp. Path.*, 1925, **6**, 21.

⁴ Constantini, P., *Rassegna internaz. clin. terap.*, 1929, **10**, 718.

⁵ Chouke, K. S., *Endocrinology*, 1930, **14**, 12.

⁶ Anderson, D. H., and Kennedy, H. S., *J. Physiol.*, 1933, **19**, 1.

⁷ Bokelman, *Arch. f. Gynak.*, 1931, **144**, 272.

⁸ Leonard, Meyer and Hisaw, *Endocrinology*, 1931, **15**, 17.

⁹ Freudenberger, C. B., and Billeter, O. A., *Endocrinology*, 1935, **19**, 347.

¹⁰ Bralet and Laprida, *Rev. Soc. Argent de Biol.*, 1933, **9**, 245.

¹¹ Korenchevsky and Dennison, M., *J. Path. and Bact.*, 1934, **38**, 231.

¹² Bates, R. W., Riddle, O., and Lahr, E. L., *Am. J. Physiol.*, 1935, **113**, 259.

¹³ Loeser, A., *Klin. Wschr.*, 1935, **14**, 4.

¹⁴ Loeser, A., *Klin. Wschr.*, 1934, **13**, 766.

thyroid gland, greater than the stimulation resulting from the implantation of the pituitary of a normal non-castrated animal. Aron¹⁵ claims that castration increases the titrable amount of thyrotropic hormone in the blood.

I. The histology of the thyroid gland of female guinea pigs, 18 to 23 days after castration was determined by a study on 37 animals in 4 groups, with weights varying from 120 to 1030 gm. A bilateral ovariectomy was performed. Eighteen to 23 days later a unilateral thyroidectomy was done. In both operations ether anesthesia was used. No iodine was given during the operations or during the experiment. The interval of 18 to 23 days was found to be the period of maximum stimulation of the thyroid after castration by Loeser,¹³ and consequently was used in this study. In general, those workers finding stimulated thyroid glands used guinea pigs weighing from 150 to 200 gm. while those reporting no stimulation used animals of greater weight and age; hence we used 4 weight groups. Group A, from 120-175 gm.; Group B, from 240-285 gm.; Group C, from 440-535 gm., and Group D, from 685-1030 gm.

Our conclusion, based on this histological study, is that there is no gross indication of increased thyroid activity after castration and in all cases the thyroid gland was found to be in a resting state with low, flattened epithelium and acini filled with colloid.

II. Using the thyroids removed by unilateral thyroidectomy in the previous study as control glands indicating a non-stimulated resting state of the remaining thyroid, and convinced by control studies 9 to 11 days after unilateral thyroidectomy, and by the work of Loeb,¹⁶ that no compensatory hypertrophy had occurred, these castrate guinea pigs were injected with thyrotropic hormone (Antuitrin T, Parke, Davis and Company). The animals were injected with 0.025 cc. per 100 gm. of body weight (approximately 5 G.P. units per 100 gm.) daily for 4 days and were autopsied on the fifth day.

The histological findings were that all of the 37 animals responded to thyrotropic hormone with a degree of stimulation inversely proportional to the weight of the animal; that is, the smaller animals responded with maximum stimulation, while the larger animals responded to a lesser degree. Control non-castrates which had been unilaterally thyroidectomized (Group E) responded to thyrotropic hormone to a comparable degree. Control castrates in which a uni-

¹⁵ Aron, M., and Benoit, J., *C. R. Soc. de Biol.*, 1931, **108**, 784.

¹⁶ Loeb, L., *J. Med. Res.*, 1919, **40**, 199.

TABLE I.

Group	No. of animals	Weight mean	Castrated	Days between		Histology removed thyroid	Days between unilat. thyroidectomy and injections		Medication Amt. Dose	No. Doses	Histology thyroids removed at autopsy
				castration and unilateral thyroidectomy	unilat. thyroidectomy and injections		Prep.	Ant. T.			
A	10	140	Yes	22	9-11	Normal. No stim.	9-11	0.025 per 100 gm.	4	4	Stim. + + + + +
B	12	265	"	18-20	"	"	9-11	"	"	4	" + + + + +
C	9	480	"	21	"	"	9-11	"	"	4	" + + + + +
D	6	875	"	23	"	"	9-11	"	"	4	" + + + + +
E Control	2	265	No	—	9	"	9	"	"	4	" + + + + +
F Control	2	270	Yes	21	"	"	—	—	—	—	Normal. No stim.
G Control	4	305	"	—	30	—	"	"	"	4	Stim. + + + + +

30 days between castration and injections.

lateral thyroidectomy was performed but which were not given thyreotropic hormone, showed a thyroid gland that was not stimulated (Group F). Control castrates (Group G) in which no unilateral thyroidectomy was performed, responded to injections of thyreotropic hormone comparable to both normal animals and unilaterally thyroidectomized castrates.

In Table I we have designated the degree of stimulation of the thyroid gland as one to 4 plus. The first grade of hyperplasia was represented by a change to cuboidal type of epithelium in the central part of the gland; the second grade was indicated by this condition throughout the gland; the third grade by an increased height of epithelium throughout the gland with some loss in colloid; the fourth (++++) by universal maximum epithelial height, loss of the circular shape of the cut alveoli, and the absence of colloid as reported by us previously.¹⁷

III. Using basal metabolism as an indication of response to thyreotropic hormone, 23 castrate female guinea pigs were injected with hormone doses varying from 0.025 per day to 0.025 per 100 gm. body weight per day. Twenty of these animals responded with an increased metabolic rate varying from +18 to +60 after 3 to 5 injections. Three animals gave no histologic or metabolic response. This response is comparable to 37 normal non-castrate female guinea pigs responding to thyreotropic hormone injections on the third to fifth day with an increased metabolism of from +20 to +65.

In summary, we found the following: (1) No gross histologic change was found in the thyroid of untreated female guinea pigs 18 to 23 days after castration; (2) castrate female guinea pigs responded to thyreotropic hormone 30 days after castration with histologic changes in the thyroid no different from those found in normal female guinea pigs given the same treatment; (3) the metabolic response of castrate female guinea pigs to thyreotropic hormone is of the same magnitude as is the response of non-castrated female guinea pigs.

¹⁷ Starr, P., Patton, H., and Bruner, R. C., *Christian Birthday Volume*, in press.