## ARTICLE IN PRESS

## THE EFFECT OF CASTRATION ON BENIGN HYPERTROPHY OF THE PROSTATE IN MAN<sup>1</sup>

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Whether benign hypertrophy of the prostate is under endocrine control or not is a problem of immediate interest, since not all workers are agreed on this point. Determination of the effect of castration on this disease is one of the most critical ways to settle this problem, but contradiction of opinion exists at the present time as to the effect of removal of the gonads on enlargement of the prostate gland.

Largely as the result of the stimulus of White, castration was carried out in more than 100 men for the cure of this disease between 1893 and 1895. Summarizing the results in 111 cases White wrote: "The theoretical objections which have been urged against the operation of double castration have been fully negatived by clinical experience, that shows that in a very large proportion of cases (thus far in approximately 87.2 per cent) rapid atrophy of the prostatic enlargement follows the operation." Discussing the findings in 79 cases who survived bilateral castration, A. T. Cabot wrote: "In 27 cases retention, which existed at the time of operation, afterwards disappeared. In 7 of these cases the retention was acute, that is, had existed for less than a month while in the other 20 the retention was of long standing"; and "Reducing these facts to percentages we find that these cases show 9.8 per cent failure; 6.6 per cent moderate improvement; and 83.6 per cent of substantial or very great improvement." Since about 1900 castration has become obsolete however as a treatment of prostatic hypertrophy but this does not indicate necessarily that the enlarged prostate does not shrink when the testes are removed.

The problem recently has been studied in 2 clinical cases by Deming, Jenkins and van Wagenen. In their first case, a man with a large prostatic hypertrophy causing acute urinary obstruction, they removed both testes with no relief of the obstruction or any noticeable diminution in the size of the gland on rectal examination during a period of 1 month; a definite adenoma of the prostate was then removed by perineal pros-

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tatectomy. They stated: "We have no evidence that castration causes atrophy of the so-called benign overgrowth of the prostate." The same group reported the case of a man who was "castrated in the early twenties" and developed symptoms of prostatic hypertrophy at the age of 74. The testicles of this man had been injured severely at 18 and 21 years of age, and at age 74 a large benign prostatic hypertrophy was present, the testes being atrophic, measuring 1 cm. in length. A perineal prostatectomy and a right castration were done, the testis showing sheets of large mononuclear cells resembling interstitial cells. They concluded that there is no histological evidence that the action produced by castration or any hormone influences the growth of prostatic hypertrophy.

In the final analysis of the problems of pathogenesis of prostatic hypertrophy, experimental results must be tested in man since benign nodular growths of the prostate composed of epithelium, muscle and connective tissue are peculiar to the human individual and are not known to occur spontaneously in other species. Unfortunately, in the series of clinical cases treated by castration in the last century very few pathological observations were reported after the operation as to its effect on the prostate gland. Cabot found no differences in the prostate 7 days following castration, while in a second case, 7 weeks following the operation, microscopic examination showed an almost complete disappearance of all glandular elements with a great increase of smooth muscle; Cabot reported 3 specimens from castrated patients in which the median lobe existed as a large and obstructing body. Griffiths reported that the prostate 17 days after orchiectomy resembled that of the dog after castration; the epithelium was cuboidal and degenerated, the lumina of the acini were reduced to a fissure and there was a proliferation of the stroma. Moullin described an adenomatous prostate 29 days after castration as follows: "although there was a distinct reduction in size as shown by the wrinkled state of the mucous membrane, no histological changes could be made out. The epithelial cells preserved their columnar shape and normal appearance and there was no evidence of proliferation."

That prepuberal castration leads to failure of development of the prostate gland and that castration of the normal adult causes atrophy of the prostate have been known at least since the time of John Hunter who wrote with regard to the bull: "The prostate gland, Cowper's glands and the glands along the urethra are in the perfect male large and pulpy, secreting a considerable quantity of slimy mucus which is salt to the taste; while in the castrated animal these are small, flabby, tough and liga-

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