around the openings of the ejaculatory ducts, is unquestionably absorbed. I believe that the large, soft, elastic, uninfamed prostates are only slightly diminished in actual size after three weeks, and it is some weeks, even months, before they are decidedly small *per rectum*. With the congested enlarged prostate it is perhaps slightly otherwise. I can conceive that a recently congested enlarged prostate is markedly reduced in volume after the first three weeks, because the diminution in its congestion removes much of its extravascular bulk, but its final reduction in size is probably as slow as that of others. I have a suspicion that the fibrous prostate, which is tough, hard, and small *per rectum*, does not become reduced so quickly as the soft, elastic, fibromyxomatous gland.

In some cases the first appearance of change in the contour of the prostate after orchectomy was a confusion between the lobes by a filling up of the interlobar groove, but of this I cannot speak definitely, because some prostates approach this type in senile enlargement. The mere reduction in size *per rectum* is, however, of secondary importance to the observed effects upon voluntary micturition.

(b) *Return of Voluntary Micturition.*—In those cases in which the muscle power was still present, though impaired, some return of normal micturition took place within the first week. But if the atony was pronounced the catheter could not be discarded. This is the weak point about all prostatic operations, a prognosis of the return of voluntary micturition depending in every case upon the muscle power of the bladder. Now, it is very evident that the muscular power of the bladder is not only impaired by prostatic obstruction but also by senile changes; and when patients apply for treatment, no matter how early the stage of the enlargement may be, some muscular weakness will be detected. And from this no aged patient ever recovers. He may be made comfortable by removing the prostatic obstruction, if this is done sufficiently early, but a strong stream is never regained. In all the cases in which I have done prostatectomy or castration in the aged, evidences of muscular weakness have remained. If the muscle of the bladder had not been placed *hors de combat* by retention or by confirmed catheterism, castration has certainly enabled the muscle to recover itself to some, often to an unexpected, extent. But the evacuating power remained capricious, and was influenced by the same conditions which affected it before the prostatic obstruction was removed. Thus, at one time the force appeared greater than at others. In the morning on rising a difficulty in emptying the bladder was still experienced, and several urinations at close intervals were necessary. Towards evening the force of the current generally improved. A cold, or an indiscretion in diet evoked frequency. If the bladder became over-distended, as in prolonged railway travelling, the stream was nearly always intermittent, the bladder being forced to complete by many efforts the work of evacuation which in middle age was accomplished in one steady expulsive contraction. The catheter even may be needed to assist the muscle if the over-distension has been great. Sudden stoppages, I have noticed, are still felt, but these may be due to the excess of mucous membrane at the base—left after the shrinkage of the subjacent enlargement—becoming rolled on to the vesical orifice.

(c) *Pus in the Urine.*—Not least among the advantages gained in some of the cases was the reduction in the amount of the pus present in the urine. Probably this may be accounted for to some slight extent by the effects of counter-irritation applied to the vertex of the bladder by means of the two wounds.

CONCLUSIONS.

1. There is no doubt that slow shrinkage of the prostatic tissue in many of the forms of senile enlarged prostate ensues upon double castration. Further experience must, however, decide as to whether every form of prostatic growth is thus affected.

2. It is certain that escape from catheter life after castration depends absolutely upon the health of the vesical muscle. The grade of the atony, therefore, should be most carefully estimated before any hopes of relief from catheterisation are held out. To promise a confirmed catheter case that orchectomy will do away with the instrument will merely bring discredit on the operation and disappointment to the

patient. Even after prostatectomy we are unable to promise such relief if the muscle is hopelessly atonic, and we cannot do so after castration.

3. It is possible that castration by diminishing the microbic infection from the inflamed senile prostate will remove a constant menace to the integrity of the kidneys, for it will control the most prolific source of ascending pyelitis.

It appears to me that double castration will prove of value in the following conditions:

1. In reducing bulky overgrowth of the lateral lobes of the prostate. It may be found that the small, tough, fibrous, median or lateral vesical outgrowths will be better removed by suprapubic prostatectomy.

2. In controlling the distress and danger of an inflamed senile enlarged prostate.

3. In lessening the frequency or difficulty of introducing the catheter in advanced or confirmed catheter life.

4. In avoiding the mechanical difficulty of crushing a post-prostatic on a post-trigonal stone, by levelling the base of the bladder, thus rendering the operation of litholapaxy feasible in a condition in which before it was impracticable.

5. In reducing chronic cystitis and recurrent phosphatic calculus in cases of confirmed catheter life.

AN ENLARGED PROSTATE GLAND EIGHTEEN DAYS AFTER BILATERAL OR COMPLETE CASTRATION.

By JOSEPH GRIFFITHS, M.A., M.D., F.R.C.S.,

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For permission to publish the account of the following case I am indebted to my colleague, Dr. Carver, under whose care the patient was while in hospital.

J. M., aged 74, a well-built and hearty-looking man, was admitted on October 10th, 1894, suffering from severe cystitis of many months' duration, the urine containing a large amount of mucus and pus. Micturition was very frequent and very painful, only a few drops being expelled at a time. Two years previously he was in the hospital for retention of urine, and since then he was in the habit of using a catheter. The prostate, as felt *per rectum*, was about as large as a medium-sized orange. As there was but little improvement from washing out the bladder and the frequent use of the catheter, and as there was much pain with little prospect of relief, he consented, as a last resource, to have his testicles removed. This was done on November 16th, 1894. The testicles were of full size, and in the left there was a large spermatocele. In each the production of spermatozoa was still going on, and in each there were numerous active spermatozoa in the seminal tubules.

On the following day (November 17th) the amount of urine found in the bladder was very small, but there was a great deal of pain in the loins, indicating partial suppression of urine. The next day more urine was secreted, and the pain in the loins was much less. There was, however, at times agonising pain in the bladder, though the amount of mucus and pus in the urine had somewhat decreased. At the end of the first week after the operation he could pass, for the first time for some weeks, a few ounces of urine without the aid of the catheter which was now only used twice daily. The urine still contained much pus. During the second week after the operation his general condition slightly improved and the bladder became quiet, and he was able to empty it fairly well; but towards the end of the second week he began to suffer from sleeplessness, which was soon followed by delirium; thus it was difficult to ascertain the condition of the urine, and on the fourteenth day after the operation the right popliteal artery became blocked, and the limb below showed signs of commencing gangrene. During the next four days he became gradually worse, the gangrene of the limb increased, and he died on December 3rd, 1894, eighteen days after the operation.

At the *post-mortem* examination the right kidney was found much enlarged from chronic hydronephrosis, and there was

suppuration of the distended pelvis and of the remaining portions of the kidney substance, which was probably subsequent to the castration. The left kidney was natural. The bladder was much thickened and its mucous membrane inflamed, as was that of the right ureter. All the other organs were healthy. In the right popliteal artery there was a mottled and slightly adherent recent clot. The prostate, which was still of large size, was somewhat firmer than an ordinary enlarged gland. In its substance there were a few small, soft, circular patches, apparently infiltrated with extravasated blood. The largest of these measured about half an inch in diameter. In some parts there were many small cysts (dilated tubules), and in others the gland substance was streaked with branching yellow lines which, as will be immediately shown, were the glandular tubules filled with fatty degenerated epithelial cells. The glandular tubules in the part of the gland streaked with yellowish lines were diminished in size and in number, and the intertubular connective tissue was relatively increased. A few of these

Fig. 1.—Section of enlarged prostate eighteen days after bilateral castration $\times 350$. (a) Contracted tubule filled with small cells; (b) tubule filled with epithelial cells undergoing fatty degeneration; (c) stroma containing proliferating connective tissue cells; (d) unstripped muscle fibres.

tubules, which were of large size, were lined by three or more layers of small compressed cells, only the nuclei of which could be defined, enclosing a large lumen filled with large epithelial cells. These epithelial cells, occupying the lumen of the larger tubules, were of polygonal shape, ill-defined, with an almost clear finely granular protoplasm and small round nuclei. Some of the central epithelial cells were in an advanced state of fatty degeneration. The remaining tubules, which formed the greater number, were small and contracted, and were lined by a single layer of small cubical, almost flattened, epithelial cells with round nuclei and very little protoplasm. The lumen, when present in these tubules, was reduced to a fissure which was empty. In some parts the stroma, which usually consists largely of unstripped muscular fibres, was very cellular, owing to the proliferation of the connective tissue cells as well as of the unstripped muscle-fibre cells, the nuclei of each of which were found undergoing division. Wherever this had taken place the muscle fibres were in great part replaced by small round cells and by fusiform cells that could not be distinguished from ordinary connective tissue cells. In other parts the cell elements of the stroma had in part disappeared, giving place to a form of fibrous connective tissue in which there were only a few connective tissue cells, and this change had especially taken place around the small and contracted tubules.

Fig. 2.—Section of enlarged prostate eighteen days after bilateral castration, stained with osmic acid $\times 250$. (a) Glandular tubules; (b) epithelial cells lining tubules, loaded with fine fat granules which obscure outline of cells and their nuclei; (c) intertubular connective tissue containing some unstripped muscle fibres.

In the cystic portions of the gland similar changes had taken place, though it was not so easy to determine them. The epithelial cells lining and those partly occupying some of the cysts were without exception in a more or less advanced state of fatty degeneration. In the small patches, which were apparently infiltrated with blood, the changes were also similar but more pronounced. The epithelial cells in the dwindled tubules were loaded with small fat granules, and where fusiform cells had formed in the stroma fatty degeneration was also marked. In one or two places the capillaries were much dilated, but there was no blood extravasated, though the naked-eye appearance of these patches suggested that.

The changes above described are: (1) Proliferation of the columnar cells lining the glandular tubules; (2) acute fatty degeneration of the cells thus accumulated in the lumen of the tubules, with their disintegration and ultimate disappearance; (3) contraction of the tubules after a conversion of their naturally tall and slender columnar cells into low cubical or almost flattened small cells; and (4) in the stroma, proliferation of connective tissue and unstripped muscle-fibre cells. It appeared that in parts many of the newly-formed cells in the connective tissue had disappeared, or been converted into fibrous stroma in which there were no muscle fibres or only traces of them. In those parts of the stroma where the changes had taken place quickly the newly-formed cells were swollen and filled with fine granules of fat.

If a comparison be made between the structure of this enlarged prostate eighteen days after bilateral castration and that of an ordinary enlarged gland from a man whose testicles had not been removed or not destroyed by disease, it will be seen that the glandular tubules and the intertubular connective tissue, with its unstripped muscle fibres, have undergone definite structural changes. In the tubules the epithelial cells had undergone, first, proliferation so as to form new cells; secondly, well-marked fatty degeneration; and lastly, disintegration followed by their complete disappearance. In this manner the tubules had, in the majority of instances, become greatly reduced in size. In the intertubular connective tissue similar changes had taken place—namely, proliferation of the connective tissue cells, fatty degeneration of the new cells, their disintegration and ultimate disappearance. In like manner the unstripped muscle-fibre cells had undergone proliferation, and the new cells thus formed were indistinguishable from the connective tissue cells among which they lie. In short, the cell elements first proliferate, then degenerate, and ultimately disappear, leaving a comparatively small amount of fibrous connective tissue in their place.

But in the ordinary enlarged prostate gland the structural changes above described as occurring after castration, so far as I have been able to observe, do not take place. There is no general proliferation of the epithelial cells lining the glandular tubules, or of the cells in the intertubular connective tissue; and no fatty degeneration of the cells followed by disintegration and ultimate disappearance. In the enlarged gland there is, however, usually a tendency, in small patches here and there in the substance of the gland, to atrophy of the gland tubules, to disappearance of the

muscular fibres in the stroma, and to the formation of fibrous connective tissue, and this may in some instances extend through the substance of the gland.

The inference, therefore, from the case I have related is that these structural changes in the enlarged prostate eighteen days after bilateral castration are preliminary to the ultimate atrophy of the glandular tubules and to the conversion of the prostate into a small, firm, and fibrous mass, containing only remnants of the tubules, and but few traces of its muscular fibres.

Changes similar in many respects to those described above as occurring after castration in man take place in the prostate of a dog after double castration. Thus in June, 1890, I castrated, while residing in Paris, a hound 3 to 4 years old, and three weeks (twenty-one days) after the animal was killed. In the gland, which was obviously small for so large

Fig. 3.—Section of prostate of full-grown dog twenty-one days after bilateral castration $\times 50$. (a) Contracted tubules lined by low cubical or flattened epithelial cells; (b) stroma composed chiefly of fibrous connective tissue.

a dog, the tubules were much reduced in size and number, and the intervening tissue was relatively increased. In many of the tubules the epithelial cells filled the lumen, and these cells were of irregular shape and size. In others the tall and slender columnar cells had given place to a single layer of small cubical or flattened cells enclosing a very narrow fissure-like lumen. In parts of the stroma the muscle fibres had to a great extent disappeared, their place being taken by connective tissue cells; in others, where the tubules had in great measure disappeared, the stroma consisted of fibrous connective tissue with hardly any traces of unstriated muscle fibres.¹

Thus the changes that arise after castration in a man with enlarged prostate are similar to those which follow castration in a dog, and no doubt the ultimate result is the same in each. The gland, whether enlarged or normal, undergoes certain degenerative changes after removal of the testicles which lead to its conversion into a small, tough and fibrous mass in which there are only remains of the glandular tubules and ducts.²

With regard to the enlargement of the prostate gland I published a paper in the *Journal of Anatomy and Physiology*, 1890, vol. xxiv, from which the following conclusions are taken:

1. That enlargement or hypertrophy of the prostate gland results from a growth of the gland tubules with their associated muscle so as to form new gland substance closely resembling that of the normal gland. This constitutes the first or glandular stage.

2. That after a variable time degenerative changes set in which ultimately convert the new tissue into a mass of more or less dense fibrous connective tissue containing only the

atrophied remains of the glandular and muscular elements. This constitutes the second or fibrous stage.

When this second or fibrous stage has been reached throughout the gland, as occasionally happens, I apprehend that castration would not cause any very marked diminution in size of the enlarged prostate and, therefore, it must not be supposed that dwindling of the enlarged gland will invariably result after castration, though this may be the usual result.

THE MILROY LECTURES ON THE NATURAL HISTORY AND AFFINITIES OF RHEUMATIC FEVER.

*Delivered before the Royal College of Physicians of London,
March, 1895.*

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[ABSTRACT.]

LECTURE III.

INFLUENCE OF TEMPERATURE.

THE marked preference of rheumatic fever for the winter season was shared by infective diseases like small-pox, measles, whooping-cough, etc. This seasonal incidence was explicable as due to the effect of climatic influences on the life-history of the specific micro-organism, or to their effect on the receptivity of the community.

A comparison of the curve of mean annual temperature at Greenwich with that of hospital cases of rheumatic fever in London showed that in the epidemic years 1866 and in 1868-9, the mean temperature was 1 to 5 per cent. above the mean for the whole period 1866-93; in the epidemic years 1874-5 the mean temperature was at the mean line. In 1879 low rheumatic fever corresponded with a low mean temperature; and in 1884 and 1893 there was again an association of high mean temperature and excessive rheumatic fever. The curves of mean temperatures for the first and fourth quarters of the year showed that higher temperatures usually coincided with excessive rheumatic fever, though there did not appear to be any definite proportion between the two.

The temperature of the earth 4 feet deep, so far as records were available, showed a much closer relationship than that of the air. The earth temperatures taken at Regent's Park since 1871 (records missing for 1877-9) showed that in 1871-4 inclusive the mean earth temperature of the year was always at or above 50° F., a temperature which was not again reached except in 1884 and 1893, which were also epidemic years. The maximum and minimum earth temperatures give similar indications. During the period in which comparison was possible in London, epidemics of rheumatic fever occurred only when the mean temperature of the soil was exceptionally high, that is, over 50° F., and the greatest epidemics occurred when the mean temperature had been thus high for two or more years in succession.

INFLUENCE OF RAINFALL.

The relationship between damp air and damp soil and the prevalence of rheumatism being almost accepted as axiomatic in medicine, rainfall might be expected to exercise a great influence in increasing rheumatism. The observations of writers on this point were hopelessly at variance. The Collective Investigation Committee of the British Medical Association reported that most cases began in damp or wet, or cold and cloudy weather; and Dr. Gabbett, from an examination of the London Hospital statistics, thought that rheumatic fever tended to vary directly with the rainfall. On the other hand, Hirsch, Edlefsen, and Longstaff, among others, had found that the amount of rheumatic fever was more or less inversely with the rainfall.

Comparing the yearly and quarterly rainfall at Greenwich with the hospital incidence of rheumatic fever, it was found that a heavy rainfall was usually associated with a low amount of rheumatic fever, and a light rainfall with excessive rheumatic fever, though no exact proportion was observable be-

¹ In one of the experiments made by White of Philadelphia, reported in the *BRITISH MEDICAL JOURNAL* of September, 1893, in which the dog was castrated seventeen days previously, there were apparently no atrophic changes in the prostate gland.

² I have, in the *Journal of Anatomy and Physiology*, vols. xxiii and xxviii, published a detailed account of the prostate gland as it is found in castrated animals and in eunuchoid persons respectively.