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Original Articles.

THE NATURE OF PROSTATIC HYPERTROPHY.

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In the introduction of this paper the writers wish to state that there is no expectation on their part that they will be able to settle definitely at once all the questions concerning the nature of prostatic hypertrophy. Their object is to place on record a somewhat exhaustive report of the histologic examination of a considerable number of prostates, to mention the results of some clinical experience and to present the conclusions to which the data have directed them. An exhaustive consideration of the theories and data of other observers must, on account of lack of space, be omitted. By confining ourselves to a consideration of the conclusions of observations made during the past five years by those who have had a large amount of material at their command and eliminating those whose conclusions have been made from theoretical considerations, the field to be looked over can be made narrow. From early times until the microscope came into general use the prostatic hypertrophy of the aged was by many considered of inflammatory origin, often thought to have been caused by a preceding urethritis. But for the past twenty years, while the theories as to its nature have been varied, there seems to have been a pretty general consensus of opinion that a true tumor formation of some sort or other was present in the prostatic hypertrophy of the aged and that the prostatitis associated with urethritis found in young men was another affair.

Gouley, who did the earliest serious work on the prostate in this country, claimed that in necropsies of young men suffering from prostatitis who died from intercurrent affections he found conditions apparently resembling those found in the prostatic hypertrophy of the aged. He suggested but did not assert an inflammatory origin in this condition. In his latest publication he considers that inflammation is the cause in some cases but adenoma in others.

The senior author of this article in a paper and discussion¹ calling attention to the frequency of prostatitis as a complication of urethritis from an examination of

216 cases, stated his belief from clinical observation that the hypertrophied prostate of the aged followed prostatitis and again later in a paper read before the Academy, but not published, expressed the same views, giving a list of men who had believed the same thing from clinical observations before the microscope came so generally into play. His views were received at the time with a lack of approval that was, to say the least, discouraging.

At the present time so many observers have noticed the very frequent connection between urethritis and prostatitis that the former may be considered as an etiological factor. Two questions which arise are: what evidence can be brought out at the present time from histologic findings that the nature of prostatic hypertrophy differs to any extent from that found in the past and what new relations, if any, can be shown to exist between posterior urethritis, prostatitis and hypertrophied prostates? Until very recently pathologists almost universally considered prostatic hypertrophy of the aged to be due to true tumor formation and while they differed among themselves as to the nature of these tumors a good many of them thought the tumors consisted of an increase in the amount of glandular tissue, which would be an adenoma; in the muscular tissue, therefore, a myoma; or in the fibrous tissue, a fibroma; or that there existed more or less of a mixture of these three forms.

Referring to important researches published during the past five years, those of Motz, Albarran, Halle and Ciencanowski seem to have been the most deserving of attention. The writers of this article gave the results of some of their observations on the prostate last June in a paper entitled "Fallacies in the Treatment of Urethral Diseases," read before the annual meeting of the American Medical Association in St. Paul.² Motz, whose article was the earliest published, arrived at his conclusions from the examination of thirty hypertrophied prostates and his conclusions seem to show that the vast majority of enlargements were of the adenomatous type, that the remaining enlargements were due to a mixture of the glandular and fibrous forms and that the purely fibrous were of a very great rarity. His researches tended to demonstrate that there was no ground for the views held by those who have considered that the changes in the blood vessels played an important part.

Prof. Dr. Stanislaus Ciencanowski³ reported a most exhaustive study on a large number of hypertrophied prostates as well as studies on the pathology of the bladder and of the kidneys. Whether or not one agrees with the conclusions he reached, every one must agree in praising the exhaustive research, both histologic and

1. Jour. A. M. A., Nov. 9, 1901, p. 1223.

2. Anatomische Untersuchungen ueber die Sogenannte Prostaten-Hypertrophie und Verwandte Prozesse, Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie, Jena, 1900. (Published originally in the Polish in 1896.)

3. Some Observations on the Prostate. Journal of Cutaneous and Genito-Urinary Diseases. Read before the American Genito-Urinary Association in 1898.

historical, and give him credit for the excellent plates published illustrating his article. As an indication of the thoroughness of his work it may be stated that the bibliography to which he refers comprises some five hundred names. Briefly stated, Ciencanowski's conclusions were that prostatic hypertrophy was an inflammatory affair, the inflammation extending from the posterior urethra and he suggested blenorrrhagia as a probable cause.

Albarran and Halle followed Ciencanowski by making a most painstaking and exhaustive research of prostatic hypertrophy.* Their conclusions were reached from the examination of 100 prostates, which were obtained from men who died from some of the complications of what is generally termed prostatism. Their conclusions—as regards the preponderance of the glandular or adenomal form over that of the myomatous or fibro-myomatous—agree with Motz, whose conclusions were reached after an examination of thirty hypertrophied prostates. They mention Ciencanowski's work, but criticise it by saying that the prostates from which Ciencanowski drew his conclusions were those of young men. While they mention hypertrophied prostate as being due to adenoma or fibro-myoma, using the old terms, so to speak, they do not by any means reject the theory of its being the result of inflammation and while they mention the two different grounds of belief, judging from their language, they seem to lean more towards the latter. It may be interesting here to note that out of the hundred cases they only found one of what they called the purely fibrous form and what has probably been called in the past the purely myomatous form. The conclusion on which Albarran and Halle dwell most emphatically is that in fourteen cases they found a condition which they termed adeno-carcinoma. In other words, they claim that cancer was present in these fourteen cases. They give a history of the cases. Upon reading the histories, two clinical facts seem to stand out prominently in opposition to their theory that those fourteen cases were cancer. One of these facts is that in but one case was there any mention of metastasis. The other is that the clinical histories of most of those cases show that the patients had suffered from their prostatic trouble for many years. Albarran and Halle claim that these are a sort of a tumor midway between the ordinary hypertrophy of old age and true cancer. They make the interesting statement that when a patient who has suffered the discomfort of a hypertrophied prostate for a long time suddenly develops cachexia and dies within a few months without other clinical evidence to account for it, cancer of the prostate is probably present.

While the writers of this paper can hardly agree with the conclusions reached by Albarran and Halle as to the frequency of cancer of the prostate from their histologic findings, as our plates show similar appearances in certain specimens to those shown in their plates and called cancer by them, which we do not consider such, yet we think that surgeons should be grateful to them for directing thought in that direction. Several other cases whose history they give were undoubtedly cancer of the prostate. They leave the impression on our minds that cancer of the prostate is probably more frequent than has been generally supposed and may be held accountable occasionally for cancers in other parts of the body occurring without any history of prolonged irritation. Some such cancers,

therefore, which have been considered primary, may after all be secondary in character.

Regarding the question as to the connection between prostatitis as it presents itself as a complication of urethritis and true prostatic hypertrophy of the aged, it may be interesting to quote here the latest views of Ciencanowski⁵: "To recapitulate, the histologic aspect of all the senile hypertrophies I have studied correspond in many regards to those upon which Mr. Fenger has written apropos of chronic prostatitis of gonorrheal origin. There exists, however, this important difference, that the alterations of the stroma of which I write are much less pronounced in the cases of senile hypertrophy of the prostate and produce the impression of a chronic inflammation of extremely slow evolution." Right here it may be well to examine an argument against the idea that hypertrophied prostate may be of inflammatory origin, which has been brought up in Europe and in St. Paul last June, and that is that any inflammatory processes found in true prostatic hypertrophy are the result of an accidental inflammatory complication such as might come from the improper passage of instruments or the remains of an ancient chronic prostatitis. It may be here stated briefly that one of the main arguments against such a supposition is the fact noticed by Ciencanowski in all his cases that the same appearance was found in all the cases of prostatic hypertrophy examined whether there was any history of the passage of sounds or not. Ciencanowski's reply to the criticisms of Albarran and Halle shows that his cases of hypertrophied prostate were those of old men, some of whom had shown symptoms of prostatism during life and some not, but the same conditions were present in both; and then, again, Ciencanowski, whose views have been confirmed by us, has been able to show the direct connection between the alterations observed, and secondly, the origin of the senile hypertrophy of the prostate.

To quote again from Ciencanowski, "Hypertrophy senile of the prostate has nothing to do with a neoplastic process. The essential cause of this phenomenon lies in chronic inflammation of extremely slow evolution, localizing itself in the glandular tissue, or in the stroma, or in both and resulting in this inflammatory process which resembles from a histologic point of view chronic post-bleorrhagic inflammations and depends in its intensity on its extent and above all on its localization. The appearance of the hypertrophy is much more pronounced if the periglandular inflammation of the stroma is most evident in the center than it is if the interglandular inflammation localizes itself at the periphery of the prostate. The inverse disposition of these lesions does not cause any hypertrophy of the glands and may even cause atrophy." The slow progress of the inflammation we would expect from our knowledge of the slow progress of chronic inflammation in the urethra generally and it should also be borne in mind here that the clinical experience of many men for decades past has led them to believe that hypertrophy of the prostate was of gonorrheal origin, although the clinical experience of some others has led them to dispute it. One argument against the theory that urethritis plays a part in causing prostatic hypertrophy is that in India, where urethritis is common, prostatic hypertrophy is unknown or very rare. An examination of India medical journals and health reports does not seem to bear this out.

4. *Hypertrophie et Neoplasies Epitheliales de la Prostate*, Par M. M. J. Albarran et N. Halle, *Ann. des Mal. des Org. Urin.*, Tome xviii, 1900.

5. *Annuaire de Malad. des organes Genito-Urinar.*, 1901, "Quelques Aperçus sur le Prostatisme."

To recapitulate briefly, the results of the work done on the nature of prostatic hypertrophy during the last five years by observers who have had the opportunity of forming their conclusions from the observation of a large number of prostates amount to about this:

1. That any former belief that prostatic hypertrophy was due to atheromatous conditions of the blood vessels is erroneous.

2. That the purely myomatous or fibrous form of prostatic hypertrophy is extremely rare, as is being shown by unanimous conclusions, resulting from investigation, by Motz, Albarran and Halle and Ciencanowski.

3. Motz, Albarran and Halle consider that proliferation of the cells of the glandular portion of the prostate, either alone or mingled with changes in the stroma, play the most important part in the hypertrophy of the gland.

4. Albarran and Halle do not dispute the fact that a chronic inflammatory process furnishes the phenomena presented, but lay special consideration on conditions found histologically in a large portion of the prostates examined by them, fourteen out of a hundred, and which they consider are either cancer in the prostate or a sort of a product midway between inflammatory and cancerous tissue.

5. Ciencanowski in his very exhaustive studies of the prostate considers hypertrophy the result of a chronic inflammation of the organ, the original seat of which can always be found if searched for long enough by means of a large number of sections. According as the original focus of the inflammation is in the periphery or in the center of the organ a corresponding form of prostatic hypertrophy or atrophy will be present.

Following is a description of the histologic work done by us on the subject. The exact number of prostates, including normal ones, that have been examined and from which the selection was made on which our conclusions are founded, it is not possible for us to state. The junior author of this paper has for six years been examining all the prostates that a large amount of necropsical work permitted him to obtain. The number would probably run into the hundreds. A hundred or over were collected, including normal ones, for the purposes of the paper read in St. Paul last June. From the total number of prostates which the writers of this paper have been able to gather, a selection was made of all those which showed marked enlargement, in other words, which were apparently abnormal prostates, whether we were able to obtain any history of the cases or not. These enlarged prostates were fifty-eight in number. We consider that they can properly be termed hypertrophied prostates from the fact that under the microscope the same or similar conditions were present in them all, whether they had been removed and we had the history of the case, or whether they were some specimen, of whose history we know nothing. We either have or are able to obtain the history of 19 of the 58.

Six of these have been removed at operation. We believe that in so large a series, selected conscientiously without regard to anything except the presence of tissue augmentation, we have included all usual varieties of prostatic hypertrophy. This condition being most frequent in the aged, we assume that the majority of our specimens have been taken from old men. The process which we have found has been of the same nature in all the cases, the difference being entirely quantitative or of degree. For this reason we state with confidence that our studies have been based on all true types of prostatic hypertrophy. The tissue removed for examination was

always selected from that portion of the gland which showed the greatest hypertrophy. Several sections were taken from a single gland, wherever from the gross appearance of the tissue considerable variation in structure was expected. The notes recorded on each specimen have been as brief as possible, only points directly bearing on the problem under consideration have been touched. No attempt has been made to sub-classify or exhaustively describe the various types of prostatic hypertrophy. The entire study has been made with the idea of detecting the cause of this common condition.

We wish to express our thanks to Dr. B. Lapowski for having first called our attention to the extremely interesting work of Ciencanowski; to Dr. John T. McGowan, who handed to us for the purpose of the paper last spring a collection of some sixty prostates which he had gathered and on which he was carrying on some histologic investigations in connection with Dr. Smith; to Drs. Howard Lillenthal, Frank Hartley, Henry Morton, Raymond Guiteras, Chas. Phelps and George Stewart, each for a prostate which they had removed by operation. Through the kindness of Dr. Charles Peck, six specimens were obtained from the Museum of the New York Hospital, some if not all of which we understand had been removed at operation, about which we have not yet had time to obtain the histories. The Museum of the Carnegie Laboratory, the morgue and various other sources supplied other specimens.

HISTOLOGICAL REPORT.

CASE 1.—N. Y. H., No. 3876. Great chronic interstitial increase with obliteration of acini in places, and marked atrophy of muscle fibers. Patches of round-cell infiltration about the acini and particularly in the neighborhood of vessels. In some places structure seems about normal, but acini are generally small and corpora amylacea few. The interstitial increase and obliteration of acini are most marked in the peripheral portions.

CASE 2.—N. Y. H., No. 2121. Acini in central portions are cystic, filled by cells and detritus. Corpora amylacea are fairly numerous. There is generally a considerable increase in the amount of connective tissue with a corresponding decrease in the muscle cells. There are a few areas of small round-cell infiltration about the periphery and occasionally about some of the central acini, but inflammation is mostly represented by the chronic connective tissue hyperplasia.

CASE 3.—N. Y. H., No. 2431. In general the tissue is normal, but in one portion there is intense round cell infiltration which has produced partial necrosis and has infiltrated deeply into the substance of the gland. Acute connective tissue hyperplasia is apparent about these areas, but the remaining portions of the gland are otherwise natural.

CASE 4.—N. Y. H., No. 6446. Moderate distension of acini, some of which are completely filled with detritus and epithelial cells. Considerable round-cell infiltration about some of the acini, particularly in the central parts of the section. In these areas there is an increase in the connective tissue stroma, with a compensatory relative decrease in muscle. Elsewhere the relative amounts of muscle and stroma are normal. Corpora amylacea are few and small.

CASE 5.—N. Y. H., No. 5265. General stroma much increased, particularly about certain acini and ducts where the hyperplastic tissue is in the adult form. Still other acini are surrounded by zones of small round-cell infiltration, in parts of which injection of vessels and true acute inflammatory changes are made out. Corpora amylacea are infrequent, though some of the acini are much dilated.

CASE 6.—N. Y. H., No. 4877. Great enlargement of glandular acini, so that appearance is of large cysts, lined by a layer of usually simple columnar epithelium and filled by detritus, cells and small corpora amylacea. The connective tissue about these dilated acini is increased and occasionally karyokinetic figures are found in the connective tissue cells. Small areas

of small round-cell infiltration are present, particularly about some of the acini. The muscle cells in places have been replaced by hyperplastic connective tissue. The blood vessels are not congested, and show but a very moderate degree of atheroma. Some are surrounded by an adventitia which is more or less infiltrated with small round cells. Apparently, some edema of the tissues is present. This specimen represents what would ordinarily be called a cystic adenoma of the prostate.

CASE 7.—Greatly enlarged middle lobe from specimen in Carnegie Laboratory Museum. The peripheral portions of the gland show a thickening of the connective tissue, particularly about the vessels, where frequent areas of round cell infiltration are also found. Muscle cells have been largely replaced in these areas and the glandular acini and ducts have been compressed by interstitial hyperplasia. The central portions of the middle lobe are made up of much dilated acini, which are mostly filled by epithelial cells, many of which are breaking down. Small round-cell infiltrations are frequent about these acini and connective tissue increase is marked. The blood vessels show slight atheroma. Corpora amylacea are infrequent.

CASE 8.—Museum specimen from Carnegie Laboratory. Great enlargement of the middle lobe. Considerable increase in connective tissue, numerous large fibroblastic cells, moderate small round cell infiltration in patches about vessels. The central acini are much dilated and are filled by broken-down cells and cell detritus. Occasional small corpora amylacea are present in these cystic acini. The blood vessels show slight arteriosclerosis.

CASE 9.—From Museum Carnegie Laboratory. Great middle lobe hypertrophy. Some of the acini are small, being compressed as a result of hyperplasia of the surrounding connective tissue, but most of the acini are enlarged and filled by one or more corpora amylacea, several of which are extremely large. In the immediate neighborhood of such acini muscle tissue has been replaced by fibrous tissue of adult form. Nearly all the acini contain such large bodies. The blood vessels show moderate arteriosclerosis.

CASE 10.—From Museum Carnegie Laboratory. Great hypertrophy of the middle lobe. Quite extensive perivascular connective tissue increase. The acini are widely separated and there is a general connective tissue hyperplasia apparently of perivascular origin. Patches of small round cell infiltration are frequent. The acini are centrally situated, usually widely distended and filled by cell detritus, polygonal epithelial cells and small corpora amylacea.

CASE 11.—Museum Carnegie Laboratory. Hypertrophy of middle lobe. Marked increase of adult connective tissue. The acini are represented by small openings and are compressed by the hyperplastic connective tissue about them. The vessels show marked arteriosclerosis. Such acini are usually filled by polygonal epithelial cells and small corpora amylacea. The interstitial hyperplasia has also resulted in muscular atrophy.

CASE 12.—Museum Carnegie Laboratory. Greatest enlargement in middle lobe. Well-marked connective tissue increase in peripheral portions of gland, showing both old and recent changes. Peripheral acini almost completely obliterated by overgrowth of connective tissue. Central acini distended somewhat and contain cells, detritus and small corpora amylacea. Patches of small round-cell infiltration frequent. Moderate arteriosclerosis.

CASE 13.—Prostate enlarged about one-third, from a man of 53 years. Morgue. Most portions of the gland are normal, but occasional patches of cell infiltration are found, particularly about certain acini which are over distended and contain epithelial cells, the central portions of which have broken down into amorphous material grouped as though forming corpora amylacea. Occasional acini are surrounded by hyperplastic connective tissue which has stenosed their ducts. This is particularly frequent in the peripheral portions of the section. The vessels are mostly congested and show but slight atheroma. The muscle has in some areas been more or less displaced by the hyperplastic connective tissue.

CASE 14.—From morgue. Subject aged 63. Enlarged about

one-fourth. Marked adult connective tissue increase extending in from periphery where acini are almost completely obliterated and where round cell infiltration is almost general. The central acini are cystic, contain detritus, epithelial cells and small corpora amylacea. The walls between these distended acini are much thinned and are almost wholly fibrous. Some of the larger acini contain very numerous corpora amylacea. The vessels show a moderate degree of atheroma.

CASE 15.—Morgue. Quite general interstitial hyperplasia with the result that nearly all parts of the gland show collapsed acini, surrounded by hypertrophied connective tissue. In some places there is considerable inflammatory infiltration, but in other areas this is wanting. Connective tissue hyperplasia in this section seems mostly limited to the periacinous tissue. Corpora amylacea are infrequent and small. The vessels show very little change.

CASE 16.—Morgue. Section is from periphery of gland. Vessels show marked atheroma, one shows endarteritis obliterans. Few acini in section. Considerable connective tissue hyperplasia, displacing much of the muscle tissue and obliterating the glands. No acute inflammatory exudate.

CASE 17.—Morgue. Tissue generally normal. Slight interstitial increase about certain distended acini. The vessels show no abnormality.

CASE 18.—General hypertrophy. From morgue. No inflammatory patches. A few areas in which perhaps there is slight increase in the connective tissue. The acini are not small, but are filled by cells and contain moderate quantities of detritus. Corpora amylacea are infrequent and are mostly small, though a few are found which nearly fill the acini. One border of section shows, however, a quite intense small round cell infiltration, with connective tissue proliferating about it—apparently this is a recent process.

CASE 19.—Morgue. Enlarged one-fourth. Contains an encapsulated whorl of connective tissue which shows both chronic and acute inflammatory diseases. General connective tissue increase, with occasional areas of inflammatory exudate and with apparently general edema, particularly about the enlarged and cystic acini in central portions of gland. Some of these enlarged acini are completely filled by a single great corpora amylacea, others contain several smaller ones. Inflammatory reaction about these acini is abundantly shown. The vessels show a moderate degree of arteriosclerosis.

CASE 20.—Morgue. Enlarged one-half. Great connective tissue hyperplasia, in places obliterating the acini, while in other places the acini are large and distended, probably from obstruction of their ducts. Great inflammatory exudate into periacinous tissue. Numerous and large corpora amylacea, some of which are surrounded by occasional epithelial cells, being otherwise encapsulated by connective tissue. A very marked and decisive specimen, showing all forms of inflammatory reaction. Blood vessels show but moderate atheroma.

CASE 21.—Morgue. Enlarged laterally, diminished in antero-posterior diameter. General connective tissue increase particularly in central portions of the gland, where the process is still active and round-cell infiltration general. Peripheral acini are largely dilated, surrounded by augmented connective tissue and many contain corpora amylacea. Such acini have but few epithelial cells and the walls are almost entirely fibrous and round cell infiltrations are quite frequent in them. Occasional acini contain only epithelial cells and detritus. The blood vessels show slight atheroma.

CASE 22.—Morgue. Slightly enlarged. Acini mostly dilated, filled by epithelial cells, though some contain corpora amylacea. The glandular epithelium shows numerous evidences of proliferation. Some contain several corpora amylacea of moderate and small size. There are occasional patches of round-cell infiltration about the acini, slight in degree. The specimen apparently represents an intra-acinal inflammation which has not extended beyond to any appreciable degree. Blood vessels natural.

CASE 23.—Morgue. Enlarged one-third. Very marked general connective tissue hyperplasia still active but not entirely acute in character. Extensive patches of infiltration in places. Interstitial growth about some acini has almost obliterated

Fig. 1.—Showing an area of small round cell infiltration. This condition is one of the most frequent manifestations of inflammation seen in hypertrophy of the prostate. Section taken from the peripheral portions of the gland. Case 34.

Fig. 3.—This picture may follow immediately on that shown in the previous plate. The inflammatory infiltration is less and is replaced by numerous fibroblasts and newly formed connective tissue fibers. The acinus shown is partly filled by proliferating epithelial cells. Case 55.

Fig. 2.—Showing general cell infiltration, edema and beginning desquamation of the cells of the acini. This stage precedes and induces interstitial hyperplasia. Case 42.

Fig. 4.—The plate shows several acini which have become compressed by the production of new connective tissue about them. This has resulted in the atrophy of the epithelium of the acini and finally terminates in complete replacement by hyperplastic connective tissue. From the periphery of the gland. Case 36.

Fig. 5.—Section of a prostatic fibroma. The hyperplastic tissue making up the substance of the fibromatous nodule is clearly defined from the more adult fibrous tissue surrounding it. We believe that conditions similar to this follow the process illustrated in the previous plate. Peripheral part of gland. Case 39.

Fig. 6.—Section from the central portion of a hypertrophied prostate. One of the excretory ducts of the glands is seen to be completely obliterated from the formation of new connective tissue in and about it. Round cell infiltration is present throughout the hyperplastic tissue. The acini in the outer portions of this gland were much dilated, forming the so-called cystic adenoma of the prostate. Case 41.

Fig. 7.—This shows the condition produced in the gland when the ducts become closed as shown in the previous figure. This lesion is commonly known as the cystic prostate, and in the fresh condition the spaces formed by the distention of the acini is filled by a semi-fluid material. Specimen taken from the outer part of gland. Case 47.

Fig. 8.—Section showing dilated acini which are filled by proliferating epithelial cells. This condition in some of its forms may be readily mistaken for carcinoma. Mitotic figures are not present in the cells in the centers of the islands, but are seen in the cells still lodged against the basement membrane, the inference is that reproduction is taking place only in the last mentioned cells. From outer portion of gland. Case 36.

Fig. 9.—Showing the presence of large corpora amylacea occupying the dilated acini. They have apparently formed from the detritus of breaking down cells in such a condition as that pictured in Fig. 8. From the peripheral portion of gland. Case 53.

Fig. 10.—Conditions of this nature result when prostates containing large corpora amylacea become infected. Pus formation is shown in one part of the section and the remaining portions show interstitial sclerosis, atrophied acini and cell infiltration. From central part of gland. Case 52.

Fig. 11.—Showing proliferation of connective tissue about large corpora amylacea when situated in the outer zones of the gland. Atrophy of acini, general infiltration and connective tissue hyperplasia. Case 54.

Fig. 12.—Carcinoma originating in the hypertrophied prostate gland. Case 45.

Fig. 13.—Carcinomatous infiltration of enlarged prostate gland. Case 50.

them, but occasional acini are dilated and these are mostly filled with epithelial cells. In the central part is found detritus, showing evident beginning formation of corpora amylacea. Blood vessels show quite extensive arteriosclerosis, but perivascular connective tissue increase is still more evident. This specimen shows to a very extreme degree a hyperplastic inflammation of the connective tissue with slight involvement of the glandular parenchyma.

CASE 24.—Morgue. Enlarged one-fifth. Acini generally dilated and filled by cells and detritus. Formation of numerous small corpora amylacea in the acini, connective tissue of gland stroma not increased. Blood vessels natural. Lesions are apparently only the distention with marked epithelial proliferation in the acini. Probably represents an early stage of prostatic hypertrophy.

CASE 25.—Morgue. Moderate hypertrophy, very hard. Increase of connective tissue marked, very extensive and general infiltration of small round cells, not only in stroma, but also in acini. Muscle tissue mostly displaced by the hypertrophic connective tissue. Acini which are not involved by cyst formation mostly filled by epithelial cells or detritus. Many acini completely collapsed from the great proliferation of surrounding connective tissue.

CASE 26.—Morgue. Moderately enlarged. Acini largely dilated, contain large corpora amylacea in various stages of formation. Other acini are filled by epithelial cells and detritus. Many are surrounded by numerous but small areas of round-cell infiltration and in the neighborhood of these connective tissue hyperplasia is evident, particularly immediately around such acini, where in some cases the process is well advanced. Other acini appear perfectly natural, and in many places the stroma is also normal, showing regular proportion of muscle and connective tissue and no inflammatory infiltration. Blood vessels show moderate atheroma.

CASE 27.—N. Y. H., No. 2431. Moderate general connective tissue hyperplasia. Acini in general show very little change, except where acute inflammatory process is present. Very intense small round-cell infiltration in peripheral portion, some places of which show pus formation and local tissue necrosis, with in places hemorrhagic extravasation. A true acute and sub-acute inflammation. Few small corpora amylacea.

CASE 28.—Morgue. Moderate general hypertrophy. General connective tissue hyperplasia of chronic form. Acini dilated and filled by proliferating cells. Perivascular connective tissue increase marked. Moderate atheroma.

CASE 29.—Carnegie Museum. Great middle lobe hypertrophy. General connective tissue hyperplasia. Areas of round cell infiltration numerous. Acini are enlarged, cystic and filled by epithelial cells and detritus, with formation of corpora amylacea. Moderate atheroma. Many vessels are surrounded by exudates of small round cells.

CASE 30.—N. Y. H., No. 3878. Moderate general chronic connective tissue hyperplasia, but the most marked lesion is a pronounced infiltration of small round cells, between the connective tissue fibers. In certain parts of the peripheral portion, particularly in the region of the prostatic urethra, this cellular infiltration has become so extreme as to result in tissue necroses and actual pus formation. In places this process has practically wiped out the acini and the infiltrations are found scattered throughout the entire gland. Some of the centrally situated acini are dilated, being filled by cells, and cell detritus. In the most acute inflammatory areas the vessels are congested and a few hemorrhagic extravasations are found in the region of the urethra, otherwise the vessels show only a slight atheroma.

CASE 31.—Prostate operated on by Dr. Guiteras. Greatly enlarged. Great hyperplasia of adult connective tissue throughout entire gland, most abundant about the dilated acini. Areas of round-cell infiltration are common and have apparently originated from or about the acini. Centrally situated acini are much dilated and are mostly filled with epithelial cells or detritus, which has resulted from disintegration of these cells. Some of the acini have apparently ruptured into their neighbors. Corpora amylacea are small and

infrequent, but formation of them is apparently taking place from cell detritus. The vessels show but very slight atheroma in most places and the interstitial overgrowth is clearly not of arterial origin. In some places small round cell infiltration of the septa between the dilated acini is very extreme. Of course where interstitial hyperplasia has been great muscular atrophy has been correspondingly marked.

CASE 32.—Enlarged prostate removed by Dr. Lilienthal. Very marked hypertrophy. General connective tissue hyperplasia, in places with actual formation of fibrous nodules, where all traces of muscle and glandular tissue are replaced by a firm mesh of hyperplastic interstitium. Areas of round cell infiltration are frequent and large and usually bear direct relation to the acini, which are mostly small, being compressed by the connective tissue growth. They are largely filled by cells and detritus. Corpora amylacea are infrequent and small, being found only in the larger acini. The vessels show a moderate atheroma.

CASE 33.—From Carnegie Laboratory Museum. General hypertrophy. Tumor projecting into bladder from middle lobe. Peripheral portions made up of a dense zone of connective tissue containing but few muscle fibers. Areas of small round-cell infiltration are frequent both in the outer and in the central portions. Central portions chiefly made up of greatly dilated acini, filled with broken-down cells and detritus. Frequent areas of inflammatory exudate about the dilated acini. Corpora amylacea frequent but small. Blood vessels normal.

CASE 34.—Carnegie Laboratory. Tumor of middle lobe. General fibrosis. Acini as a rule are atrophied, apparently from the pressure of the surrounding hypertrophic connective tissue. Some of the acini are, however, greatly dilated and are filled with cells, detritus and small corpora amylacea. Numerous areas of small round-cell infiltration surrounded by zones of fibrosis. The walls of the blood vessels are slightly thickened.

CASE 35.—From Carnegie Museum. Prostate measures 6 by 10 cm. Hypertrophy involving all portions equally. Enormous distention of acini which are filled by broken-down cells, detritus and small, but frequent corpora amylacea. Stroma very scant in central portions, but peripheral portions show hyperplastic connective tissue and are almost devoid of muscle fibers. Blood vessels apparently normal.

CASE 36.—From Carnegie Laboratory Museum. Entire prostate enlarged, particularly the middle lobe, which is about three times the usual volume. Walls of bladder hypertrophied and sacculated. Marked general increase of fibrous connective tissue. Muscle fibers are still abundant, but many are degenerated, as though from pressure. Many of the acini are distended with broken-down cell detritus, but others are atrophied and show marked increase of the connective tissue about them with resulting complete atrophy of the acinus. In these areas inflammatory changes are very marked surrounding the alveoli. Blood vessels show a marked atheroma.

CASE 37.—From Carnegie Laboratory Museum. General hypertrophy with tumor of middle lobe. Sections of the middle lobe tumor show an encapsulated fibromatous nodule 1 cm. in diameter. This area shows a well-defined capsule of adult connective tissue enclosing acini atrophied or dilated. In either case the lumen is filled by detritus and small corpora amylacea. Blood vessels are numerous and thick walled. Round-cell infiltration about the acini is frequent and it is also present about the small blood vessels.

CASE 38.—From Carnegie Laboratory Museum. Enlarged about four times. Hypertrophy most marked in the left lobe. Peripheral portions made up of thickened and infiltrated connective tissue. In the central parts the acini are either much atrophied or distended. In the latter case the central portion of the acinus is filled with a fine granular debris and the walls are covered by a thin layer of columnar or squamous epithelium. The connective tissue cells show many evidences of proliferation. Muscular atrophy is clearly shown, particularly about the enlarged acini, where more or less inflammatory infiltration is present. Blood vessels show no change.

CASE 39.—Carnegie Laboratory Museum. General hyper-

trophy of prostate and of the walls of the bladder. Very marked connective tissue hyperplasia with general glandular atrophy, particularly where the acini are compressed by the hyperplastic connective tissue. Patches of inflammatory infiltration are present about nearly all of the acini and also about the smaller blood vessels. Small fibromata, highly vascular and evidently of recent origin, are present in places (see plate). Blood vessels slightly thickened.

CASE 40.—Carnegie Laboratory Museum. Great enlargement of the middle lobe with less marked hypertrophy of the lateral lobes. Peripheral portions show marked fibrous increase. Central portions made up of greatly dilated acini, between which thin connective tissue walls intervene. These walls are almost universally infiltrated with small round cells. Blood vessels moderately thickened.

CASE 41.—Specimen removed by Dr. Morton. General augmentation of the connective tissue stroma. Frequent areas of inflammatory exudate. Acini are generally small and are frequently surrounded by zones of infiltration. Walls between the acini are atrophied. Most of the acini contain proportionately large corpora amylacea. Blood vessels natural.

CASE 42.—Carnegie Laboratory Museum. Prostate enlarged about 6 volumes. Abscess cavity in anterior portion 2 cm. in diameter communicating with posterior urethra through dilated duct of prostate. Section taken from portion of gland distant from abscess cavity. The entire interstitium of gland is edematous and is infiltrated with numerous small round cells and plasma cells. This infiltration is most pronounced about the acini, which are filled for the greater part by broken-down cells and by inflammatory exudate. Some of the acini are compressed by the exudate about them. Pus formation is not present in these sections. Under high magnification the epithelial cells of the inflamed acini show frequent karyokinetic figures.

CASE 43.—From Carnegie Laboratory Museum. Moderate degree of general hypertrophy. Muscle tissue almost completely absent and in some portions the glandular elements are represented by spaces lined with a layer of simple squamous epithelium filled by a single large amyloid body and invested by a capsule of hypertrophic fibrous connective tissue. In other portions of the same gland the sections show but very numerous small acini with thin walls, evidently formed by the distention of the acinus by the pressure of its own secretion since the walls of the acini show numerous evidences of distention.

CASE 44.—Carnegie Laboratory Museum. Moderate hypertrophy limited in the lateral lobes. Great general connective tissue hyperplasia. One side of the section shows a few atrophied voluntary muscle fibers surrounded by a greatly augmented endomysium. The acini are large, mostly filled by cells and by corpora amylacea and frequently surrounded by an edematous infiltrated interstitium. The blood vessels show thickened walls.

CASE 45.—Carnegie Laboratory Museum. General hypertrophy, particularly of the middle lobe. Walls of the bladder are hypertrophied and ulcerated. Very marked hypertrophy of the connective tissue with almost complete atrophy of the muscle fibers. Acini for the greater part filled by cell detritus and inflammatory exudate, but in certain of the acini the epithelial cells have taken on very active proliferative changes with the result that they are filled with large epithelial cells supported by connective tissue stroma which has grown in from the walls of the altered acinus. The nuclei of these cells show numerous karyokinetic figures and the specimen is undoubtedly one of carcinoma, originating from the inflamed acini of the gland. Blood vessels greatly thickened throughout the section and in places endarteritis obliterans is shown.

CASE 46.—Carnegie Laboratory Museum. Marked hypertrophy of lateral lobes. The interstitium throughout the entire section is greatly increased, particularly about the glandular acini, where evidences of recent connective tissue proliferation are abundant. The acini are atrophied and contain frequently but a single large amyloid body. Other acini are filled by the epithelial cells and small quantities of detritus. The adventitia of the blood vessels is generally thickened.

CASE 47.—Carnegie Laboratory Museum. Moderate hyper-

trophy. Numerous small semi-pedicated nodular masses project from the surface of the prostate. Marked general connective tissue increase with consequent muscular atrophy. The acini are greatly dilated and are usually lined by a thin layer of simple squamous epithelium. They contain detritus which has apparently remained after the evaporation of fluid. Corpora amylacea, where present, are usually single and completely fill the acinus in which they are lodged. The vessels show marked endarteritis.

CASE 48.—Carnegie Laboratory Museum. Great hypertrophy of the middle lobe. Peripheral portions show a very marked fibroid increase which is of less pronounced degree in the central portions of the gland. The central acini are distended by epithelial cells and detritus. Corpora amylacea are small and frequent. There is a general inflammatory exudate throughout the entire section. Blood vessels normal.

CASE 49.—Carnegie Laboratory Museum. Great enlargement of the entire gland. Small pediculated tumor projects from middle lobe into cavity of bladder. This last portion shows in section almost complete substitution of glandular tissue by dense fibrous connective tissue which encloses frequent corpora amylacea of large size and surrounded by connective tissue only. Blood vessels moderately thickened.

CASE 50.—From Carnegie Laboratory Museum. Moderate hypertrophy involving all portions of the gland. Wall of bladder thickened and the seat of several carcinomatous ulcerations. The connective tissue of the gland is greatly increased and is infiltrated in almost all portions by columns of actively proliferating epithelial cells. A few large corpora amylacea are found situated in atrophied acini and the acini throughout the section are compressed by the greatly augmented connective tissue and by the infiltration of this stroma by cancer cells. Blood vessels moderately thickened.

CASE 51.—Carnegie Laboratory Museum. Moderate hypertrophy of the lateral lobes, great enlargement of the middle lobes. Great thickening of the walls of the bladder. Peripheral portions of the gland show an advanced connective tissue hyperplasia with inflammatory infiltration. Central portions show distension of the acini with atrophy of their walls and formation of numerous small corpora amylacea. Blood vessels moderately thickened.

CASE 52.—From autopsy. Man aged 57. Patient died of meningitis following abscess of the prostate, pyonephrosis and general sepsis. Prostate enlarged about six volumes. Abscess cavity of prostate measuring 2x3 cm., communicating with posterior urethra through ducts of prostate gland. This case gave a history of long standing but "cured" posterior urethritis. Acini throughout entire gland are infiltrated with pus cells. In this exudate are found frequent large corpora amylacea. The connective tissue stroma is greatly augmented throughout, the increase being in adult fibers. There is inflammatory exudate of the entire glandular substance, even where far distant from the abscess cavity.

CASE 53.—From autopsy. Man aged 60. Cause of death acute on chronic alcoholism. Prostate enlarged about one volume. Peripheral portions show a marked increase in connective tissue. The stroma throughout the entire gland is infiltrated with small accumulations of round cells. In the peripheral portions of the gland the acini are greatly dilated and contain very large corpora amylacea. In the central portion of the gland the amount of connective tissue is more abundant and the glandular acini are smaller and are either empty or contain less detritus. Corpora amylacea are numerous, though small. The blood vessels are moderately thickened. In the areas of greatest connective tissue hyperplasia, that is in the central portions of the gland, muscular atrophy with connective tissue substitution is very pronounced. Blood vessels normal.

CASE 54.—From the autopsy of a man aged 53, dead of alcoholism and pneumonia. History of chronic prostatitis obtained. Marked hypertrophy, particularly of the lateral lobes. General connective tissue hyperplasia. Infiltration of small round cells through entire stroma, especially about the acini, which are generally atrophied and contain large corpora amylacea. Blood vessels moderately thickened.

CASE 55.—Specimen removed at operation by Dr. Geo.

Stewart. Patient aged 57. Has had difficulty in passing urine for past ten years. Entered Bellevue Hospital with retention of four weeks' standing. Urine drawn for three weeks by prostatic catheter. When in good condition, operated on by Dr. Stewart. Bloodless specimen weighed 115 gm. Acini generally dilated and filled by proliferating epithelial cells, cell detritus and numerous small corpora amylacea. Several acini are largely filled by pus cells. Inflammation has apparently traveled from these acini to others in the neighborhood. The connective tissue stroma is hyperplastic and contains many areas of small round-cell infiltration. Interstitial hyperplasia has been so marked about certain acini as to produce marked glandular atrophy. This is more observable about the ducts in the neighborhood of the posterior urethra.

CASE 56.—Removed at operation by Dr. Chas. Phelps. Patient an old man who gave typical history of enlarged prostate of long standing. Mass of tissue removed measured 8x7x5 cm., very nodular. Gross diagnosis of cancer of prostate. Entire tissue greatly infiltrated with serum, stroma very edematous and shows exudate of small round cells, occasional leucocytes and many plasma cells. General hypertrophy of interstitium, particularly in region of posterior urethra where there are many evidences of a chronic inflammatory process of long standing with the result that hyperplasia of connective tissue has constricted the prostatic ducts, producing great distension of glandular acini in peripheral portions of gland. Acini about border of gland largely filled with proliferating epithelial cells, cell detritus and numerous small amyloid bodies. Acini in central portions of gland often occupied by single very large amyloid concretions and surrounded by zone of infiltration. The blood vessels show no abnormality.

CASE 57.—Specimen removed at operation by Dr. Hartley. The specimen is divided histologically into two distinct parts. The largest of these is located in the anterior portion of the tissue and extends from the periphery to the central parts of the gland. It is made up of large hyperplastic fibers of connective tissue in which beginning sclerosis is apparent. Numerous fibroblasts are also present and many of the connective tissue cells show karyokinetic figures. Areas of small round cell infiltration are frequent and include occasional plasma cells intermingled with the round cells. The acinal arrangement is wholly obliterated in these portions by the overgrowth of the connective tissue, but in several places multiplying epithelial cells are found, mostly in rows infiltrating between the connective tissue fibrils and in places forming small islands of actively dividing cells. Apparently the epithelial proliferation is a recent process and it probably is developing into carcinoma of the scirrhus type. The histological picture is found only in certain parts of the posterior portions and near the center of the gland. These show an active connective tissue hyperplasia, but the fibers are more of the embryonic type than those found in the previously described portion. The epithelium in this portion of the gland has more of the normal arrangement and though the cells are dividing they do not have the appearance of cancerous growth. The blood vessels show slight thickening. Corpora amylacea are few, found only in the second portion and are small in size.

CASE 58.—Tumor removed from the lateral lobe of an enlarged prostate of an old man at autopsy. The sections show marked hypertrophy of the interstitium, the increase being in adult tissue only. The acini are small and are much encroached upon by the overgrowth of connective tissue about them. Several acini are partly filled by epithelial cells which are largely broken down. The blood vessels are slightly thickened. Corpora amylacea are of small size and few in number.

A review of this series of 58 cases shows that abundant evidences of inflammation are present in every gland. Naturally, the precise character of the inflammatory lesion differed considerably and often a single gland showed several types. The most common lesion noted was interstitial hyperplasia and this was almost invariably accompanied by resultant atrophy of the muscle cells of the gland. Thus, in 41 of the 58 cases, the prostatic hypertrophy was entirely or largely due to increase

of the fibrous connective tissue. A considerable percentage of these cases showed fibroblasts and newly-formed fibers as well as other evidences of recent proliferation of the connective tissue, as shown in Fig. 3.

Thirty-six cases show areas of inflammatory infiltration, usually consisting principally of patches of small round-cell infiltration, though some showed a more extreme change, characterized by the presence of plasma cells and marked edema, as shown in Case 42 from which Fig. 2 was taken. In 5 cases pus formation was present; in 3 of these infection had clearly taken place from the posterior urethra. It is probable that had all the sections been so cut as to include the posterior urethra we should have found that this were even more frequently the case. Nineteen of the 58 cases showed more or less cystic formation. The true character of these cysts and their mode of formation from inflammatory disease of the prostate will be discussed later in the paper. These 19 cases are such as would ordinarily be classified as cystic adenomata of the prostate; that they are in no way adenomata will be shown later. Of the 6 specimens, in which marked proliferation of the glandular epithelium was present, 3 belong also to the cystic prostates. Only 5 neoplasms of the prostate were found. Of these 2 were carcinomata and 3 fibromata. Case 57 also probably represents an early stage of cancerous growth. Neither fibro-myomata, myomata nor true adenoma were present. Atheroma or endarteritis of moderate to marked degree was present in 17 cases.

To recapitulate briefly: in the 58 cases studied all showed evident inflammatory lesions. In 41 the increase in size was entirely or chiefly due to fibrous proliferation, but in 36 inflammatory infiltration played a leading or contributory rôle and in 19 cystic distension of the alveoli was present in sufficient degree to notably increase the size. Six tumors were present, 3 of which sprang from the interstitium (the fibromata, Cases 19, 37, 39) and 3 from the epithelium (the carcinomata, Cases 45, 50 and 57). No cases of true glandular or muscular hypertrophy were found.

Interstitial hyperplasia is then found to be the most frequent cause of hypertrophy of the prostate. That interstitial increase after adolescence is the result of inflammatory disease is so generally recognized that it is not necessary to discuss this point at this time. Nevertheless, since it is the most frequent factor in the production of prostatic hypertrophy, it must be considered in its relation to this condition at some length.

It is our purpose to discuss later the origin of the process so we shall assume a condition of acute or sub-acute prostatitis as a starting-point. In all organs, acute or sub-acute inflammation gives rise to interstitial hyperplasia; small wonder, then, that the process becomes marked in the prostate, an organ abundantly supplied with blood vessels and highly cellular connective tissue. The interstitial hyperplasia, coupled with more or less edema and cell infiltration, always associated in so highly vascular a tissue, gives rise to the acute prostatic hypertrophy, such as is found in the young. With a cessation of acute inflammation following a removal of its cause and normal reaction on the part of the tissues of the organism, interstitial hyperplasia should cease and retraction and atrophy follow from the sclerosis of the fibers, as the embryonic tissue takes on the adult form. Such a result does follow in favorable cases of prostatitis in the young and healthy, and, as the sclerosis of the newly-formed tissue continues, the atrophic or small hard prostate follows to a greater or less extent, always

provided, however, that this same fibrous sclerosis does not excite secondary changes in the glandular epithelium. But in the middle aged or old man, particularly where more or less general or arterial disease exists, resolution and healing do not so readily follow and instead of cessation of connective tissue hyperplasia the condition becomes chronic. With the increased fibrosis, consequent thickening of the walls of the veins and lymphatics follows and chronic congestion is added to the factors tending to prolong and increase interstitial hyperplasia, edema and inflammatory exudation. So it happens that in the enlarged prostate of the aged, acute and sub-acute proliferations are found mingled with the thickened masses of adult sclerosed connective tissue. As an inevitable result of this overgrowth of stroma, atrophy of the smooth muscle cells follows. This may be of greater or less degree, greater if the inflammation partakes more of the acute type where parenchymatous degenerations are most rapid, less if the process be more chronic.

As a result of this overgrowth alone, when continued for months or years, considerable prostatic hypertrophy may follow, but to this process is added secondary changes, taking place in the glandular tissue, which increases the enlargement of the prostate.

If the fibrosis be most marked in the peripheral portions of the gland it results in encroachment upon and fibrous thickening of the walls of the alveoli which finally become compressed and obliterated—Fig. 4. If the hyperplasia be most marked in the central portions of the gland or about the ducts this results in obstruction or occlusion of the ducts—Fig. 6. After occlusion of the ducts continued secretion on the part of the glandular epithelium causes a distension of the acini and alveoli, producing the familiar cystic adenoma of the prostate—Fig. 7. When now desiccation or condensation of this secretion follows, corpora amylacea form—Fig. 9. Even though the duct be partly pervious the formation of these bodies and the inspissation of the secretion, mingled with desquamated epithelium, renders normal drainage of the alveolus impossible and cysts of considerable size result. If absorption through the walls be marked and the surrounding fibrosis sufficiently active a single amyloid body may later be found surrounded by a thick connective tissue capsule, perhaps still lined by a layer of atrophied squamous epithelial cells—Fig. 11.

Although three small encapsulated fibromata were found in our series of specimens, and though their structure is identical with that of fibromata found elsewhere, we are still loath to classify even these as true neoplasms of idiopathic origin. When the proliferation of stroma is especially active about a group of acini, the actively growing fibroblasts compress these gland sacs more and more until, as shown in Fig. 4, atrophy of the epithelium takes place and fibroblasts grow in, filling up the space, producing a nodule of highly cellular young connective tissue enclosed by a capsule of more dense adult fibers—Fig. 5. Undoubtedly a true fibroma may originate from the prostate gland, but our study of these specimens leads us to the above explanation for the formation of the prostatic fibromata seen by us.

Albarran and Halle have recently called our attention to the frequency with which carcinoma originates in hypertrophic prostates. While we concur with these authors in their general statement, we do not accept as cancer most of the cases which they picture and classify as such; of this more later. Careful study of our three cases of hypertrophied prostates, in which carcinomatous

growth was present, we believe throws some light on this very important subject. In two of our cases cancerous invasion of the walls of the bladder was present, but after careful study of the gross and microscopic specimens we feel justified in concluding that the growth was primary in the prostates. In our cases, the cancer involved but a limited part of the enlarged gland and the usual interstitial and inflammatory infiltrations of the ordinary enlarged prostate were present—Figs. 11 and 12. For these reasons we believe that the cancer had attacked the glands subsequent to their hypertrophy, as is undoubtedly the case with specimen 57. It is universally admitted that the chronic or sub-acute inflammation of glandular stroma tends toward the production of malignant epithelial proliferation. Surgeons and pathologists admit that these conditions predispose toward cancer of the mammary gland and so in the enlarged prostate we have a chronic interstitial proliferation compressing and irritating the alveolar epithelium; with these most favorable conditions we can only express surprise that cancer of the hypertrophied prostate is not more frequent.

In a certain number of enlarged prostates we find an epithelial proliferation of an entirely innocent character. These are those cases in which dilatation of the glandular sac is followed by a proliferation of the epithelium which finally completely fills the gland sac and gives rise to an appearance frequently resembling carcinoma—Fig. 8. It is this condition, in certain of its modifications, which we believe Albarran and Halle have in some cases mistakenly called cancer. Six of the specimens studied by us show this lesion in its most exquisite type. Ordinarily it can easily be distinguished from carcinoma by the fact that the cells resting on the basement membrane are distinctly columnar and that those in the central portions of the cell islands show many degenerative alterations of both nucleus and cytoplasm without karyokinetic nuclear figures, except in the cells resting on the basement membrane. When, however, such acini become greatly compressed by the interstitium about them, they resemble cancer very closely, but this new growth should not be diagnosed unless it be found that the proliferating epithelial cells are invading the tissues about the acini—Fig. 13. We fully agree with Albarran and Halle, nevertheless, in their statement that primary carcinoma of the prostate is much more frequent than generally recognized, and it is highly probable that the hypertrophied organ is more than seldom the site of unrecognized primary carcinoma. Undoubtedly, true adenoma of the prostate may exist. We have, however, not yet seen a case and we contend that the condition ordinarily described as such is not adenoma and that its origin is due to the occlusion of the glandular ducts after the process described above.

Atheroma has been considered by some as an etiological factor in the production of prostatic hypertrophy. Moderate to extreme atheroma was found in seventeen of the cases of this series, but in each instance it was accompanied by other and more pronounced lesions more directly bearing on prostatic hypertrophy. It is now generally admitted that when atheroma is found in the prostate it only represents a local manifestation of a general condition and that it is just as frequent in normal or atrophic prostates taken from men of like age as in the hypertrophied gland.

The question has doubtless occurred to many of our readers, if these inflammatory changes noted by us may not be secondary or accidental in character, caused by the

prostatic hypertrophy and not its cause. We believe that this legitimate question can be answered in the negative. We have endeavored to show in the above examinations that the increase in size of the glands was either immediately or secondarily due to the direct inflammatory exudates or to the reaction on the part of the tissues to these processes, i. e., interstitial hyperplasia.

Granting that our observations in this series of specimens is correct, the origin of the inflammation is yet to be ascertained. In certain of our cases (30, 52, 55, and 56) the sections apparently indicated that the primary inflammatory process had originated about the posterior urethra. Had all our sections been chosen with the determination of this point in view, it is probable that a larger percentage would have shown this condition. But at best, such deductions from the histologic picture are uncertain and more or less speculative. In our opinion clinical evidence is much more trustworthy. It will hardly be questioned that prostatitis most frequently results from, or follows, posterior urethritis, and posterior urethritis is usually primarily or secondarily of gonococcic origin. Asserting as we do, however, that prostatic hypertrophy is the direct result of chronic prostatitis, by the same chain of clinical evidence we are forced to the conclusion that it follows posterior urethritis from whatever cause. For the reasons stated above chronic proliferative prostatitis is more frequent in the aged than in the young.

From our study of prostatic hypertrophy we believe that the usual story of this disease is as follows: Given a posterior urethritis, infection of the ducts and alveoli follows. This is accompanied by inflammatory infiltration about the walls of the infected sac. Following this inflammatory exudate (Fig. 1), which may involve large portions of the gland, fibroblasts and plasma cells appear and acute interstitial hyperplasia becomes inaugurated, as shown in Figs. 2 and 3. The changes which now follow depend largely on what portion of the gland is involved. If the hyperplasia be most marked in the peripheral portions, the acini become compressed and the epithelium atrophies (Fig. 4) and from such acini small fibromata may result—Fig. 5. If the process be more slow and infiltration still active, the condition shown in Fig. 6 may follow. Should the fibrosis be most marked about the ducts or the glands, constriction of these tubes may produce pictures like that shown in Fig. 7, which may be followed by that shown in Fig. 9. Now, if fibrosis be marked about the acini the condition shown in Fig. 11 may happen; on the other hand, acute inflammation with pus formation may take place, as seen in Fig. 10. If proliferation of the alveolar epithelium be excited, pictures like that of Fig. 8 are produced and if this irritation result in malignant cell proliferation true cancer may form (Fig. 12) finally with carcinomatous infiltration of the interstitium—Fig. 13.

This work on prostatic hypertrophy has purposely been founded on histologic findings only, for the reason that in the early days, when the study of prostatic hypertrophy was necessarily purely clinical, or aided only by gross observations or rude microscopic methods, the general impression was that the disease was inflammatory in nature. This fact has already been stated in our introduction. This idea held until, after incomplete sporadic microscopic studies, a theory was formed, founded purely on the histology of the disease, that prostatic hypertrophy was a true tumor formation and

idiopathic in its origin. Nearly all text-books on general pathology now give this view and the greatest of pathologists have favored the theory either by copying what others have written or by confining their personal observations to a few specimens only. Serious histologic studies of the hypertrophic prostate have not been numerous and for this reason, if for no other, we are much indebted to the recent, most careful and thoroughly scientific study of Ciencanowski, who has fully demonstrated by his histologic observations that hypertrophy of the prostate is an inflammatory disease.

This study was taken up by one of us with the idea of disproving the statements of Ciencanowski and satisfying himself of the truth of the idea expressed in nearly all works on pathological anatomy. The result has been a complete conversion to the views of Ciencanowski, whose conclusions we endorse fully, as far as our work has covered his field. We therefore take no credit to ourselves for originality of thought or discovery, leaving all credit to the clinical observers who first advanced the theory and to Ciencanowski who first fully and finally proved its truth.

We may briefly state our conclusions as follows:

1. Prostatic hypertrophy of the aged is the result of chronic prostatitis.
2. It most frequently arises from chronic posterior urethritis, of whatever cause.
3. True neoplasms of the prostate are rare and are not concerned in the production of prostatic hypertrophy.
4. Carcinoma is apt to occur in the hypertrophied prostate as a result of the chronic inflammatory process.

SARCOMA OF THE UTERUS.

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CLINTON, IOWA.

During the present year a lady 65 years of age came under my care presenting the following history and symptoms. The mother of several children, she had enjoyed good health until about two years ago, when she began to be troubled with constipation and pain in the lower part of abdomen and a sense of weight and pressure in the pelvis. These symptoms gradually increased. About six months prior to coming under my observation the symptoms became more acute, when she had, according to her statement, a discharge of fluid from the bowels. This gave her a measure of relief, but soon the same chronic condition she had previously suffered from appeared and continued on with some increase in severity until she came under my care in August of last year. A physical examination revealed the uterus to be uniformly enlarged to two or three times its normal size and appeared to be firmly impacted in the pelvis. There was no discharge from the organ and the symptoms seemed to be largely due to pressure. The general condition of the patient appeared to be good, although she had lost in weight and was somewhat anemic. This could be accounted for, in part at least, on the ground of constipation and impaired digestion.

The age of the patient and the fact of the growth appearing after the menopause suggested malignancy, but the absence of positive symptoms of cancer indicated the possibility of a non-malignant growth. Assuming the probability of an enlarged and myomatous uterus I opened the abdomen. The peritoneum was very much thickened and there was found a considerable quantity of free fluid in the abdominal cavity. The abdominal