

larger ones will at times cause a very severe colic, and since there is no accurate clinical method of determining the size and location of such a stone, every case in which stone is suspected as being the cause of colic should be studied in conjunction with the roentgenologist. If necessary, repeated roentgenograms should be made until one is satisfied as to the size and location of the calculus. Only then is one able to form any opinion as to whether operation should be performed without further delay, or whether the stones, because of their size and position, will probably pass either with or without the assistance of such maneuvers as can be carried out through the operating cystoscope. Case 3 is a case in point.

CASE 3.—J. L., a fireman, aged 31, was admitted (J. S. R.), July 20, 1921, complaining of left renal colic three months before. The history and physical examination were negative.

Cystoscopy revealed a normal bladder and normal right ureter; a catheter passed without obstruction, yielding clear urine. The left ureter was normal; the catheter met obstruction 10 cm. from the meatus and no urine was obtained.

Roentgen-ray examination revealed a stone the size of a pea in the lower end of the ureter.

The treatment consisted of repeated ureteral dilations and oil injections. The stone passed three months later, following a dilation.

Although no fixed rule can be laid down which will cover the entire question as to what is the proper procedure to advise in dealing with the smaller calculi, it is our belief, based on our experience, that unless the calculus is so impacted that it will in all probability be the cause of a hydronephrosis or pyonephrosis in a short time, these cases should be kept under observation for a certain period in order that the stone may be given an opportunity of passing spontaneously. If after six or seven months it is still in the same position, one may be reasonably sure that it will not pass of itself, and then the decision as to the method of removal must be made.

CONCLUSIONS

1. Renal colic is a constant symptom in all but the "silent" calculus cases.
2. Patients seek relief from pain more frequently than from any other symptom associated with calculus.
3. An early and complete urologic and roentgenologic examination should be made in every instance in which stone is suspected.
4. Early operative intervention is indicated as a measure of prevention against destruction of the kidney.
5. Stone in the kidney, if allowed to remain, eventually results in total destruction of the organ.
6. Small calculi should be observed for a reasonable time before operative removal is attempted. Many of them will pass spontaneously or can be assisted by repeated dilation of the ureter.

CARCINOMA OF THE PROSTATE*

ROBERT H. HERBST, M.D.

AND

ALVIN THOMPSON, M.D.

CHICAGO

In this brief report, we wish to discuss some observations and conclusions based on a review of the literature and our personal experience with the prostatic cancer problem.

The literature is crowded with case reports, methods of treatment and statistics of results, but few have considered ways and means by which a larger percentage of these patients may be discovered early enough to give them permanent relief.

The incidence of cancer of the prostate to that of benign hypertrophy varies in reports from 15 to 25 per cent. The differentiation of cancer by our present methods of local examination is at times impossible, so

that it is probably safe to estimate that at least one in four tumors of the prostate is malignant.

Fully one third of these patients give evidence of bone metastases at the time they seek relief, and many who do not show such evidence have extensive local involvement, or metastases which are not demonstrable.

For these reasons, it is evident that a rather small proportion of the patients we treat are seen sufficiently early to give them permanent relief by any known method of treatment.

Unfortunately, the symptoms which might attract attention to the prostate gland do not appear until late in the course of the disease, in many instances after metastases

have developed. Therefore, if we hope to discover these cases early they will have to be found in the course of a general physical examination. The prostate gland has been sadly neglected in the course of physical examinations, unless the patient happens to complain of some urinary disturbance, and unfortunately those suffering from cancer of this gland do not develop these symptoms until late.

The importance of a thorough investigation of the prostate gland in men more than 40 years of age undergoing a general physical examination cannot be overestimated, and this is the only measure by which we may expect to obtain better results by our present methods of treatment. The appeal for early diagnosis is applicable to all forms of cancer, but is more so in cancer of the prostate because symptomatically it is a silent disease until far advanced. We may improve these methods, but the great hope of the future in these

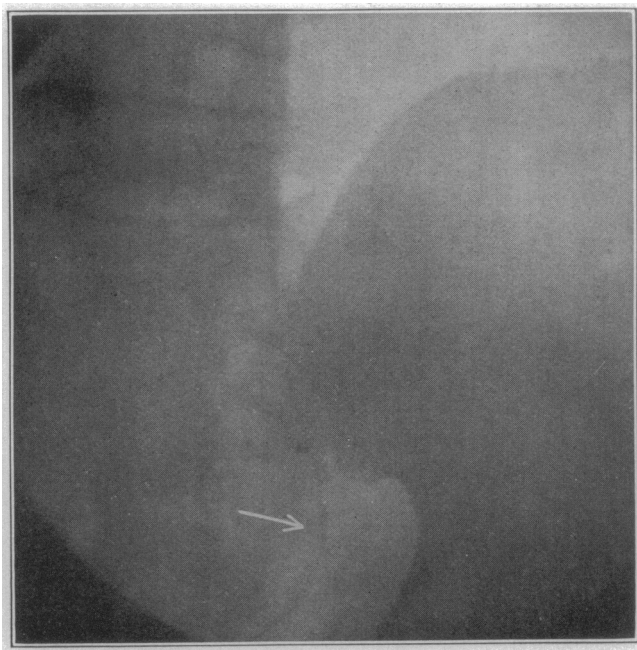


Fig. 5 (Case 3).—Left ureter with an opaque catheter in position, showing relation of the shadow to the ureter.

* Read before the Section on Urology at the Seventy-Third Annual Session of the American Medical Association, St. Louis, May, 1922.

unfortunate cases rests in our ability to teach the general profession to include careful examination of the prostate in their diagnostic routine.

Early malignancy in the prostate gland may be difficult to determine by ordinary palpation in the rectum, especially in the early stage, with one or more small areas of involvement. These can be felt more readily if a sound or a cystoscope is introduced into the urethra.

In reviewing the literature of the last six or seven years, it is evident that most of us, in our early experience, subjected patients to radium therapy who had both glandular and bone metastases. Most of those with bone metastases are now being eliminated, owing to present day methods of roentgenologic study. However, we are still unable to rule out glandular metastases, except in a small percentage, when the pelvic glands are palpable. It is quite evident that a fairly large proportion of patients treated with radium have glandular involvement, or at least the lymphatic channels which drain the prostate contain cancer cells, and this explains why we frequently fail to check the progress of the disease.

SIGNS AND SYMPTOMS

The urinary symptoms so characteristic of benign hypertrophy do not appear until late, unless the malignancy is associated with benign hypertrophy in the superior segment of the gland. Blood is not commonly found in the urine until late except in the adenocarcinoma type, because most of these growths develop behind the urinary tract rather than in it. Pain along the sciatic nerve is the one symptom associated with early malignancy that should attract our attention to the prostate in men of prostatic age. Pubic and sacral pain and pain in the back are usually significant of extensive local involvement, but may be caused in some cases by glandular or bone metastases.

In addition to the characteristic rectal findings of a stony hard "frozen" gland in which one can usually feel some irregular nodules, we wish to emphasize the significance of the increased resistance which is often found in the inters vesicular space, just above the prostate gland.

This infiltration produces an elevation of the trigon which is termed the "subtrigonal" plateau, when seen on cystoscopic examination. It can be felt more distinctly if a cystoscope is introduced into the bladder and the beak turned downward toward the trigon. Obliteration of the interlobular sulcus is also a characteristic rectal finding in malignancy.

The rich lymphatic drainage of the prostate gland explains the frequency and often early development of metastases and our failure to arrest the progress of the disease. Even though the gland is not extensively involved and metastases are not demonstrable, the lymphatic channels may be loaded with cancer cells.

The degree of local involvement does not necessarily bear any relationship to the possibility of metastases. For this reason, a careful necropsy examination of the prostate gland should be made in persons dying from otherwise unexplained secondary carcinoma. In spite of our present day methods of roentgenologic and neurologic study, we fail to recognize the presence of metastases in some cases, especially those which occur in the pelvic and prevertebral lymph nodes. These patients usually complain of severe abdominal pain and pain in the back, which is probably due to pressure on nerve roots by the enlarged lymph nodes. We have found that many of these are not controlled by radium, and they progress rapidly and show glandular metastases at necropsy.

Although in these cases the lungs are rarely involved, one of our patients presented extensive metastases of the lung developing from a rather small prostatic tumor, without evidence of the existence of any other metastases.

PATHOLOGY

From the standpoint of therapy, a classification of cancer of the prostate into three pathologic types seems rational.

1. A scirrhus type, which usually begins in the posterior lobe in the form of small flat or nodular areas. These are harder than the normal gland tissue, but are at times difficult to diagnose by rectal palpation. This type may invade the entire posterior lobe and spread upward along Denonvillier's fascia between the seminal vesicles, sometimes involving them. Metastases are common and frequently develop early in the course of the disease.

Here we have a process developing and spreading behind the urinary tract rather than into it, so that these patients do not have any urinary symptoms until

late, and not infrequently the symptoms caused by metastases are the first to appear.

The inters vesicular area and the region of the seminal vesicles should attract our most earnest attention, if we hope to control the spread of the tumor. It is difficult to determine when this invasion occurs, but it is safe to state that at least the lymphatic channels which pass through this region carry cancer cells before any infiltration can be determined by palpation in the rectum.

2. Type 2 is a combination of Type 1, associated with a benign hypertrophy of the superior portion of the prostate. This is a rather common form of tumor and at times difficult to differentiate from simple hypertrophy, the malignant area often being discovered at the time of operation. When attempting to enucleate the adenoma, it is found adherent to the posterior lobe, or, on bimanual palpation after removal, the malignant areas are felt. In this type, urinary symptoms develop early, owing to the change in contour of the neck of the bladder and obstruction produced by the adenoma-

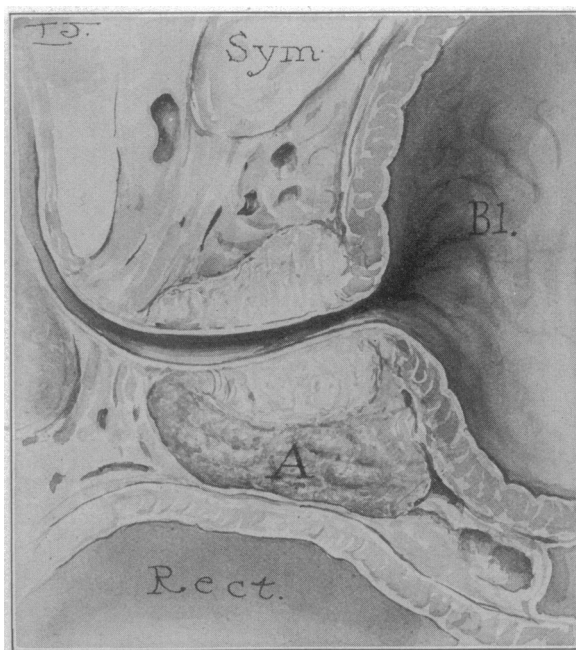


Fig. 1.—Malignant lower posterior segment of prostate (A), with benign hypertrophy in the superior part of the gland.

tous part of the tumor. In our experience, this type has been easier to control than Type 1 because, owing to the symptoms, the patients present themselves earlier for treatment.

A variation of this type is found in some of these tumors when the adenomatous portion is invaded by the cancer from the posterior lobe. These tumors were described by some of the earlier writers as adenomas of the prostate which had undergone malignant degeneration.

3. Type 3 is a less common form of tumor, in which the entire gland is the seat of an adenocarcinoma. These tumors are as a rule smooth and symmetrical but are harder than the adenoma. Enucleation, when attempted, is found difficult or impossible owing to the absence of a line of cleavage. Symptoms of obstruction occur early, owing to invasion of the prostatic urethra and bladder, but metastases do not occur as frequently as in Type 1 and Type 2. When patients suffer from this type, the condition is easier to control, because they are disturbed by urinary symptoms and seek relief before metastases have developed.

Many variations of the foregoing classification could be described, but a simple division of this kind is helpful in applying various methods of radium therapy used in the control of prostatic cancer.

Type 1 and Type 2 must be looked on as the most malignant forms of the disease, owing to the probability of early metastases; nevertheless, direct extension of cancer into the bladder and surrounding bony structure is not an unusual finding in Type 3.

We have obtained better results in Type 2 and Type 3 because the early development of urinary symptoms leads the patients to present themselves before metastases have developed. Also, in Type 2, the enucleation of the adenomatous part of the tumor gives opportunity to implant and apply radium more accurately to the malignant posterior lobe.

TREATMENT

More than six years ago, we began treating carcinoma of the prostate by embedding needles containing radium in the involved areas of the gland, through the opened bladder. Our reason for applying treatment through the opened bladder was twofold: (1) it gave easy access to the tumor and especially the subtrigonal area, and (2) it gave relief from urinary retention.

Later, following the reports of Barringer and others, we treated some of these patients by introducing needles

through the closed perineum, but we found that it was most difficult and often impossible to carry the needles well up into the subtrigonal tissues and the region of the seminal vesicles.

In many instances, the extent of the infiltration above the prostate cannot be accurately determined by rectal examination; but, with a good suprapubic exposure, one is able to outline accurately the extent of the subtrigonal infiltration. Knowing that most of these cancers spread in this direction and get beyond control, we feel that it is most important to irradiate these areas first. Cancer cells are undoubtedly present in these tissues before any thickening can be made out, and it is our practice to irradiate this area even though nothing is felt, applying the same principle that we do when we attempt to cut through healthy tissue in the

excision of malignant tumors; in other words, we go a little beyond the limits of the growth with the hope of preventing its progress.

In our efforts to control cancer, we frequently lose sight of the fact that many of these patients suffer from retention of urine, the obstruction being caused by the malignant tumor or an associated hypertrophy of the middle lobe. Under these circumstances, radium will neither relieve the retention nor improve the function in time to protect the upper urinary tract. Repeated catheterization, if not impossible, is usually painful and not well tolerated. Therefore, a suprapubic cystotomy, in addition to giving an excellent opportunity for the introduction of radium, protects the upper urinary tract and does much to make the patient comfortable during the weeks or months that treatment is carried on.

A part of the failure to secure good functional results following irradiation of the malignant prostate can be attributed to the fact that, in a large percentage of cases, the carcinoma is associated with benign hypertrophy, the radium having little or no effect on the adenomatous lobes. This usually occurs in the middle lobe, and the hypertrophied tissue must be enucleated if we may hope to relieve the obstruction. Again, many of these patients cannot be examined cystoscopically and the middle lobe will not be found until the bladder is opened; all sound arguments in favor of suprapubic cystotomy.

Some of our best results have been obtained in those cases in which we have been able to enucleate an adenomatous middle lobe; following which, a tube of radium is fitted into the cavity and several needles containing radium are inserted into the malignant part of the remaining shell. This may be repeated if the

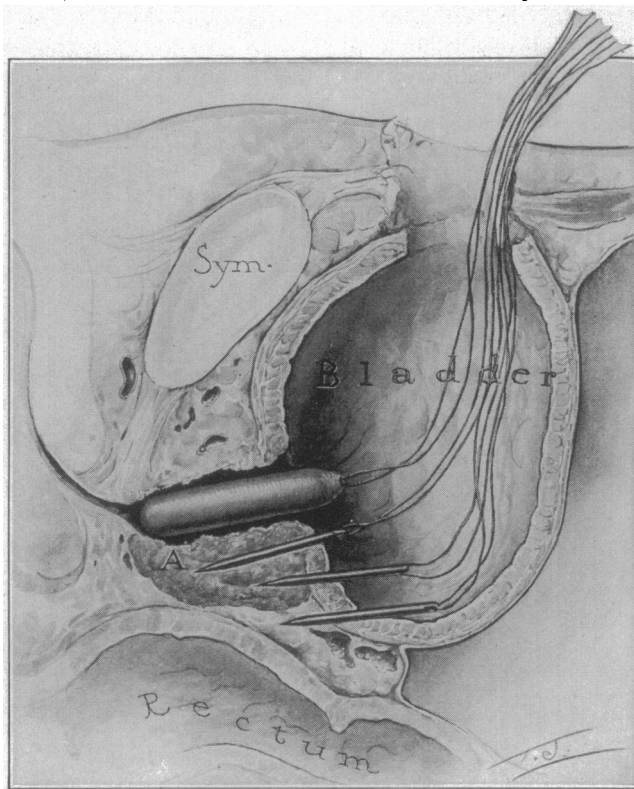


Fig. 2.—Tube of radium fitted into cavity left after enucleation of benign part of tumor; also radium needles embedded in malignant area (A). Two lower needles are passed through the posterior wall of the bladder, irradiating the subtrigonal area and the region of the seminal vesicles.

bladder is kept open; or subsequent applications are made by passing a staff carrying a tube into the urethra or by introducing long needles through the perineum, or both.

In the treatment of these cancer patients, we must not forget that many of them are suffering from the effects of retention and that we have the same problems of elimination that we have in the man with benign hypertrophy. Severe toxemia may be mistaken for cachexia, and it is surprising how some of these patients improve following preliminary treatment such as flushing with large quantities of water, relief of retention and attention to the bowels. It is just about as irrational to apply radium therapy in the case of the severely toxic patient without preliminary drainage as it is to attempt the enucleation of the benign prostate under the same circumstances. Patients with demonstrable metastases may get two or three fairly comfortable years from a suprapubic permanent drain. Even patients who carry a small amount of residual urine will be relieved of pain and show a temporary improvement in general health following the institution of such drainage.

A fibrosis, with narrowing of the neck of the bladder, has interfered with urinary function in some cases. In this condition, dilation has been extremely difficult, and in one of our patients in whom the cancer appears to be controlled we have been compelled to continue suprapubic drainage, although we have dilated the neck of the bladder for a year and a half. In another case, we excised a wedge-shaped piece of tissue from the internal urethral orifice without much improvement in function.

Most observers agree on the value of the roentgen ray in conjunction with radium therapy. The relative value of each is difficult to determine, but here, as in most fields, treatment must be carried out by one of large experience in order to obtain results.

After giving perineal insertions a fair trial, we have again returned to our original method of suprapubic exposure and embedding of needles, utilizing the perineal method and the intra-urethral applications as supplementary forms of treatment.

(Abstract of Discussion will be found on page 1688, this issue.)

Syphilis Statistics in Japan.—Dr. Hata has collected data on the reproductive power of women married for three years or more who show a positive Wassermann reaction. He gives the following percentages: Not impregnated, about 40 per cent; impregnated, about 60 per cent. Among the children of these syphilitic mothers, there were 28 per cent. premature and only 30 per cent. survived more than two years, only a third of whom will live a natural healthy life. Maternal syphilis is one of the most serious factors in the problem of repopulation.

THE ANILIN DYES IN THERAPEUTICS*

JOHN W. CHURCHMAN, M.D.

NEW YORK

Of the various features of the anilin dyes which make them an attractive subject for experimental investigation, I will consider the three with which my own studies of gentian violet (and more recently of acid fuchsin) have been chiefly concerned.

THE SELECTIVE POWER OF THE ANILIN DYES

One of the most striking examples of selective bacteriostatic power is furnished by gentian violet. The behavior of bacteria toward this dye follows pretty closely the Gram reaction, and this feature is characteristic also of other triphenylmethane dyes, among them magenta.¹ These facts are now well known; but I have recently been able to show that the behavior of bacteria toward acid fuchsin (a sulphonated triphenylmethane) is, in certain respects, the exact reverse of their behavior toward the basic dyes. If bacteria are exposed to acid fuchsin and planted on plain agar, it is found that it is now the gram-positive spore-bearing aerobes which survive, and the commoner gram-negative bacteria which die. A plate streaked, for example, with *Bacillus paratyphosus* and *Bacillus pseudo-anthraxis* which have been exposed to acid fuchsin will show vigorous growth of the latter, and none whatever of the former; while if the experiment is done with gentian violet or magenta there will be vigorous growth of *B. paratyphosus* and none whatever of *B. pseudo-anthraxis* (Fig. 1). I have previously shown that it is quite a simple matter to rid a culture of gram-negatives of contaminating

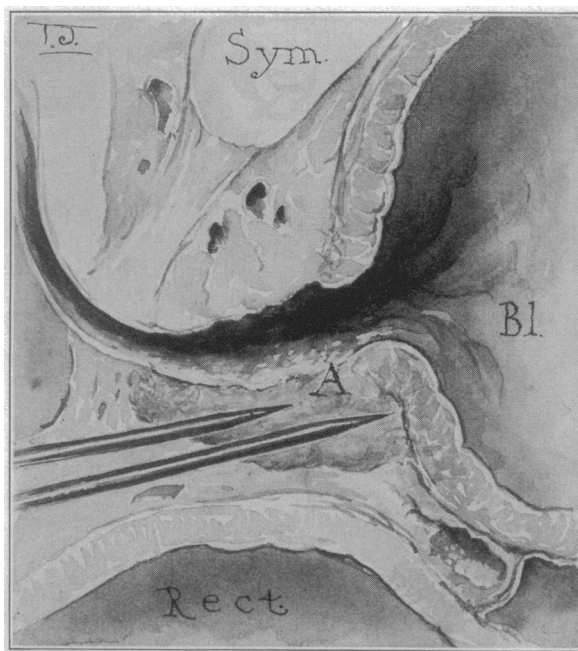


Fig. 3.—Long needles embedded in malignant posterior segment (A) of prostate. These have been passed through the perineum.

gram-positives by exposing the mixture of the two organisms to gentian violet, previous to plating; and it is equally easy to rid gram-positive spore bearers of contaminating gram-negatives by exposing the mixture to acid fuchsin. One can thus quite easily from a mixture, let us say, of *Bacillus pyocyaneus* and *Bacillus megatherium*, pick out at will either organism in pure culture by the use of these two dyes (Fig. 2).

It proves, moreover, to be the case (experiments with sulphanilic acid, chromotropic acid and ethylsulphonic acid furnished the proof) that it is the sulphonic acid group in the acid fuchsin which accounts for this reverse selective power. We have succeeded, therefore, for the first time in determining which part of a dye molecule is responsible for its

* From the Department of Hygiene, Cornell University Medical College.

* Read before the Section on Pharmacology and Therapeutics at the Seventy-Third Annual Session of the American Medical Association, St. Louis, May, 1922.

1. Churchman, J. W.: J. Exper. Med. **16**: 221 (Aug.) 1912; **17**: 373 (April) 1913.