

administered to only 1 recipient, then an infective donor can cause, at most, 1 case of homologous serum jaundice. The elimination of pooling would necessitate radical changes in the operation of blood banks, one of which would be the requirement that plasma should be typed and cross matched, or treated with group-specific substances.¹⁶ The allocation of a particular pool to a particular patient until there is no chance of his needing more plasma would cut down on the multiple chances for infection resulting from the present random system of distribution.

2. Methods of Future Control: Possible methods of prevention of homologous serum jaundice in the future may be sought along two lines: treatment of the blood or blood product or treatment of the recipient.

The infective principle is extremely rugged. It resists storage in the frozen and dried state, filtration, a temperature of 56 C. for one hour, exposure for months in mediums containing 0.5 per cent each of phenol and ether or 0.2 per cent tricresol and ether extraction.¹⁷ Oliphant and Hollaender have found that the exposure of icterogenic serum in a specially constructed apparatus to ultraviolet light of 2,537 Å may reduce the icterogenic capacity of the serum decidedly.¹⁸ The products of plasma fractionation¹⁹ do not seem to transmit the icterogenic agent.²⁰ Since these fractions are specific and superior agents for many purposes for which human plasma and serum are employed, their use instead of the latter might be the most effective preventive. Moreover, the use of whole blood should be encouraged for the treatment of traumatic shock, since it is not only probably safer than plasma from the point of view of homologous serum jaundice but also a more physiologic and effective replacement fluid.

Attempts have been made to reduce the incidence of homologous serum jaundice by the intramuscular administration of the gamma globulin fraction of human plasma²¹ to the recipients of blood or plasma. The evidence gathered to date²² does not show conclusively that such treatment is as effective as in infectious hepatitis, but further studies are needed.

CONCLUSIONS

1. Homologous serum jaundice is a disease which must be seriously considered in the operation of a hospital blood bank and in the use of pooled human plasma from any source. In the Peter Bent Brigham and Children's hospitals, over a one year period a minimum estimate is that approximately one in every two hundred plasma or blood transfusions was followed by the disease. If, as is more likely, almost all the infections were the result of the transfusion of pooled plasma, preserved in the frozen state, the minimum incidence was one in every eighty-six plasma transfusions. The criteria for selecting our cases have been presented. Four of these cases were fatal, representing

an unexpected late sequel of an original illness from which the patient had apparently recovered.

2. Two methods of control may be immediately instituted in the operation of a blood bank: (1) better detection of possible infective donors by history and physical and laboratory examination, and (2) elimination of the practice of pooling plasma or reduction of the size of pools to a minimum, with limitation of the number of recipients of plasma from each pool as far as possible.

3. Methods of control which may be of value in the future are: (1) the ultraviolet irradiation of plasma or serum; (2) the use of whole blood and the products of plasma fractionation rather than plasma, and (3) the administration of gamma globulin to recipients of plasma or blood.

SUMMARY

1. Eleven cases of hepatitis which was probably due to the prior infusion of human plasma or blood were observed in the course of a year in which 2,443 transfusions of blood and plasma were given.

2. Methods for control of this disease in civilian hospitals include better detection of infectious donors, reduction in the size of plasma pools and elimination of the practice of administering a particular pool to multiple recipients. The use of whole blood and plasma fractionation products in preference to pooled plasma should be encouraged.

ENDOCRINE THERAPY IN CARCINOMA OF THE PROSTATE

Preparation of Patients for Radical Perineal Prostatectomy

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As soon as the efficacy of the endocrine management of carcinoma of the prostate, whether by orchiectomy, the administration of estrogens or a combination of the two had been established by numerous observers, chiefly through the fundamental investigations of Herbst¹ and of Huggins,² carefully compiled studies soon became available concerning the extent of regression of the primary neoplasm and its metastases following the various types of therapy. From extensive reviews of statistics to date, as well as from experience gained in treating 200 patients with prostatic cancer at the Brady Urological Institute by the administration of diethylstilbestrol, we have come to expect objective regression of the primary growth in approximately 75 per cent of the cases and of its metastases in approximately 45 per cent.

In our clinic we have found it advantageous to classify cases of prostatic carcinoma into four main groups:

I. Early, in which the malignant process is confined to the gland itself and is therefore admirably suited for radical extirpation.

II. Moderately advanced, in which the growth has spread into the bases of the seminal vesicles, into the apex of the gland, or both.

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22. Stokes, J., Jr., and Neefe, J. R.: The Prevention and Attenuation of Infectious Hepatitis by Gamma Globulin, *J. A. M. A.* **127**: 144-146 (Jan. 20) 1945. Gressman, Stewart and Stokes.¹⁶

III. Advanced, in which, on initial examination, there exists obvious extension throughout the region of the seminal vesicles, inferolateral ligaments and membranous urethra and with fixation of the outer layers of the rectum.

IV. Metastatic: metastases may occur in all three of the aforementioned groups but are, of course, most commonly seen in group III.

During the past three years we have encountered a number of cases in group II which have responded so satisfactorily to diethylstilbestrol therapy that radical surgery subsequently has been undertaken in order to afford these patients the chance of a complete cure. It is with the management of these cases, which may properly be classified as moderately advanced, that this paper is primarily concerned.

THE ACTION OF DIETHYLSTILBESTROL

The mode of action of the endocrines in prostatic cancer is not yet completely understood, nor has the question of diethylstilbestrol therapy versus castration been settled. It is apparent, however, that the actively growing malignant cells require androgen for their viability, and when it is denied them, as after orchiectomy or when it is neutralized, as seems to occur after the administration of diethylstilbestrol, these cells undergo certain changes which can be demonstrated histologically and chemically. As Huggins³ has stated, "androgen control seriously disturbs the enzyme mosaic of the cancer cells, at least with respect to the important energy-producing protein-catalysts, the phosphatases. As a contribution to the general problem of cancer treatment, it is well to emphasize that any interference with an important enzyme system of a cell, normal or malignant, will cause in that cell a decrease of size and function."

The cytologic changes in the cancer cells following diethylstilbestrol therapy have been intensively studied by Kahle and others.⁴ These observers were able to demonstrate definite regressive changes in the nuclear and cytoplasmic material. These changes consist at first of pyknosis of the nuclei and vacuolization of the cytoplasm. Later there occur progressive fragmentation and disappearance of nuclear material, rupture of cell membranes, loss of cellular outline and finally replacement by fibrous stroma, smooth muscle and round cells.

The fact that recrudescence usually occurs after varying lengths of time has been adduced by most observers as evidence that the cancer cells are not actually destroyed but simply remain dormant until becoming reactivated.⁵ However, it is common clinically to note that, despite extensive and progressing metastatic manifestations elsewhere during the administration of diethylstilbestrol, the prostate itself remains soft, even atrophic, and in many instances the diagnosis of carcinoma cannot be made by subsequent rectal palpation. Moreover, from a histologic standpoint, as shown by Kahle and others, it would seem that actual cell death had occurred following diethylstilbestrol therapy.⁴

Clinically, after the administration of estrogens one notes in about 75 per cent of the cases a generalized softening of the primary neoplasm associated with a shrinkage in size. These changes are variable, and this variability may be related to the histologic pattern of the tumor, as has been suggested by some, or to the total dosage of estrogen employed. In those patients in whom the carcinoma by rectal palpation is classified as moderately advanced (group II), we have gained the impression from serial examinations during diethylstilbestrol treatment that the earliest signs of regression appear in the periphery of the growth. This has led to the supposition that possibly the marginal cells are more actively growing and therefore show the effects of androgen deprivation more acutely than do those located nearer the center.

Whatever the explanation, the clinical observation has been that, under the influence of diethylstilbestrol, the cancerous process first seems to recede out of the bases of the seminal vesicles and apex of the prostate. This observation has been responsible for our feeling that patients with what has hitherto been considered inoperable prostatic cancer can be given the possible opportunity of cure by radical surgical excision following adequate estrogenic preparation.

THE RADICAL OPERATION

From the insidious nature of the growth of carcinoma of the prostate, it is obvious that early diagnosis is extremely difficult and, in the majority of cases, when the diagnosis is first made the primary neoplasm has extended beyond the capsule into the contiguous structures. The actual percentage of cases deemed suitable for radical surgical removal varies in different clinics. Prince and Vest⁶ performed the operation on 9 per cent of patients with prostatic cancer examined at the University of Virginia in a period of two years. In an earlier study⁷ it was found that 22.7 per cent of all patients admitted to the Brady Urological Institute between 1937 and 1942 with a diagnosis of carcinoma of the prostate were subjected to radical surgery. The latter percentage is higher than ordinarily would be expected because numerous patients in whom a diagnosis of early carcinoma had been made elsewhere were referred to this clinic in the hope that they could be cured by the radical operation. However small the actual figure, it must be borne in mind that those patients who fulfil the conditions for radical extirpation must not be denied the chance of cure by this method.

It is well to review the clinical criteria for radical surgery in carcinoma of the prostate:

1. On rectal palpation the growth must not extend beyond the capsule into the bases of the seminal vesicles or the region of the membranous urethra. The gland must be freely movable, since fixation indicates spread into the periprostatic tissues.

2. No demonstrable metastases must be present. Acid phosphatase estimates are helpful in many cases but often may remain at normal levels in the presence of extensive metastatic lesions.

3. The patient must be a good surgical risk, and his life expectancy should be reasonable. It is doubtful whether patients in the eighth or ninth decades should

3. Huggins, C.: Treatment of Cancer of the Prostate, *Canad. M. A. J.* **50**: 301-307 (April) 1944

4. Schenken, J. R.; Burns, E. L., and Kahle, P. J.: The Effect of Diethylstilbestrol and Diethylstilbestrol Dipropionate on Carcinoma of the Prostate Gland: II. Cytologic Changes Following Treatment, *J. Urol.* **48**: 99-112 (July) 1942. Kahle, P. J.; Schenken, J. R., and Burns, E. L.: Clinical and Pathological Effects of Diethylstilbestrol and Diethylstilbestrol Propionate on Carcinoma of the Prostate Gland, *ibid.* **50**: 711-732 (Dec.) 1943.

5. Barringer, B. S.: Prostatic Carcinoma, *J. Urol.* **47**: 306-310 (March) 1942.

6. Prince, C. L., and Vest, S. A.: Carcinoma of the Prostate, *South. M. J.* **36**: 680-685 (Oct.) 1943.

7. Colston, J. A. C.: Carcinoma of Prostate: Study of Percentage of Cases Suitable for Radical Operation, *J. A. M. A.* **122**: 781-784 (July 17) 1943.

be submitted to the operation, especially in view of the essentially slow growing characteristics of the tumor in these older persons.

RESULTS

The postoperative results of the radical operation at the Brady Urological Institute have been reviewed in detail in earlier publications.⁸ It has been pointed out that the operative mortality ranges between 5 and 6 per cent, a figure which compares very favorably with the results of surgery performed for the cure of cancer elsewhere in the body. In the last series of cases reported there occurred 4 hospital deaths in a total of 73 radical prostatectomies done from 1937 to 1942, a mortality percentage of 5.5. Since 1942 there has been only 1 death directly attributable to operation. There are several reasons for the progressive reduction in mortality since 1904, when Young performed the first radical perineal prostatectomy for cancer. These include better methods of hemostasis, including the liberal use of blood transfusions, as well as chemotherapy and the antibiotics. The use of spinal anesthesia has provided better relaxation of the perineal musculature, thus materially improving the technic and shortening the duration of the operation.

THE PREOPERATIVE ADMINISTRATION OF DIETHYLSTILBESTROL

The preparation of patients for radical perineal prostatectomy by the use of diethylstilbestrol has been recommended before,⁹ and Vallett¹⁰ has reported a case in which the radical operation was successfully performed after castration.¹⁰ Hitherto, however, no reports have appeared in the literature where a series of cases so managed has been carefully followed and studied from that standpoint. At the Brady Urological Institute 200 cases of cancer of the prostate have been treated with diethylstilbestrol, in all of which the primary neoplasm was considered too extensive on first examination to justify radical extirpation. The 7 cases reported here were classified as moderately advanced on rectal examination. All were then maintained on diethylstilbestrol therapy for varying periods, during which time serial rectal examinations were performed. The response of each of these patients to the administration of estrogen was so gratifying that it was deemed worth while to perform the radical operation in order to attempt a complete eradication of the disease. In several other patients similar regression occurred, but their general physical condition and life expectancy contraindicated extensive radical procedures.

In the 7 patients submitted to radical prostatectomy, the preoperative dosage of diethylstilbestrol was 1 to 2 mg. per day. No essential difference in the rapidity or degree of regression of the primary neoplasm has been noted with larger doses. The use of diethylstilbestrol in the dosage recommended has not been attended by untoward symptoms, save for slight swelling and tenderness of the nipples, and, as the growth has receded very satisfactorily on this dosage, larger amounts have not been employed.

8. Young, H. H.: The Cure of Cancer of the Prostate by Radical Perineal Prostatectomy, *J. Urol.* **53**: 188-252 (Jan.) 1945. Colston, J. A. C.: Surgical Removal of Cancer of the Prostate Gland: Radical Operation, *J. A. M. A.* **127**: 69-72 (Jan. 13) 1945.

9. Colston, J. A. C., in discussion on papers by Huggins and McDonald, Rathbun and Nesbit and others, *Tr. Am. A. Genito-Urin. Surg.* **37**: 235-236, 1944. Parlow, A. L.: Advanced Cancer of Prostate: Consideration of Value of Radical Prostatectomy in Selected Cases, *New York State J. Med.* **45**: 383-386 (Feb. 15) 1945.

10. Vallett, B. S.: Radical Perineal Prostatectomy Subsequent to Bilateral Orchiectomy, *Delaware M. J.* **16**: 19-20 (Feb.) 1944.

REPORT OF CASES

CASE 1.—J. E. A., a white man aged 68, first examined Nov. 9, 1943, presented increased urinary difficulty, moderate frequency and nocturia one to four times of one year's duration. He gave no history of back or perineal pain or apparent weight loss. He had been examined elsewhere six weeks previously, at which time a small, hard, oval nodule had been discovered in the right lobe of the prostate. He had therefore been referred here for possible radical perineal prostatectomy.

Physical examination revealed that the patient was in good condition. The penis showed moderately advanced induration of the corpora cavernosa (Peyronie's disease). The scrotal contents were normal. On rectal examination the prostate was slightly broader than normal. Both lateral lobes were irregular and contained areas of stony hard induration, more pronounced on the right. There was evidence of extension to the apex of the prostate and region of the membranous urethra. Both seminal vesicles were palpable but not indurated. There was no x-ray evidence of bony metastases. The acid phosphatase was normal.

Because of the extension of the disease toward the apex, the condition was considered unfavorable for radical cure at that time. Therefore the patient was begun on diethylstilbestrol 1 mg. per day and maintained on this regimen for almost seven months. During this time serial rectal examinations showed progressive shrinkage and softening of the neoplasm.

On May 27, 1944 the patient was readmitted and prepared for operation. Laboratory studies showed hemoglobin 96, white blood cells 6,100, phenolsulfonphthalein excretion 65 per cent in two hours. The urine was normal except for an occasional white blood cell; culture was sterile.

May 29 a radical perineal prostatectomy was carried out, followed by an uneventful convalescence.

Pathologic studies showed adenocarcinoma of the prostate and involvement of the bases of both seminal vesicles.

The patient was discharged from the hospital on the twenty-ninth postoperative day, voiding a good stream with perfect control. On the last visit, one year after operation, the patient was found to be in good general condition with no evidence of local recurrence or distant metastases. He was passing a stream of good caliber and force.

CASE 2.—K. H. B., a white man aged 59, first seen Feb. 3, 1944, came here after a diagnosis of carcinoma of the prostate had been made elsewhere and orchiectomy advised. There was no history of urinary symptoms, weight loss or pain. Previous x-ray studies had been negative for metastases, and acid phosphatase was normal.

On examination the patient was found to be in good condition. The external genitalia were negative. The prostate was slightly broader than normal, fixed, irregular and stony hard throughout. There was evident extension into the apex as well as into the bases of both seminal vesicles.

Radical extirpation was thought to be contraindicated at that time, and the patient was placed on diethylstilbestrol 2 mg. per day. This was maintained for approximately two months. During this time serial rectal examinations demonstrated such satisfactory regression of the carcinomatous process that it was thought advisable to carry out radical perineal prostatectomy. Laboratory studies showed hemoglobin 13.3 Gm., white blood cells 5,600, blood urea 20 mg., phenolsulfonphthalein excretion 75 per cent in two hours. The urine was normal; culture was negative.

April 12, 1944 radical perineal prostatectomy was done. Convalescence was uneventful except for one febrile rise after passage of a sound. The patient was discharged twenty-three days after operation, voiding well and with good control.

Pathologic sections showed extensive adenocarcinoma of the prostate with involvement of the bases of both seminal vesicles.

Four days after leaving the hospital the patient had acute urinary retention and was treated elsewhere for a stricture at the site of anastomosis. A suprapubic cystostomy was done and a urethral catheter left in place. The tube was removed five days later, and the patient was able to void satisfactorily. At the present time the voided stream is free and urinary control

satisfactory. The patient has now resumed full activity. He frequently plays eighteen holes of golf a day and experiences no urinary leakage whatever. However, at the end of an especially strenuous day, the patient occasionally notices slight dribbling.

CASE 3.—Dr. W. N. F., a white man aged 61, a physician, was first examined at the Brady Urological Institute Feb. 11, 1944. In the course of a general physical examination elsewhere the prostate was observed to be hard and irregular. The patient was followed periodically for several months. A bilateral orchietomy was advised and, on the suggestion of a colleague, he came to the Brady Urological Institute. No nocturia was noticed at any time, and only slight hesitancy. There was no history of pain or weight loss. The patient had a long history of alcohol addiction.

On physical examination the patient was in good general condition. The external genitalia were normal. There was a small, reducible hernia present at the right external ring. Rectal palpation showed the prostate to be moderately broader than normal. It was irregular, indurated and stony hard throughout. The right lobe was especially prominent. The induration had extended into the apex of the prostate and up into the bases of both seminal vesicles. There was no x-ray evidence of metastases. Acid phosphatase studies were normal.

Although the growth had not spread beyond the confines of the capsule, it was thought to be too extensive at that time to insure a complete cure by radical operation. For this reason diethylstilbestrol 2 mg. a day was advised. Rectal examination six weeks later revealed definite regression of the neoplasm both in size and in degree of induration.

The patient was readmitted March 28 and prepared for radical operation. Laboratory studies revealed hemoglobin 12 Gm., white blood cells 5,200, blood urea 20 mg. per hundred cubic centimeters, phenolsulfonphthalein excretion 82 per cent in two hours. The urine was normal; cultures were sterile.

On April 1 a radical perineal prostatectomy was carried out followed by a completely uneventful convalescence except for slight leakage after removal of the urethral catheter on the fourteenth postoperative day. The patient left the hospital nineteen days after operation, voiding well and with good control.

Pathologic studies showed extensive adenocarcinoma of the prostate involving the bases of both seminal vesicles.

Two months later symptoms of urinary difficulty developed, and he required several efforts to empty his bladder. Urinary control, however, was excellent.

He was reexamined July 11. No evidence of local recurrence or distant metastasis was found. However, a stricture had developed at the site of the anastomosis. The residual urine was 30 cc. The patient therefore was readmitted to the hospital and the stricture dilated under spinal anesthesia. He was discharged after several days, voiding an excellent stream and with normal control.

CASE 4.—C. E. H., a white man aged 60, first examined at the Brady Urological Institute on March 24, 1944, was referred by his physician, who had followed him for about one year because of increased urinary difficulty and hesitancy as well as an enlarged, rather hard prostate. There had been no history of back or perineal pain and no weight loss.

On physical examination the patient seemed to be in good general condition. The external genitalia were normal. On rectal examination the prostate was moderately broader than normal and especially prominent on the right side. The right lobe was of stony hard induration, especially toward its outer edge and well down toward the apex. The left lobe was firm but not of third degree. The seminal vesicles were thickened but not involved. The growth had apparently extended beyond the capsule on the right side, and particularly into the membranous urethra. Residual urine was 85 cc. There was no x-ray evidence of metastases.

Radical operation was thought to be unjustified because of the extent of the malignant process. The patient therefore was started on diethylstilbestrol 1 mg. per day. He was seen again one month later, at which time he was voiding with considerably less difficulty. Definite regression of the neo-

plasm had occurred. Diethylstilbestrol was continued another month, and at the end of that time on rectal examination it was difficult to detect any areas of stony hardness or make a gross diagnosis of carcinoma.

The patient was readmitted May 23, 1944 and prepared for radical perineal prostatectomy. Laboratory studies disclosed hemoglobin 100, white blood cells 8,500, blood urea 28 mg. per hundred cubic centimeters, phenolsulfonphthalein excretion 85 per cent in two hours. The urine contained a trace of albumin and 4 to 5 white blood cells. May 24 radical perineal prostatectomy was carried out and followed by an uneventful convalescence. The urethral catheter was removed on the fourteenth postoperative day. The patient voided an excellent stream and remained dry perineally. Pathologic studies showed carcinoma of the prostate not involving the seminal vesicles. It was predominantly adenocarcinoma in type, with a multiplicity of form and showing diethylstilbestrol changes. The patient was discharged nineteen days after operation, voiding well and with good control.

After returning home he did well for about fourteen months. At that time he noticed some diminution in the size and force

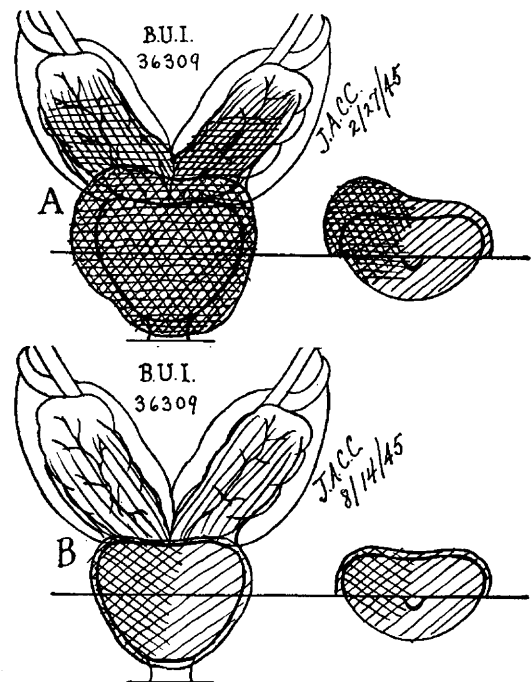


Fig. 1 (case 5).—A, diagrammatic representation of rectal findings on initial examination. B, six months after institution of diethylstilbestrol.

of the stream. He was reexamined Sept. 6, 1945 and found to be in excellent general condition. There was no evidence of local return of the cancer or distant metastases. A soft stricture at the site of the anastomosis was easily dilated, following which the patient developed acute retention. He was hospitalized twenty-four hours and discharged voiding easily with normal control.

CASE 5.—M. W., a white man aged 68, was first examined at the Brady Urological Institute Feb. 27, 1945. For the preceding year he had suffered from vague gastrointestinal symptoms manifested chiefly by gaseous distention. His local physician had discovered a suggestive nodule in the prostate and referred him to a urologist, who diagnosed carcinoma of the prostate but considered the process too extensive for radical operation. The patient was referred to this clinic. He had no history of any urinary symptoms whatever. Rectal examination disclosed the prostate to be considerably broader than normal. The left lobe was nodular and of stony hard induration, and there was nodularity of the right lobe, which also was stony hard but not quite so prominent as the left. The bases of both seminal vesicles were invaded, particularly on the left (fig. 1 A). There was no x-ray evidence of bony metastases. The serum acid phosphatase studies were normal.

The initial impression was that the growth was too extensive for radical operation. Diethylstilbestrol 1 mg. a day was started. When seen six months later a most remarkable change in the palpatory findings had occurred. The gland was only slightly broader and was more prominent than normal. No nodules were present, and the elevation on the left side had disappeared. The entire gland was elastic and compressible and not adherent. The vesicles and the base of the bladder above the gland were quite soft (fig. 1B). Another x-ray again demonstrated no evidence of metastases.

The patient was readmitted Aug. 15, 1945 and prepared for radical perineal prostatectomy. All laboratory findings were negative. August 17, radical perineal prostatectomy was performed. The convalescence was smooth. The urethral catheter was removed the eleventh postoperative day, following which all urine drained by way of the perineum until reinsertion of the catheter on the seventeenth postoperative day. The catheter was finally removed the twenty-second day, after which the perineum remained completely dry. For the first three days the patient was almost totally incontinent, but at the end of that time he regained control gradually, so that when he was discharged

tenderness and soreness of the nipples, but there was some lessening in frequency and nocturia. The stream was perhaps slightly better. He was again examined May 31, 1945, at which time the prostate felt distinctly smaller. The left lobe was slightly larger than normal, smooth and elastic throughout, and of second degree induration. In the lower portion of the left seminal vesicle there was induration, but the remainder felt soft. The membranous urethra was uninvolved, and the rectal mucosa smooth.

The patient was admitted to the hospital June 2, 1945. General physical examination was essentially negative. Preoperative laboratory studies included hemoglobin 13, 7 Gm.; white blood cells 13,550, blood urea 20 mg. per hundred cubic centimeters, phenolsulfonphthalein excretion 75 per cent in two hours. Urine was normal.

On June 11 radical perineal prostatectomy was carried out. At operation there was obvious extension into the tip of the right seminal vesicle and laterally to the pelvic wall on the right side. After removal of the prostate and seminal vesicles there apparently still remained some neoplastic tissue on the right side. Postoperatively the patient had a smooth convalescence. The urethral catheter was removed on the fourteenth postoperative day, following which the patient voided an excellent stream with good control. On the sixteenth postoperative day he suddenly developed a left hemiparesis, which manifested itself as a seventh nerve palsy and decided motor loss of the left arm and leg. This cleared rapidly after about two weeks and was considered to have originated on an angiospastic basis. The patient was discharged on the thirty-fifth postoperative day, voiding satisfactorily with excellent urinary control.

Pathologic studies showed adenocarcinoma of the prostate with considerable anaplasia and with some diversity of the histologic pattern.

The patient was seen three weeks after leaving the hospital. A soft stricture at the site of the anastomosis was easily dilated. He was again seen after another three weeks period and found to be voiding a good stream with normal control. The patient died in May 1946. His physician said that he could feel some evidence of malignancy on rectal examination.

CASE 7.—Dr. W. T. B., a white man aged 70, a physician, was admitted to the Brady Urological Institute Oct. 3, 1945 complaining of nocturia and burning on urination for approximately three to four years. He had been referred by his own physician, who had discovered a hard nodule in the prostate on rectal examination.

On physical examination the patient seemed to be in excellent general condition. The external genitalia were entirely normal. On rectal examination the prostate was somewhat broader than normal. Both lateral lobes were irregular and stony hard throughout, with the induration extending into both seminal vesicles, particularly on the left side (fig. 1A). Laboratory studies revealed hemoglobin 14 Gm., white blood cells 9,600, blood urea 20 mg., phenolsulfonphthalein excretion 73 per cent in two hours. The urine contained 8 to 10 white blood cells per high power field; cultures were sterile. There was no x-ray evidence of bony metastases.

It was believed that, although this could be classed as a moderately advanced carcinoma of the prostate which had extended into both seminal vesicles, the radical operation should be deferred in the hope that following a course of diethylstilbestrol, the growth would regress sufficiently to permit an easier operative procedure and insure a better functional result. The patient was discharged and placed on diethylstilbestrol 2 mg. per day.

He was readmitted to the Brady Urological Institute for the second time on Nov. 13, 1945. Rectal examination disclosed the prostate to be only slightly broader than normal. The right lobe was smooth and firm but elastic and compressible throughout. The left lobe contained no evidence of stony hardness and was also smooth and compressible (fig. 2B). There had been a very definite and gratifying response to diethylstilbestrol therapy. It was decided that the patient was now suitable for radical operation. Preliminary laboratory studies revealed hemoglobin 14.2 mg., white blood cells 8,700, blood urea 20 mg. per hundred cubic centimeters. The voided urine contained 4 to 6 white blood cells per high power field.

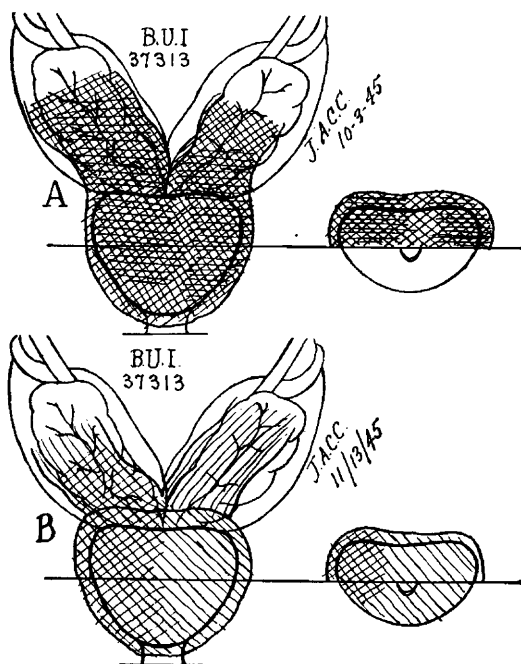


Fig. 2 (case 7).—A, diagrammatic representation of rectal findings on initial examination. B, six weeks after institution of diethylstilbestrol.

on the twenty-sixth postoperative day he was voiding a normal stream with excellent control.

Pathologic studies showed adenocarcinoma of the prostate involving the bases of both vesicles, chiefly the left, with scattered areas of diethylstilbestrol change.

The patient has not been seen since, but a letter from him one month after operation stated that he was in excellent health and voiding satisfactorily.

CASE 6.—E. R., a white man aged 62, first seen March 1, 1945, had a history of onset of urinary difficulty and frequency one year prior to the first examination. Six months before examination he had been seen elsewhere and had been treated periodically by urethral sounds and posterior urethral irrigations.

The patient was in good general condition. The external genitalia were normal. On rectal palpation there was evidence of third degree induration and nodularity throughout the prostate, but chiefly on the right side, with infiltration of the perirectal tissues over an area 1.5 cm. in diameter on the right side. Except for this the carcinomatous process seemed to be confined within the capsule of the prostate. There was no x-ray evidence of metastases. No serum acid phosphatase studies were obtained. The patient was placed on diethylstilbestrol 2 mg. per day. On this medication he developed some

Nov. 14, 1945, radical perineal prostatectomy was carried out. The postoperative course was entirely uneventful. The urethral catheter was removed the twelfth postoperative day, following which the patient voided a good stream with excellent control. The patient was discharged sixteen days after operation, to be followed by his own physician.

Pathologic studies showed adenocarcinoma of the prostate, fairly well differentiated, with involvement of both seminal vesicles.

Several weeks after leaving the hospital the patient developed acute retention and was seen by a urologist elsewhere who, after several dilations, performed a transurethral resection. Following this procedure the patient became totally incontinent, but this condition has gradually improved, so that he now has no nocturnal leakage but has to wear a clamp during his surgical activities, which he has resumed.

SUMMARY

Endocrine therapy in the treatment of carcinoma of the prostate, either by the administration of estrogen or by orchiectomy or by a combination of the two, has been proved by many competent observers to have a definite and most valuable place in the treatment of carcinoma of the prostate. Regression of the primary growth, as measured by rectal examination, has been noted to occur in approximately 75 per cent of the cases, and regression of metastases in 45 per cent. It has been postulated that this inhibitive effect results from an interference with the enzyme balance by endocrine therapy, and probably this effect is more pronounced on the younger, actively growing cells of the tumor, which are more dependent on androgen for their metastases. In spite of the intensive laboratory studies and many clinical observations that have been made on endocrine therapy of carcinoma of the prostate, no case has yet been reported in which complete disappearance or clinical cure has been obtained by endocrine therapy alone. From the results of experimental laboratory work and clinical research, it would appear at present that a permanent cure with endocrine therapy of carcinoma of the prostate cannot be obtained.

The regression of the prostatic growth which occurs in an appreciable percentage of cases under endocrine therapy has led us to follow a series of 7 cases in which on first examination the growth was considered too far advanced for complete extirpation by radical operation. In these 7 cases it was considered that the regression of the neoplasm as far as could be judged by rectal palpation had progressed to a sufficient degree to permit the radical operation which was successfully carried out in these cases. There has been no operative mortality in this series, but 2 patients have developed complications resulting from stricture formation at the site of the anastomosis. One patient has died of recurrence and metastases one year after operation.

The patients in this series have all been operated on within the last two years, so that the presentation is in no sense intended as a study of ultimate mortality.

It is our impression that endocrine therapy for the preparation of patients to undergo the radical operation is of the utmost value in that:

1. We have observed numerous cases of moderately advanced carcinoma of the prostate in which orchiectomy or transurethral resection has been advised in the belief that the disease was too far advanced for radical extirpation.

2. Regression of the growth, which usually occurs, materially facilitates the operative technic in moderately advanced cases.

3. It is our hope that five year cures will be obtained in some of the cases in which on physical examination the observer's opinion was that the prognosis for radical cure was unfavorable.

In view of the regression of the primary growth which usually occurs in cancer of the prostate following endocrine therapy and which is attributed to death of at least some of the malignant cells, presumably at the periphery of the lesion, it would seem advisable to institute endocrine therapy in all cases of carcinoma of the prostate, even those which fulfil the criteria for the radical operation.

ORTHOPEDIC CAUSES OF PELVIC PAIN

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This paper presents the problem of pelvic pain in a deliberately simplified form. My purpose is to show that measurements of pelvic mobility are essential to an accurate diagnosis.

The fundamental structure of the pelvis consists of bones, muscles and joints. The massive ring formed by the two innominate bones and the sacrum gives origin and insertion to the most powerful muscles in the body; muscles that go far afield for attachment to other bones. The intrapelvic sacroiliac joints and symphysis pubis allow the bony ring to change its shape. The extrapelvic hip joints, sacrolumbar and sacrococcygeal joints allow motion of other bones on the pelvic ring. The ligaments of the pelvic joints are tremendously strong and are elaborately arranged in all planes, so that the slightest change in the position or shape of the pelvic ring alters the total ligamentous tension.

Flexion and extension are the normal motions of the intrapelvic joints (fig. 1). The sacrum may flex or extend on the ilia at the sacroiliac joints. The axis of sacral motion is a horizontal, transverse line that passes through the ligamentous portions of the sacroiliac joints and the body of the second sacral vertebra. Sacral flexion increases the lumbar lordosis, narrows the pelvic inlet and enlarges the outlet: sacral extension reverses the process. Furthermore, either innominate bone may flex or extend on the other at the symphysis pubis. The axis of innominate motion is a horizontal, transverse line that passes through the center of the symphysis. Innominate flexion by elevating the ilium produces lateral tilting of the sacrum and by carrying the ilium forward produces rotation of the sacrum toward the opposite side: innominate extension reverses the process. Abnormal motion may occur when the symphysis pubis is relaxed or torn, allowing a small amount of opposed flexion and extension of the innominate bones at the hip joints. Abnormal motion appears in appropriate roentgenograms as a vertical shift at the symphysis pubis.¹

The curve of intrapelvic mobility is high at birth, goes down slightly during childhood and rises to a peak at puberty. During adult life the curve gradually descends, and it remains at a low level during old age. Age and other factors, such as training and build, influence articular mobility in general, but the action

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1. Chamberlin, W. E.: The Symphysis Pubis in the Roentgen Examination of the Sacro-Iliac Joint, *Am. J. Roentgenol.* 24: 621, 1930.