CARCINOMA OF THE PROSTATE

(A STUDY OF EIGHTY CASES DIAGNOSED FROM 1930-1940 INCLUSIVE)

A Thesis

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by

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CHAPTER I

THE PROBLEM, MATERIALS AND METHODS

I. THE PROBLEM

There are large gaps in our knowledge of cancer of the prostate. Not only why or how the lesion begins, but also its rate of growth and mode of extension are not fully understood. The desirability of obtaining a microscopic classification, which would indicate the probable clinical course, has long been appreciated. The study of proven cases of carcinoma is an approach to the solution of the latter problem. Approximately one hundred and sixty-five clinical cases of carcinoma of the prostate were confirmed by tissue section in the laboratory of the Winnipeg General Hospital during the perior between 1930-1940 inclusive. Only a few, if any, of these cases would be expected to survive until the present time, so that this series of cases may be expected to show a possible correlation between a clinical classification, a histological classification and the ultimate clinical course of the disease.

II. MATERIALS AND METHODS

Approximately one hundred and sixty-five cases of carcinoma of the prostate were diagnosed clinically and confirmed by tissue section in the Winnipeg General Hospital between 1930-1940 inclusive. The clinical histories and charts of these cases were reviewed and summarized. The data obtained were recorded on summary sheets based on the cancer

record sheets used by the American College of Surgeons and adopted by the Manitoba Cancer Institute. No history was recorded in thirty cases, and in a few others the information was insufficient. Tissue blocks sections of all cases were drawn from the files of the laboratory, except in eleven cases when neither paraffin blocks nor sections could be found. Approximately one quarter of the original paraffin blocks were re-cut and re-stained. Of those cases in which sufficient history had been recorded and sections were available, an attempt to determine the outcome and final history was made through three main sources: (a) the Manitoba Cancer Institute; (b) the hospital records; (c) the office records of the surgeons who had been in charge of the cases concerned. History subsequent to diagnosis and final notes were not obtained in twenty-four cases. Tissue sections, sufficient history and follow-up notes were obtained in eighty-seven cases. On review of the tissue sections, histological evidence of carcinoma was insufficient or lacking in seven cases, so these cases were not included in the series. Thus eighty cases were classified according to the clinical method of Ferguson, and the clinical method found on the summary sheets of the American College of Surgeons. The microscopic sections were classified according to the method proposed by Edwards (1950).

CHAPTER II

REVIEW OF THE LITERATURE

Age incidence. The average age at the time of clinical recognition of carcinoma of the prostate is between 61 to 66 years[14,52], although there is a wide clinical age range[45] and no adult period is entirely exempt[28].

Carcinoma of the prostate is extremely rare clinically before the age of 40 years[2,14,15,46]. Some reported series[4,5,16,28,52] include a few cases below the age of 40 years. In the opinion of Bumpus[14] any case of prostatic tumor discovered before the age of 40 years should be considered a sarcoma clinically until proven otherwise. Huggins[32], writing in 1943, had seen only one case (47 years old) younger than 50 years of age. Other authors[3,28,36,37,39,43,54] report series which include an occasional case of carcinoma in a patient less than 50 years of age.

Incidence of cancer of the prostate. Cancer of the genito-urinary tract including the prostate contributed 16.2 per cent of the 84,108 male cancer deaths in Canada between the years 1931-1944 inclusive. Cancer of the prostate accounted for 8.9 per cent of these deaths. During the period of 1931-1944 inclusive, cancer of the digestive tract and the peritoneum was most common for men and women accounting for nearly 52 per cent of the 168,885 cancer deaths in Canada during that period. Cancer of the genito-urinary tract was

second most important cause of cancer deaths in males.*

Statistics dealing with the incidence and death rate of cancer of the prostate in Manitoba have been obtained through the co-operation of Miss P. L. Ellis of the Manitoba Cancer Institute. These figures are given in the following tables.

TABLE I

INCIDENCE OF CANCER OF THE PROSTATE AND NUMBER OF DEATHS DUE TO THE DISEASE IN MANITOBA FROM 1930-1949.

Year	Number of Cases Reported	Number of Deaths Reported
1930	-	34
1931	-	19
1932	-	20
1933	-	27
1934	-	24
1935	-	34
1936	-	28
1937	43	40
1938	40	24
1939	51	35
1940	59	60
1941	58	45
1942	58	37
1943	54	37
1944	56	42
1945	61	34
1946	71	49
1947	83	53
1948	70	63
1949	83	61

* Reference--Cancer mortality in Canada and the provinces 1921-44. Vital statistics analytical report No. 3. The Dominion Bureau of Statistics, Department of Trade and Commerce. Canada. 1947.

TABLE II

INCIDENCE RATES OF CANCER OF THE PROSTATE IN MANITOBA DURING THE PERIOD OF 1937-1949, PER 100,000 POPULATION.

Year	Crude Rates*			Age Adjusted*		
	urban	rural	general	urban	rural	general
1937	16.20	8.75	11.61	20.54	9.36	14.95
1938	11.87	10.00	10.72	14.18	10.62	12.40
1939	18.67	10.36	13.56	21.10	10.60	15.85
1940	22.03	11.64	15.64	23.84	11.90	17.87
1941	21.26	11.63	15.34	22.58	11.16	16.87
1942	17.09	14.47	15.49	16.88	13.78	15.33
1943	17.54	12.36	14.41	17.25	11.81	14.53
1944	17.22	13.27	14.85	15.84	12.13	13.98
1945	19.55	13.78	16.12	17.28	12.45	14.87
1946	25.47	14.56	19.04	22.12	12.61	17.36
1947	29.10	16.64	21.82	25.19	14.48	19.84
1948	19.05	17.40	18.10	15.63	14.38	15.00
1949	23.68	18.87	20.92	19.11	15.17	17.14

*Crude rates are expressed in terms of "rate per 100,000 population."

Age adjusted rates are the crude rates corrected to a standard population (1931) in order to eliminate the effect of changing age structure of the population from year to year.

TABLE III

DEATH RATES FROM CANCER OF THE PROSTATE PER 100,000 POPULATION IN THE PROVINCE OF MANITOBA, 1930-1949

Year	Age Adjusted		Crude	
	urban	rural	urban	rural
1930	16.80	11.54	9.67	9.16
1931	10.95	5.73	6.17	4.50
1932	13.56	3.90	8.94	3.12
1933	13.10	7.26	8.99	6.21
1934	10.32	7.13	6.98	6.19
1935	13.27	10.06	9.85	8.82
1936	10.38	8.29	7.80	7.47
1937	18.46	9.12	14.79	8.31
1938	9.35	5.93	7.68	5.65
1939	12.67	8.36	11.06	8.21
1940	22.49	13.12	20.65	12.93
1941	16.12	9.72	15.09	9.90
1942	10.19	8.99	10.26	9.64
1943	12.91	6.98	13.49	7.51
1944	10.37	9.98	11.26	11.06
1945	10.78	6.52	11.73	7.11
1946	15.84	8.49	18.29	9.55
1947	16.95	8.37	19.61	9.89
1948	15.56	11.36	19.05	14.28
1949	11.94	12.51	15.39	15.36

Note: Urban Manitoba includes Winnipeg and all its suburbs except Charleswood.

TABLE IV

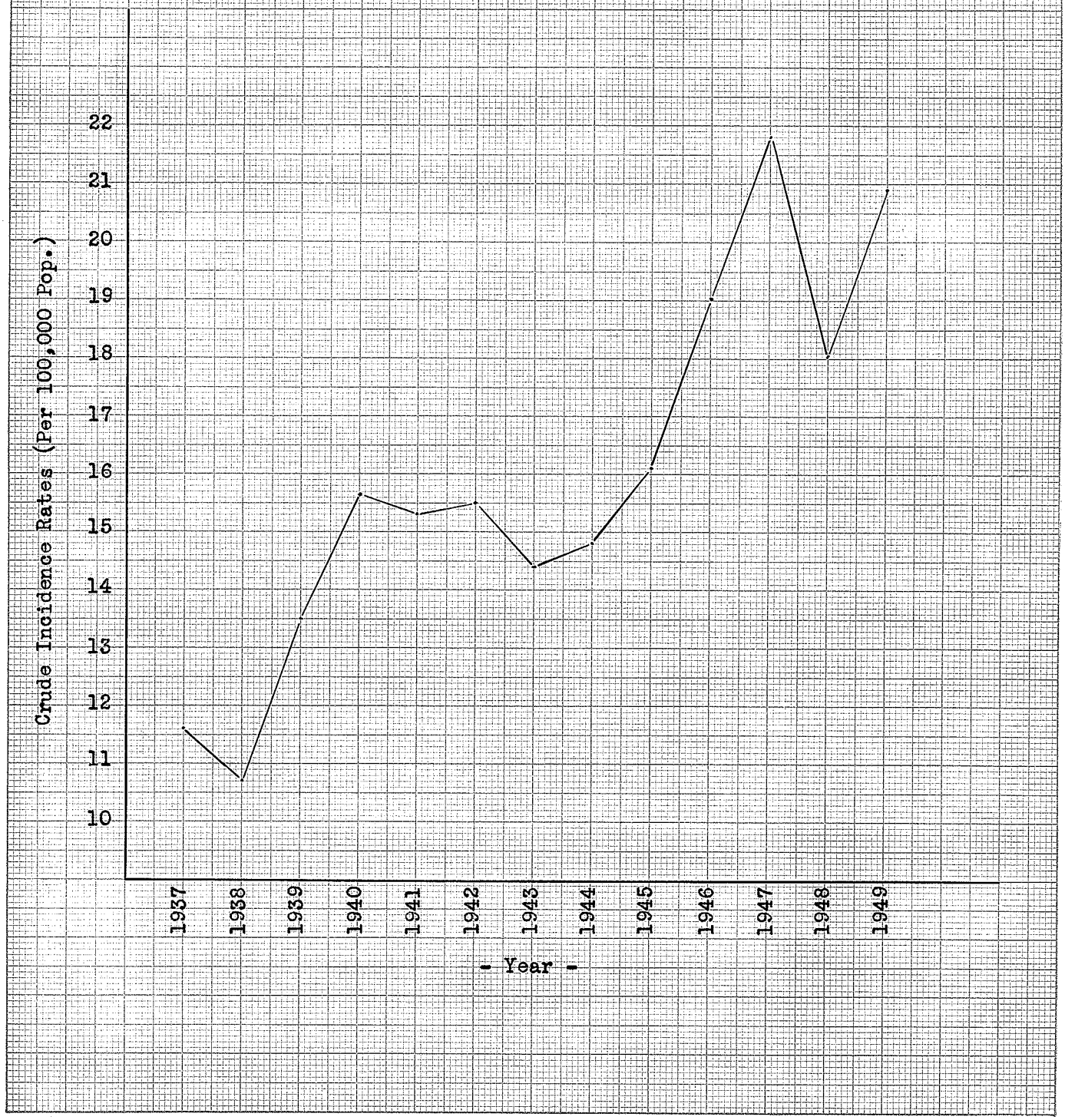
THE TEN YEAR AVERAGES OF DEATH RATES PER 100,000 MALE POPULATION DUE TO CANCER OF THE PROSTATE, 1930-39 and 1940-49.

	1930-1939		1940-1949	
	Age Adjusted	Crude	Age Adjusted	Crude
Urban	12.89	9.19	14.32	15.48
Rural	7.73	6.76	9.60	10.72
Manitoba	10.31	-	11.96	-

The large increase in the crude rates is due to the increase in the population of the older age groups. In Winnipeg the number of men over the age of 70 years increased from 2895 in 1931 census to 6219 in 1946, an increase of 66 per cent in the average of the two decades. In rural Manitoba, the number of men over 70 years of age increased from 6818 in 1931 to 10,097 in 1946, an average increase of 29.6 per cent.

CHART 1

THE TREND OF CANCER OF THE PROSTATE IN MANITOBA, 1937-1949.
CRUDE INCIDENCE RATES (PER 100,000 POPULATION)



Etiology. In this connection, it is interesting to note that the development and maintenance of the prostate requires the male hormones of the normal testes[18]. Eunuchs have never been known to develop carcinoma of the prostate[42]. Kahler[37] could establish no relationship between carcinoma of the prostate and associated atrophy, nodular hyperplasia, inflammation, or calculi. Moore[39] on the other hand, believes that carcinoma is intimately associated with senile atrophy and that carcinoma rarely occurs in acini already hyperplastic. However, as with cancer occurring in other sites of the body, the etiology is not known at the present.

Edwards[21], in agreement with Andrews[2], concluded on the basis of statistical analysis, that benign prostatic hypertrophy and carcinoma of the prostate showed a definite relationship, although the nature of this relationship remains obscure.

Symptoms. The onset of carcinoma of the prostate is elusive and without signs or symptoms[29]. Even when the disease is moderately advanced, symptoms when present are not distinctive[4,6] since carcinoma and benign prostatic hypertrophy both produce obstructive symptoms in the same age group[4]. Carcinoma of the prostate often begins in the periphery or in the posterior lobe of the gland at a distance from the urethral lumen, so that obstruction to urination appears late in the course of the disease[18].

Symptoms depend upon (a) interference with urinary drainage by tumor invading the prostatic urethra and base of the bladder, (b) pain

produced by metastases to bone, (c) edema produced by metastases to lymph nodes, and (d) cachexia of carcinomatosis (Cf. Huggins[35]).

The initial symptoms are either urinary[6] due to obstruction[10], or pain due to extension, or metastases. Barringer[6] found frequency and difficulty the two most common initial urinary symptoms, occurring in 82 per cent of 280 cases. Other common initial symptoms are nocturia, retention, urgency and incontinence. There is considerable confusion in the literature regarding the importance of hematuria as an initial symptom, but the consensus appears to be that hematuria is uncommon[35] and of no significance[10]. Bumpus[14] in 1000 cases did not find hematuria as an initial sign in any instance. Carnett[15] states that hematuria and pyuria are found in only 1-2 per cent of cases when first seen. Usually patients complain of three or more symptoms at their first consultation. The most common triad in Barringer's[6] series consisted of frequency, difficulty and nocturia.

Obstructive symptoms range anywhere between frequency of urination to complete retention. Frequency and nocturia head the list of urinary symptoms (initial) of any series. The onset is insidious. Gradually the frequency and nocturia may become so marked that the patient has no hour free from the demand to urinate. Difficulty in initiating the flow, stammering and inability to completely empty the bladder are added in time to the list of symptoms and compel the patient to seek advice, if hematuria, complete retention, or pain have not already done so. The onset of complete retention in the presence of relatively mild symptoms is considered to be suggestive of carcinoma

by some authors[11].

Pain may be manifest as painful urination, backache, sciatica, lower abdominal and pelvic pain or pain in the hips, groin, penis, rectum or perineum in that order of frequency[6]. Pain localized in the perineum, rectum, and penis is due to involvement of nerves by local extension of the tumor, while pain in the hips, low back, and long bones is due to distant metastases.

Vesical pain, which is infrequent in benign prostatic hyperplasia in the absence of calculus or infection[15], is apt to be constant and independent of nocturia in carcinoma[36].

Extravesical pain associated with urinary symptoms should always be considered suspicious of metastases[10]. In one fifth of the cases of carcinoma reviewed by Carnett[15], pain was an outstanding symptom in patients when first seen. In the series reported by Bumpus[13], pain was absent in one quarter of all cases with metastases, and urinary symptoms were absent in approximately 11.5 per cent of those cases with metastases. Bilateral leg pain in men over fifty is commonly due to carcinoma. The pain may be only a soreness[15]. The onset of sciatica in a man over forty demands a rectal examination[35].

One of the chief causes of the bizarre clinical picture is the varying and widespread dissemination of the metastases[3]. The pelvis and the lumbar vertebrae are the common sites. Pain in the lower back, the hips and the pelvis is common. Metastases in the long bones are found in the proximal ends.

Several cases are well nourished and even obese in the presence

of advanced disease[26]. Occasionally symptoms (such as diarrhoea and rectal bleeding) are referable to the gastro-intestinal tract[6].

A considerable delay between the onset of symptoms and the time of the first consultation is noted by most authors. In Barringer's series[6], twenty-four months was the average time between initial symptom and first examination. Bryan[12], writing in 1912, in an attempt to explain this delay states:

> ". . . There is an unconscious adjustment of the patient to the condition. He pays no more attention to the increased calls for urination or the slightly stuttering stream than that patient who puts on spectacles for the first time: both conditions are regarded as one of the natural phenomena of advancing years. At the instant pain or haemorrhage is noticed, the patient now knows something is wrong and seeks the advice of a surgeon."

Clinical findings. Early clinical carcinoma is found as a firm nodule just beneath the capsule of the posterior lobe. The single hard nodule is to be differentiated from prostatic calculi, tuberculous infection, non-specific infection and benign prostatic hypertrophy[32]. The nodule is often masked by edematous prostatic tissue. The edema disappears after exposure to x-ray leaving the nodule clearly defined[6].

The single nodule of carcinoma is not a common clinical finding. The literature contains many reports regarding the extension of the carcinoma at the time the patient is first seen. Thus, Barringer[4] found the lesion confined to the prostate in only two, perhaps three, cases of a series of 145 patients. In another paper, Barringer[5] states that in 98 per cent of cases the carcinoma had extended beyond the prostate when the patient was first seen. In one quarter of the cases

studied by Carnett[15], bone metastases were demonstrable at the time the local lesion was diagnosed. Caulk and Boon-itt[16] report that 51.3 per cent of 197 cases presented demonstrable lesions beyong the prostate when the patient was first examined. Only 36 cases of 1040 studied by Colston and Lewis[17] were considered eligible for radical surgery. In the series reported by Wear and Schoenenberger[52], 170 of 400 cases had metastases at the time of the first admission. These reports constitute only a fraction of the literature but illustrate the stage to which the disease has usually progressed when the patient first seeks advice.

The usual lesions fall into one of two groups: (a) the large bulky carcinoma which grows slowly, filling and infiltrating the pelvis, and (b) the small hard carcinoma which produces few local changes but which metastasizes relatively early in its history. Between these two extremes which in the pure type are rare, all gradations are seen[4].

The usual type is a slowly growing tumor which is limited posteriorly by the limiting fascia of Denonvilliers and the base of the bladder anteriorly. The line of least resistance is followed and the tumor grows upwards into the lymphatics, around the seminal vesicles and metastasizes early in its history[4].

In the well established case, the findings are fairly characteristic, for a high degree of clinical accuracy can be attained. The prostate is enlarged, firm or stony hard, nodular and fixed. Only one lobe may be involved. The median groove is often obliterated, although its presence does not rule out carcinoma[6].

Metastases to lymph nodes may be very extensive and still not be

felt or reached by the examining finger[13]. The nodes must produce an abdominal mass or be increased to such a size to be felt per rectum[13].

Clinical classification. A number of classifications have been proposed, none of which are entirely satisfactory. Each classification is based on different aspects of the disease. Barringer[4] and Bumpus[13] prefer to divide the cases into two groups: (a) those cases with large bulky carcinomata and late metastases, and (b) those cases with the small stony hard carcinomata and early metastases. Both extreme forms are rare and all gradations are found. Bothe[10] proposes three types: (a) those cases which have urinary obstruction and no evidence of metastases where the prostate is stony hard and nodular; (b) those cases where there is evidence of metastases and no local evidence of the primary lesion, the variable symptoms depending on the site of the secondary tumors (occult); (c) those where there is no evidence of malignancy before study of the tissue after extensive sectioning (latent).

Ferguson's classification[23], given below in detail, recognizes three groups. The classification is based upon differences in prognosis, clinical findings and symptoms. The following table is taken from Ferguson's paper.

TABLE V

CLINICAL INDEX OF MALIGNANCY

AFTER FERGUSON[23]

Index factors	Group A Least malignant	Group B Intermediate	Group C Most malignant
Age	More than 65	55 to 65	Less than 55
Residual urine	200 ml. and over. Frequently complete retention.	100-200 ml.	Less than 100 ml.
Duration symptoms	More than 20 months	10-20 months	Less than 10 months
Extent of disease	No pain. No demonstrable metastases.	Pain. No demonstrable metastases.	Pain and demonstrable metastases.
Prognosis, untreated cases	30 months to many years.	7-30 months. Average 18.	Up to 1 year. Average 6 months.
Percentage of 501 cases reviewed by Ferguson[23]	62 per cent	26 per cent	12 per cent

Survival figures. Survival figures are usually given as the length of life after the onset of symptoms and after the time of diagnosis. Bumpus[14] in reviewing 485 untreated cases found the average duration of life from the onset of symptoms until death to be thirty-one months. Two thirds of those cases with metastases when first seen died within nine months, while those cases with no demonstrable metastases on their first examination averaged one year of life after the first consultation. Of the 485 cases, 58 per cent died within one year after

their first examination. Nesbitt and Plumb[43] give the figures for their series of 605 cases, in which the shortest duration of life from the onset of symptoms until death was two months, the longest 324 months, and the arithmetic mean was 50 months.

Survival figures actually mean very little when a case on hand is being considered from the standpoint of prognosis. An attempt of classification to correlate the clinical and pathological findings may be expected to reveal some constant factors. Foot[25] has attempted such a classification but could demonstrate no correlation between the histological picture and the time of survival.

Duration of the lesion. Any conclusions based on the study of reported series recording the duration of symptoms from onset to death will be erroneous and misleading with respect to the duration of the lesion. An estimation of the time from beginning to end is presumptive. When the facts regarding latent carcinoma and metastases are considered, it seems possible that the carcinoma of the prostate may exist for many years without causing symptoms or spreading from its place of origin[29]. Flynn[24] reports a case of carcinoma which was proven microscopically nine years before there was evidence of local and widespread disease and twelve years before death. Such reports are rare. Ockerland[44] estimates on empirical grounds that the average victim of carcinoma of the prostate has had the lesion for five years by the time he seeks relief.

Gross appearance. The gland should be sliced with a sharp knife at regular intervals of not more than 4 mm thickness if early lesions are to be found. Thick pieces of punch material should be divided with the knife in the longitudinal plane. Tissue with yellow streaks and dots, which represent aggregates of degenerating and desquamated cells, should be blocked for section and staining as such areas are most likely to be carcinoma. While the lesions are usually firm, whitish-yellow or hemorrhagic compared with the oozing surface of the surrounding tissue, the following exceptions should be noted. The consistency varies with the amount of stroma and the degree of cellularity. Areas of fibrosis subsequent to a healed infarct or focal atrophy and chronic hyperplastic conditions may produce a firm lesion. White areas are produced by areas of fibrosis of old healed infarcts, while yellow colour is seen in areas of hyperplasia, tuberculous lesions and in acute or chronic pyogenic infections[37].

Spread of the tumor. The most characteristic mode of spread of the carcinoma is by way of the perineural lymphatics. Kahler[37] found the perineural lymphatics involved in practically all his cases regardless of size or microscopic grade. Moore[39] found carcinoma in the perineural lymphatics of 77 per cent of the 52 early cases reported. In 15 of the 17 early cases studied by Andrews[2] the perineural lymphatics were involved, while Edwards[21] observed it in 12 of his 28 cases of latent carcinoma. Hinman[29] points out that the early invasion of the lymphatics does not necessarily mean distant metastases. According to

Hinman[29], this early invasion of the perineural lymphatics may be confined within the capsule of the prostate for a long time.

The size of the lesion often bears no relation to the extent of the metastases[42]. A small growth may give rise to widespread metastases[5,15,19,26], while in other cases[5] the pelvis may be filled with tumor and yet no distant metastases have occurred. Distant metastases occur by way of the lymphatics and blood stream[42], although spread by blood stream is late[29]. Invasion of the blood vessels was not common in the series studied by Andrews[2] and not seen by Edwards[21].

Bone and lymph node metastases constitute 66 per cent of the metastases of some series[3]. According to some authors the lymph node metastases are more frequent than those in bone and are less readily diagnosed clinically[15]. The lesions in the lymph nodes occur more frequently than is possible to demonstrate clinically because of the inaccessibility[13] of the nodes. Graves and Melitzer[26] place metastases to lymph nodes second to those of the bone. With such a division, it is probable that the metastases to lymph nodes and bone are about equal.

The mechanism of bone metastases has been a matter of considerable speculation. Roberts[47] stated that spread occurred along the normal abdominal lymph drainage of the pelvic organs in probably all cases and suggested that the path of the lymph vessels and tissue spaces of the spinal laminae with associated ligaments may account for widespread metastases. Warren et al[51] regarded the perineural lymphatics as pathways leading the cancer into intimate contact with cortical bone. Thence the growth through the ostia is relatively simple and invasion

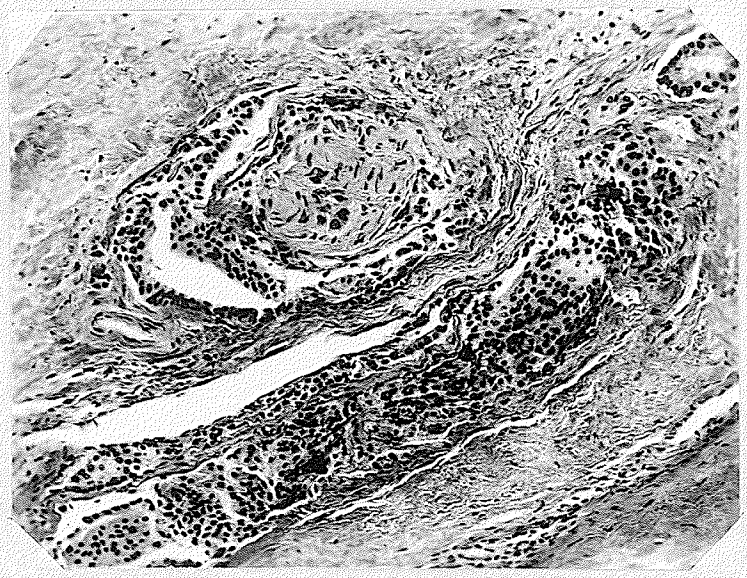


FIGURE 1

Perineural lymphatic invasion by carcinoma. Tumor is also seen in an adjacent blood vessel. Hematoxylin and eosin stain. 150 x.

FIGURE 2

A mass of tumor cells found in a blood vessel in a shred of prostatic tissue. Hematoxylin and eosin stain. WGH 900-40. 200 x.

of the bone follows. Batson[9] by injecting the deep dorsal vein of the penis was able to demonstrate connections between the veins draining the pelvic organs and the vascular sinuses of the sacrum, pelvis and head of the femora. Under certain conditions a retrograde flow was demonstrable. Batson[9] has termed this system of veins, which is continuous with the veins of the skull, neck, viscera, vertebral column and body wall, as the vertebral system of veins.

Carcinoma of the prostate is the most common source of bone metastases in men[15,22]. Kaufmann (quoted by Caulk and Boon-Itt[16]) states that 70 per cent of prostatic carcinoma, 37 per cent of thyroid carcinoma and 14 per cent of breast carcinoma give rise to bone metastases. The pelvis is always involved[32]. The pelvis and sacrum were involved in 85 per cent of cases with metastases in the series reported by Graves and Melitzer[26] and the lumbar spine in 59 per cent of the same group. Pathological fractures occurred in only 5 per cent of the cases. In a series of 50 advanced cases of carcinoma reported by Huggins[32], 31 had x-ray evidence of bone metastases. The metastases are never found beyond the knee or elbow joint[32].

The local spread of the tumor into the seminal vesicles and the base of the bladder are late manifestations in the natural history of the tumor, although by the time the tumor produces symptoms it is seldom confined within the prostate itself. Colston and Lewis[17] found only 36 of 1040 cases suitable for radical extirpation of the tumor.

When an ulcerating tumor is found on the anterior wall of the rectum, it is usually an adenocarcinoma of the rectum, originating in

its mucosa and not an extension of carcinoma of the prostate into the rectum. Young[56] found that in 800 cases of prostatic carcinoma, the rectal mucosa was involved in only 12 instances.

Autopsy findings. The autopsy findings are usually those of the advanced case. Towards the latter part of the disease, the patient may have considerable pain and be bedridden, evidence of which is found at autopsy in the form of wasting of muscle and fatty tissue, trophic changes of the skin over pressure areas and edema of the extremities. Bronchopneumonia is a frequent contributing factor in the death of the patient. Tumor may partially or completely fill the true pelvis. Invasion beyond the capsule of the gland into contiguous tissue such as the base of the bladder and the seminal vesicles is common. The tumor may extend upwards and partially obstruct both ureters to produce hydroureter, hydronephrosis and pyelonephritis, the last being a common contributing factor in the death of the patient. If the obstruction of both ureters is more or less complete, terminal uremia may be present. Soft tissue metastases, for example, to the lung, liver and skin, are usually small and seldom explain symptoms of importance. Enlarged lymph nodes replaced by tumor tissue may form masses in the pelvis or along either side of the aorta. Secondary growths are usually obvious, but the real extent of these will depend upon the thoroughness of the examination. While it is impossible to examine all bony structures, special attention should be paid to any areas showing radiological changes. Approximately 90 per cent of the bony metastases are osteo-

sclerotic in nature.

Occasionally the carcinoma may be occult, in which case the primary tumor is small and the metastases widespread. Extensive sectioning of the prostate may be necessary to demonstrate the primary tumor.

Site of origin of carcinoma. That carcinoma begins most frequently in the so-called posterior lobe was first stated by Young and supported subsequently by several authors[7,5,39,42,45]. When occult and latent carcinoma were studied, others found that the carcinoma begin in the periphery of the gland with no special predilection for the posterior lobe[46,29]. Most authors[6,7,39,42] agree that the vast majority of the carcinoma arise in the posterior lobe but can and do originate anywhere in the prostate gland or its accessory glands. Bugbee[11], however, found that the carcinoma originated in the median or lateral lobe in six of seven early cases diagnosed by tissue section where the lesion was small and the origin could be determined. Moore[39] in a study of 52 early carcinoma, in which only one lobe was involved, found 73.5 per cent in the posterior lobe, 8.8 per cent in the lateral lobe, 14.8 per cent in the anterior lobe and none in the median lobe. Of 40 foci of carcinoma found in 26 cases by Edwards[21], 21 were in the posterior lobe, 13 in the lateral lobe and 6 anterior to the urethra. The foci may be multicentric in origin. Edwards[21] found more than one carcinoma in 8 of 28 cases studied. As many as 5 foci were observed in a single gland in his series. The possibility must be considered,

however, that some of those cases interpreted to have multicentric foci, may merely represent irregular-shaped extensions of a single tumor cut in one plane.

Neller and Neuburger[41] (1926) found in 40 cases of men dying from unrelated causes, 7 cases with atypical epithelium which they interpreted as beginning carcinoma. Since this time Muir[40], Moore[39], Rich[46], Kahler[37], Baron and Angrist[8], Andrews[2] and Edwards[21] have reported the incidence of latent carcinoma to range between 2.1 to 46 per cent. Much of the variation in the figures is due to the method of examination and the criteria of malignancy.

The following table summarizes the number of cases studied and the percentage of latent carcinoma found by different authors.

TABLE VI

REPORTED INCIDENCE OF LATENT CARCINOMA OF THE PROSTATE IN CASES OVER 50 YEARS OF AGE

Author	No. of cases studied	No. of latent carcinoma found	Percentage of cases having lat. carcinoma
Neller and Neuburger[41]	40	7	17.5
Muir[40]	54		13
Moore[39]	375	52	13.9
Rich[46]	292	27	
Kahler[37]	381	53	13.9
Baron and Angrist[8]	50	23	46
Andrews[2]	142	17	12
Edwards[21]	150	28	18.7

The incidence of latent carcinoma of the prostate in males over the age of 50 years appears to be in the neighborhood of 15 per cent of all cases coming to autopsy. Only those reports should be considered which state rigid criteria of malignancy and which have included unselected series of consecutive autopsies except for age, where the lesion is small and confined to one lobe and not diagnosed clinically.

The study of latent carcinoma of the prostate is more than academic in importance. Data are being accumulated regarding the site of origin and the association of the early lesions with other conditions of the prostate. It is only possible to make such studies on autopsy material, so that the important question of how these tumors might behave in living patients is still incomplete. Tissue obtained at operation does not lend itself to determining the important question of how many of these latent carcinomas become clinically manifest. The entire gland is not removed usually at operation. Only adenomas are removed in the suprapubic approach so that the true prostatic tissue compressed in the periphery of the gland is left in the "rim" or "capsule." Most of the early or latent carcinomas are found in the periphery of the gland. Much of the tissue removed by transurethral resection is median lobe tissue, in which latent carcinoma is seldom found. If carcinoma is found in a shred of tissue removed by transurethral resection, the lesion is probably advanced. In the present series a few cases were reported as early or even latent, but on further examination the tumor was found on the edge of one shred and it is likely that the surgeon's knife touched the tumor at its periphery.

Microscopic criteria of malignancy. The criteria of malignancy in the prostate are similar in many respects to those of carcinoma elsewhere. A few features are unique. Many cases are straightforward and present no problem. Small lesions and lesions present in one or two shreds of punch material often require considerable study. Distortion of the microscopic picture by a previous operation and infection may produce a lesion simulating carcinoma. Andrews[2] and Moore[39] have given their criteria of malignancy of the prostate in detail.

The relationship of the epithelium to stroma is very important[2,39] since adenocarcinoma is often composed of small, well differentiated acini in which nuclear changes and mitotic figures are rare or absent[2]. In the normal prostate, the acini are surrounded or invested by a narrow band of collagenous connective tissue devoid of capillaries. This layer, which is termed the tunica propria, follows all the irregularities of the acinus. In the earliest malignancies, a loss of the tunica propria occurs and the acini are arranged irrespective of the whorls of smooth muscle, connective and elastic tissue. A "back to back" arrangement results where the acini are found in close approximation with no intervening stroma. An abnormal stromal relation together with any nuclear changes or lymphatic or blood vessel invasion, supports a diagnosis of malignancy.

The acini may be small, round or oval with no papillae but an irregular lumen border. Many of the acini are distorted with the lumen narrowed to a slit-like space. The cells may be two layers thick or

there may be intra-acinar proliferation. The basal layer of epithelial cells is not present. The cells lining the acini have a faintly eosinophilic staining cytoplasm which is usually finely granular. They are usually cuboidal but there is wide variation in shape and size. Variation in staining qualities is noted together with relatively larger than normal nuclei (Cf. Moore[39] and Andrews[2]).

Often the diagnosis is made using a low power magnification in which the details of stroma and acinus relationships may be appreciated. Inclusion of epithelial elements with muscle bundles is diagnostic. At times the muscle fasciculi appear to be "fractured." Perineural lymphatic invasion is an early and reliable sign of malignancy[2,37]. The tumor cells may be arranged in sheets and cords with no attempt to form acini.

Histological classification of carcinoma of the prostate. Edwards (1950) noted the similarity between the histological picture of carcinoma of the prostate and carcinoma of the breast. On the basis of microscopic appearance, he proposed a descriptive terminology and divided carcinoma of the prostate into four groups, namely: (1) duct carcinoma, (2) acinar carcinoma, (3) intratubular or intra-acinar carcinoma, and (4) anaplastic carcinoma.

(1) Duct carcinoma. The histological picture of duct carcinoma is characterized by small, irregular or incomplete glands, which are frequently single and have intervening stroma. The epithelium is low and cuboidal, with scanty cytoplasm and large hyperchromatic nuclei.

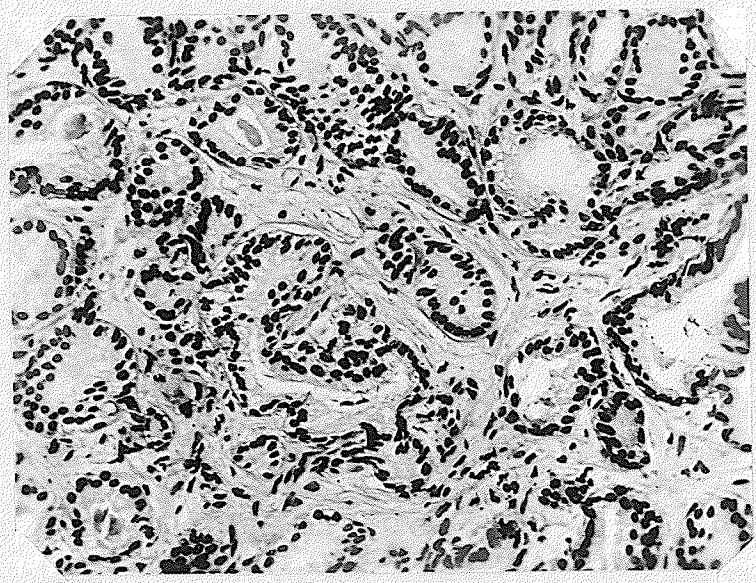


FIGURE 3

An example of duct carcinoma of the prostate. The cells are small, have deeply staining nuclei and there is abundant intervening stroma. Hematoxylin and eosin stain. WGH 1717-36. 200 x.

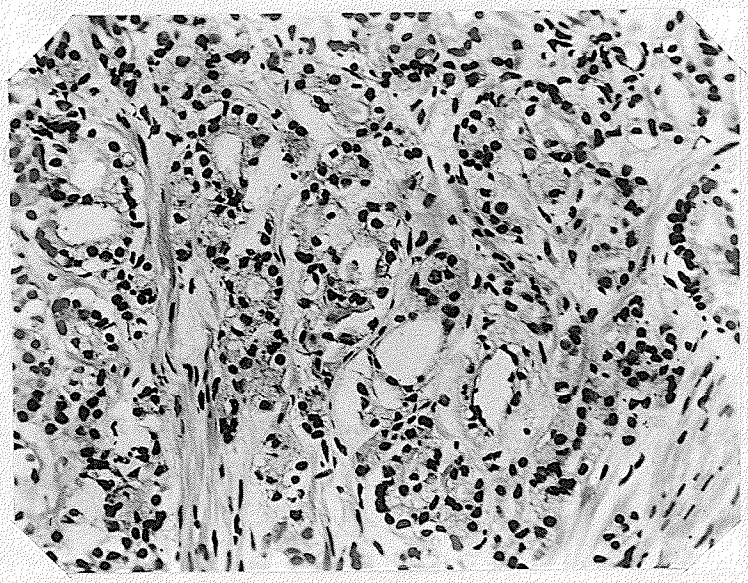


FIGURE 4

An example of acinar carcinoma of the prostate. There is little intervening stroma between the glands. Hematoxylin and eosin stain.
WGH 3426-39. 200 x.

FIGURE 5

Acinar carcinoma of the prostate showing the "back to back" arrangement of the acini. Some of the acini have calculi in their lumen. Hematoxylin and eosin stain. WGH 1439-38. 200 x.

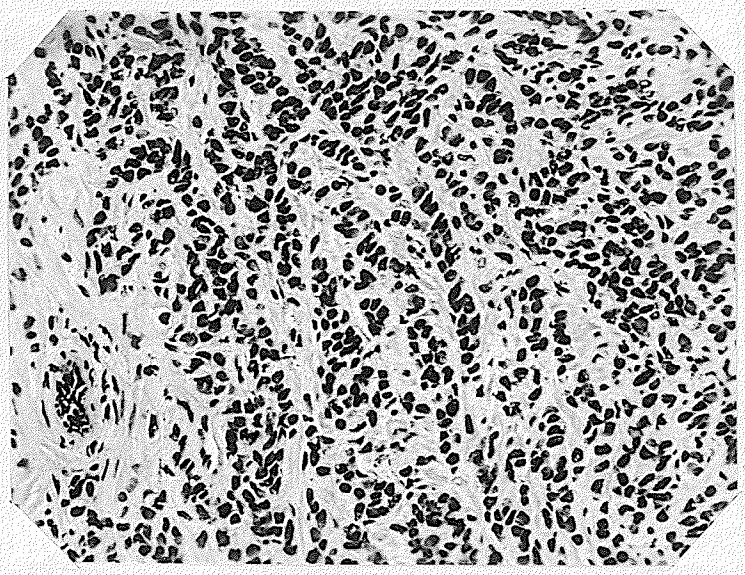


FIGURE 6

Anaplastic carcinoma of the prostate. The cells have large irregular nuclei which are deeply stained by the hematoxylin. Hematoxylin and eosin stain. WGH 5626-36. 200 x.

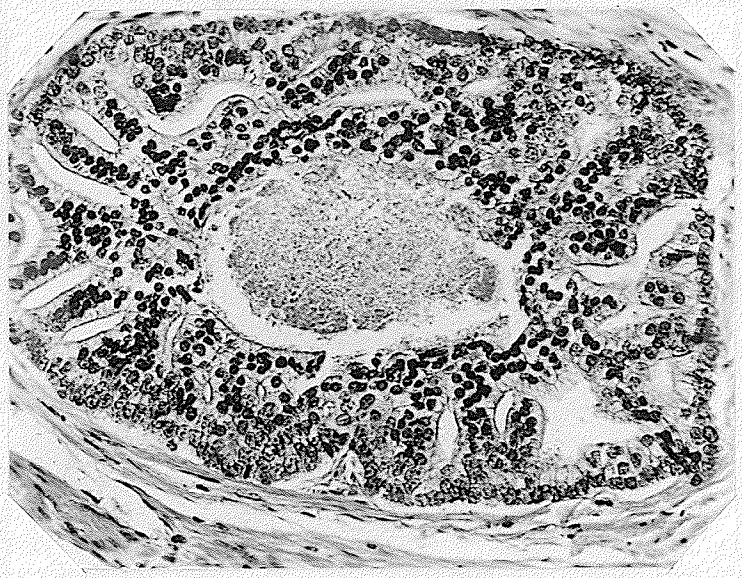


FIGURE 7

An example of intratubular carcinoma of the prostate, showing multiple lumina and cells which have pale-staining cytoplasm. A false capsule surrounds the gland. Hematoxylin and eosin stain. WGH 71-1937. 200 x.

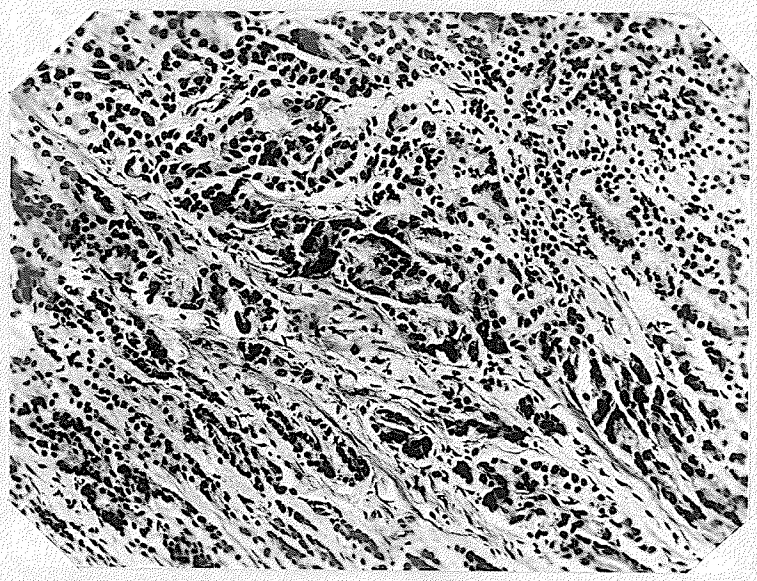


FIGURE 8

An area of carcinoma of the prostate which shows the features of more than one histological type. In the upper right hand corner of the photomicrograph, the histological type is predominantly acinar, while in the centre, running diagonally is an area of duct carcinoma. In the lower left hand corner the histological type is mostly anaplastic. Hematoxylin and eosin stain. WGH 907-38. 150 x.

(2) Acinar carcinoma. In acinar carcinoma, the glands are relatively larger and have little or no intervening stroma, when compared with duct carcinoma. The glands have usually only one layer of epithelium, the cells of which have paler staining cytoplasm, smaller, paler staining nuclei than the duct type of carcinoma.

(3) Intratubular carcinoma. Intratubular proliferation of epithelium showing multiple lumina within one gland is the distinguishing feature of this type of carcinoma. The cells have abundant, pale-staining cytoplasm and nuclei which are normochromatic. Edwards found this intratubular pattern always in association with one or more other types.

(4) Anaplastic carcinoma. In anaplastic carcinoma, the cells are arranged in sheets or strands and show no attempt to form acini or glands.

Phosphatases. A phosphatase is an enzyme which splits the phosphoric acid esters of carbohydrates. There are many phosphatases, which may be divided into two groups, namely, acid phosphatases and alkaline phosphatases. Acid phosphatases have optimum activity in acid medium and the alkaline phosphatases have their optimum activity in an alkaline medium. They are separate enzymes and have different origins[53]. The "activity" or the amount of enzymatic splitting varies with several factors, among which are pH, substrate or the substance being acted upon and the amount of enzyme present. The different methods of estimation of phosphatase activity standardize these factors so that

differences are due to the amount of enzyme present. The enzyme activity is expressed in arbitrary units. Many methods of estimation have been devised, each method having a different arbitrary unit. Since the activity of the phosphatases varies with substrate and pH, the arbitrary units in general cannot be converted by a simple arithmetic process from one unit into another[53]. Small amounts of acid phosphatase are found normally in the serum of both males and females. The source of this serum acid phosphatase is not known. Similarly, there is normally a small amount of alkaline phosphatase in blood, the source of which is mostly from bone[53].

Kutscher and Wolbergs (quoted by Dean[20]) in 1935, during their investigation to determine the source of urine phosphatase, discovered that the human prostate tissue is extremely rich in acid phosphatase. This phosphatase has a wide range of activity between pH 4.5 - 6.5 and an optimum between pH 5 - 6. It was later shown that the concentration in human prostatic tissue ranges from 500 - 2500 units per gram (Gutmans) fresh tissue as compared with less than 5 units activity in kidney, liver and duodenal mucosa[48].

The prostates of infants have insignificant amounts of acid phosphatase[48]. There is a great increase at puberty[20] when a physiological maturity of the prostatic glandular epithelium occurs[48] under the influence of the testicular hormone. Gomori (1941) using enzyme staining techniques showed that acid phosphatase is present only in the adult epithelial cells of the gland.

In 1936, the Gutmans and Sproul confirmed the high acid

phosphatase activity of normal prostatic tissue and in prostates which were carcinomatous. They noted also that the metastases of prostatic tumor retains capacity to elaborate acid phosphatase in high concentration at the site of the metastases. In 1938, the Gutmans[27] demonstrated increases in the amounts of serum acid phosphatase in patients with metastatic carcinoma of the prostate. Patients with other diseases of the prostate such as benign prostatic hyperplasia, prostatitis, tuberculosis and lymphosarcoma of the gland had normal serum acid phosphatase. Thus, carcinoma of the prostate is the only condition where the serum acid phosphatase is significantly elevated and then only if these are metastases[48]. The method is considered a consistent and specific enough though not infallible supplement to clinical judgment and other procedures[48]. Apparently the acid phosphatase of the prostatic cancer tissue does not enter the circulation as long as the capsule of the gland is intact[53]. The test does not differentiate benign prostatic hyperplasia and carcinoma of the prostate which has not metastasized[48] or infiltrated beyond the capsule.

In many cases, a malignant prostatic tumor is an overgrowth of well differentiated prostatic tissue[31]. The phosphatase activity of the normal prostate is usually the same magnitude as prostatic carcinoma except in cases of anaplastic carcinoma where it is diminished[53]. Less than 10 per cent of cases do not show an elevation of the serum acid phosphatase even in the presence of extensive disseminated disease[53]. When the metastases produce only osteolytic lesions in bones, neither alkaline or acid serum phosphatases are raised[32].

Alkaline phosphatase occurs in kidney parenchyma, intestinal mucosa and bone. Serum alkaline phosphatase originates mainly in the bones and is excreted by the liver. In liver disease, where there is less excretion, the serum alkaline phosphatase levels may be raised. Production of alkaline phosphatase is increased with the formation of new bone. Since metastases from carcinoma of the prostate are nearly always osteoplastic, an elevation of serum alkaline phosphatase occurs in 90 per cent of cases with metastases. Sometimes the elevation is evident before symptoms referable to bone are manifest. (Cf. Woodard[53])

From the standpoint of carcinoma of the prostate, serum alkaline phosphatase is less specific than serum acid phosphatase. Significant elevations of serum alkaline phosphatase in liver disease have already been mentioned. Other diseases which affect the osseus skeletal system such as Paget's disease, osteogenic sarcoma, multiple myeloma and fractures will also elevate the values. These conditions, however, do not affect the serum acid phosphatase values. In the absence of liver disease and diseases of bone, an elevated serum alkaline phosphatase warrants strong suspicion that metastases to bone have taken place[20].

Huggins[32] has given normal values which are now widely accepted. The normal serum acid phosphatase may be regarded as 4.5 King-Armstrong units per 100 cubic centimetres serum and the serum alkaline phosphatase as less than 12.5 King-Armstrong units per 100 cubic centimetres serum. Values of serum acid phosphatase between 5 to 10 K.A. units per 100 cubic centimetres serum are considered by Huggins[32] to be presumptive in the diagnosis of carcinoma of the prostate and values over 10 K.A. units as diagnostic. (Cf. Huggins[32])

CHAPTER III

HISTORY

Marital status. As may be expected, the majority of the patients were married (63), a few were widowers (10), and some were single (9). The marital status of 11 patients was not recorded.

Occupation. The majority of the patients were farmers. A large group were listed as retired, labourer, or no occupation. The following table, which summarizes the occupational status of the patients of this series, does not appear to show any relationship between the disease of carcinoma of the prostate and occupation.

TABLE VII

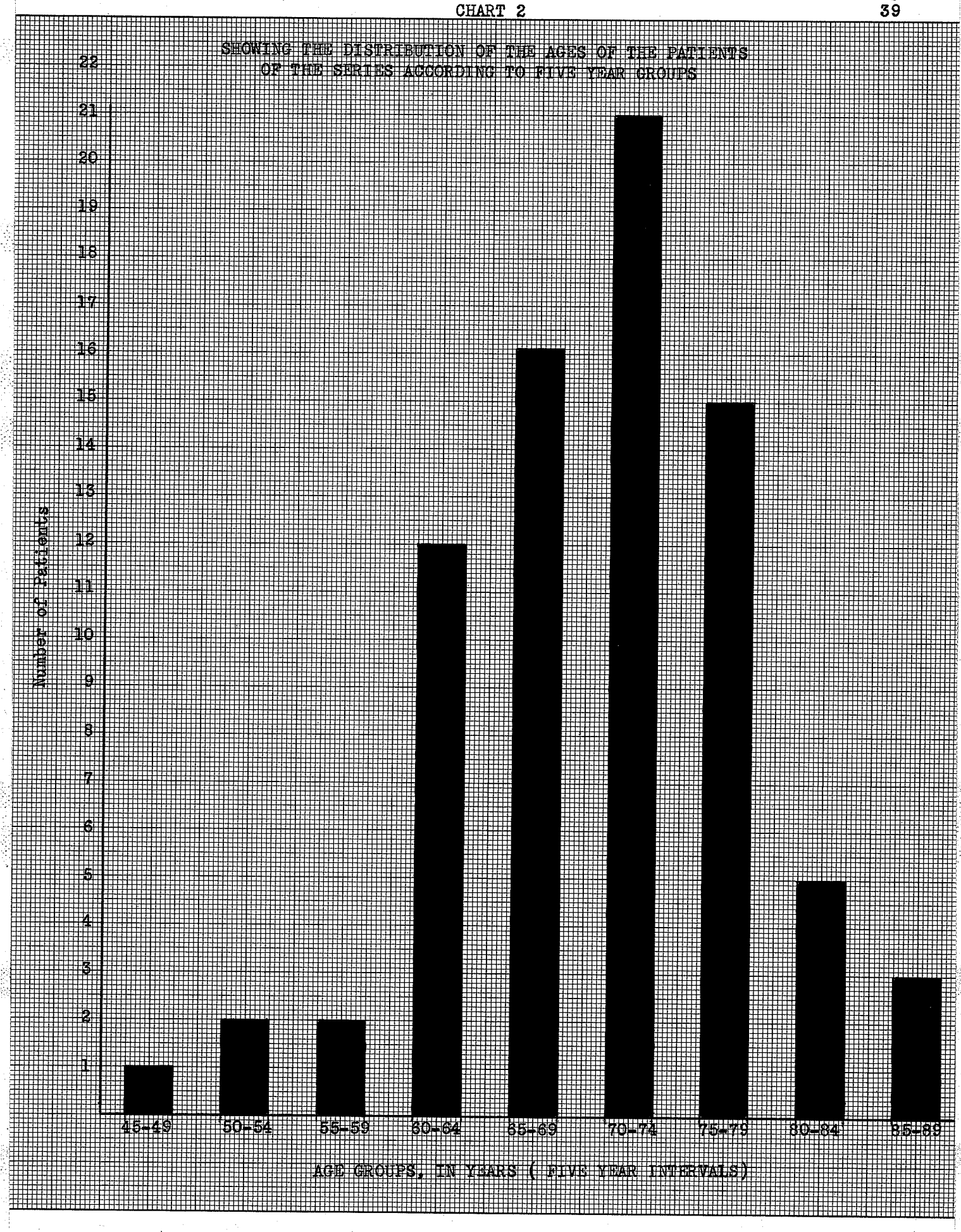
OCCUPATIONS OF THE PATIENTS OF THIS SERIES

Farmer	29
Retired	13
Labourer	8
None	3
Agent	3
Contractor	3
Engineer	3
Carpenter	2
Butcher	2
Salesman	2
Constable	1
Electrician	1
Postmaster	1

Age. Of the 80 selected cases, the age was recorded in 77 instances. The youngest patient at the time of diagnosis was 48 years of age, the next youngest patient was 50 years of age, while the oldest

CHART 2

SHOWING THE DISTRIBUTION OF THE AGES OF THE PATIENTS OF THE SERIES ACCORDING TO FIVE YEAR GROUPS



in the group was 88 years of age. The average age for the group was 71.4 years. The preceding graph indicates the distribution of the ages. From it is seen that the largest number of cases occurred between the years 70-74, when the whole group is divided into five-year age groups. Thirty-six patients were in the eighth decade at the time of diagnosis, while 28 were in the seventh decade.

TABLE VIII

AGE OF THE PATIENT AT THE TIME OF DIAGNOSIS IN SEVENTY-SEVEN CASES OF CARCINOMA OF THE PROSTATE

Age in years	No.	Age in years	No.
48	1	72	4
50	1	73	1
53	1	74	5
55	1	75	4
58	1	76	5
60	2	77	1
62	3	78	2
63	2	79	4
64	5	80	1
65	1	81	1
66	2	82	2
67	4	83	1
68	4	85	1
69	5	87	1
70	4	88	1
71	7		

Family history of cancer. A family history of cancer was recorded in six cases. In one case, two brothers and a sister had died of cancer of the stomach. In another case, the father, mother and sister had died of cancer, the sites of which were not recorded. Both mother and grandmother had died of cancer of the face in the third case.

A sister of the patient had died as the result of cancer of the breast in the fourth case, while in the fifth case an aunt had died of the same disease. A brother of the patient in the sixth case had died of cancer of the stomach. No case had a history of a relative who died of cancer of the prostate or genito-urinary tract.

Previous genito-urinary tract disease. Eleven patients had a history of previous genito-urinary tract disease, independent of their illness due to carcinoma of the prostate. A positive blood Wasserman reaction was recorded in one case. The following list indicates the nature of some of the diseases which were recorded. Qualifying statements or definite diagnoses are not possible in most of the cases.

(a) inflammation of the bladder

(b) urethral burning for 25 years

(c) urethral injury - traumatic

(d) previous transurethral resection

(e) retention for 10 years

(f) slight urethral discharge for years

(g) incontinence for 30 years

(h) difficulty for 13 years

(i) mumps orchitis

(j) hematuria when young

(k) previous suprapubic prostatectomy

Complaints. Complaints recorded on first or subsequent admissions were divided into two categories, i. e., (a) initial

complaints suffered by the patient at the onset of the disease or at the onset of prostatism, and (b) entrance complaints which were usually the initial complaints together with other complaints which had been added in time and which had forced the patient to seek advice.

Frequency of urination and nocturia head the list of initial complaints, followed by difficulty and dysuria, when the recorded symptoms are listed in order of their occurrence. Retention, occurring either at the onset of the illness or shortly afterwards, was noted in six patients. Hematuria, as an initial symptom, usually in combination with some other symptom, was recorded in four cases. Pain was less common as an initial complaint than as an entrance complaint.

Frequency and nocturia were also the most common entrance complaints. Difficulty and retention, together with such complaints as incontinence, loss of force, pain and loss of weight were noted more often in entrance complaints than in initial complaints. The most frequent combination of two symptoms were frequency and nocturia, occurring in twenty cases.

TABLE IX

SUMMARY OF COMPLAINTS, AS LISTED IN THE HISTORIES

Complaint	Number of times as initial complaint	Number of times as entrance complaint
frequency of urination	52	63
difficulty in urination	26	44
nocturia	45	58
dysuria	16	29
retention	9	55
backache	5	11
pain, in thigh or leg	1	3
urgency	4	18
incontinence	4	24
constipation	2	2
pain in hips	1	5
loss of weight	1	14
pain, lower abdominal	0	19
rectal pain	0	5
penile pain	0	4
poor stream	3	28
testicular pain, voiding	1	0
hematuria	4	6

Hematuria. Painless hematuria as a single initial symptom occurred in two cases. Hematuria as an initial symptom, in association with other symptoms occurred in an additional two cases. Hematuria, as one of other entrance symptoms was noted in six cases, two of which are the same cases mentioned above.

Acute retention. Twenty-one cases had acute retention in association with other symptoms requiring them to be admitted to hospital. Two cases suffered acute retention in association with other symptoms as initial complaints, later to be admitted with acute retention. Acute retention in four cases was the only initial complaint of the onset of their illness. In addition, one case had acute

retention due to a urethral stricture resulting from a fall. Another case suffered from acute retention, requiring hospitalization, resulting from a fall. Partial retention ranging from a few ounces to as many as 27 ounces was recorded in another 18 cases.

Duration of symptoms before admission and diagnosis. From the following table it is seen that averages are of little value in assessing any given case. The duration of the symptoms of prostatism ranged anywhere from one day to 30 years. Four cases suffered from the onset of acute retention with no previous symptoms to suggest prostatism. It is of interest to note, however, that 28 patients or approximately one third had symptoms for less than one year, while 44 or approximately one half of the patients had symptoms for less than 2 years prior to their first admissions and surgical treatment.

TABLE X

DURATION OF SYMPTOMS OF PROSTATISM
BEFORE THE FIRST ADMISSION

Time in months	No. of patients	Time in months	No. of patients	Time in months	No. of patients
0	3	13	4	61	1
½	2	16	1	64	1
1	2	20	2	70	2
1½	2	22	1	72	2
2	2	23	2	84	1
3	1	24	3	96	1
3½	1	27	1	118	1
5	1	28	1	127	1
6	3	35	1	135	1
7	2	36	3	190	1
8	2	38	1		
9	1	42	2	30 years	1
12	6	44	1	no record	15
12½	1	48	1		

CHAPTER IV

CLINICAL FINDINGS

General condition of the patient on first admission. The general condition of the patient was recorded in sixty cases, as follows:

good	29
fairly good	10
obese	3
thin	2
poor	7
fair	4

Not all those cases listed as fair or poor had generalized carcinomatosis. Parkinsonism, congestive heart failure, and hypertensive cardiovascular disease were responsible for the patient's plight in some instances. On the other hand, some of the cases listed as being in good general health had advanced local disease or demonstrable metastases. Thus, of the cases listed as having good general health, 18 had a lesion more or less confined to the prostate but not resectable, 7 had demonstrable local infiltration of adjacent tissues, and 2 had demonstrable metastases, while 2 were diagnosed clinically benign. Of the patients whose general health was listed as fairly good, 6 had local disease (1 a diabetic also), 3 had local infiltration and 1 distant metastases. Of the cases listed as "fair" 3 had local disease and 1 had infiltration into adjacent tissue. The 3 obese patients had local disease. No adequate explanation of the three thin cases was found in the records; all had local disease. Those listed as having poor general health form an interesting group. Five of these patients had localized

disease, and their general poor health can be attributed to reasons other than carcinoma at the time of their first admission. Two cases had advanced disease and their general poor health can be attributed to their carcinoma.

I. RECTAL EXAMINATION

Size of the gland. The relative size of the prostate was recorded in 61 cases. The prostate was described as "enlarged," qualified in 42 cases by plus signs. The prostate was considered normal in size in only three cases, and small in four. The other terms used together with the frequency of their occurrence are listed below.

TABLE XI

Term used to describe the relative size of the prostate	Number of times found in descriptions of 61 cases
enlarged, qualified by plus signs	42
very large	3
large, unqualified	1
small	3
normal	3
slight enlargement	2
general enlargement	1
moderate enlargement	1
considerable enlargement	1

Consistency. A number of terms were found to describe the consistency of the gland. Most of them indicate that the gland was harder than normal and nodular or irregular in outline. These terms are listed on the following page.

TABLE XII

Terms used to describe the relative consistency of the gland, as felt per rectum	No. of times listed
hard, unqualified	17
firm	6
nodular and hard	11
stony hard	5
smooth and hard	4
nodular and irregular (with or without "hard")	7
not hard	1
firm and elastic	3
deep firmness	1
hard nodule	1
soft	1
very firm	4

Portion of the gland involved. In the present series, the right lobe was involved with the carcinoma process about as commonly as the left. In only 9 cases was a single nodule recorded. The following table summarizes the portion involved, as determined clinically by rectal palpation.

TABLE XIII

Portion of the gland involved with carcinoma, as determined by digital examination per rectum.	No. of cases in which the portion was involved.
right lobe	2
left lobe	4
median	1
diffuse involvement	6
single nodule-	
position not recorded	2
left lobe	3
right lobe	4
lateral lobes	6

TABLE XIII (Continued)

Portion of the gland involved with carcinoma, as determined by digital examination per rectum.	No. of cases in which the portion was involved.
unequal, right more than left	2
unequal, left more than right	2
deep mass	1
commisure obliterated	4
median groove present	1
normal contour	1

Fixation. The fixation or relative mobility of the gland was recorded in 28 cases as follows: fixed, 19; movable, 5; slightly movable, 1.

Cystoscopic examination. Trabeculation of the urinary bladder in varying degrees was the most frequent recorded cystoscopic finding, other than those describing the relative enlargement of the lobes. Evidence of tumor invasion of the urethra or bladder base was noted in 22 cases. Cystitis and diverticulae were the next in order of frequency.

TABLE XIV

Lesions recorded as found by cystoscopic examination, (enlargement of the lobes excepted)	No. of times recorded
trabeculation of urinary bladder	20
evidence of tumor invasion	22
-constriction of bladder neck	11
-"ragged" or irregular urethra	3
-mass fungating into bladder	2
-bullous edema	1
-edema of uretral orifice	1
-tumor bulging into bladder	1
-areas of blanching	1
cystitis	5
diverticulae	4
calculi	3
atonic bladder	1
"negative"	3

CHAPTER V

LABORATORY FINDINGS

I. LABORATORY AND ROENTGEN STUDIES

Plain films of kidneys, ureters and bladder (KUB). In the majority of cases, the plain film studies revealed no disease. In a few cases, invasion of bone by carcinoma was noted. Of those cases in which plain film studies were made, 28 were reported as normal. In two cases, associated bladder calculi were shown, and in another case the bladder was noted to be small and irregular. Intravenous pylegrams were used to demonstrate dilatation of the ureters in three cases.

Hemoglobin. Hemoglobin estimations were the most frequently used hematological examination. More complete blood studies were done in a few cases, but their number is too small to warrant study. Twenty patients had a hemoglobin estimation of over 90 per cent at the time of their admission, 17 between 75 and 90 per cent, and another 17 below 75 per cent.

Urinary sediments. Pus cells and red blood cells were the most frequent pathological microscopic findings in the urinary sediments. The table below lists the microscopic findings of the centrifuged specimens of the recorded cases.

No. of cells per high power field	Pus cells	Blood cells
few (0-15)	35	16
many (15-80)	26	10
loaded (90 /)	8	2

Blood urea nitrogen estimations. Pre-operative blood urea nitrogen estimations were done on 86 cases. Most of the cases had been decompressed before the estimation was performed, when obstruction was present, so that the estimations are of little value from the standpoint of the degree of urea nitrogen retention present when the patient was first admitted. The results are recorded below, where it is seen that many fall within the normal range.

Blood urea nitrogen, mgms per cent	No. of patients
10 - 15	14
15 - 20	31
20 - 25	23
25 - 30	6
30 - 35	5
45 - 50	2
over 50	4
over 100	1

Blood creatinine studies. Only a few blood creatinine studies were done, as listed below:

1.6 mgms %	1
1.7	3
1.8	1
1.9	2
2.6	2
3.0	1
3.5	1
8.1	1

CHAPTER VI

CLINICAL CLASSIFICATION

Two methods of clinical classification were used in the study of this series, namely: (1) the method used by the American College of Surgeons and Manitoba Cancer Institute, and (2) Ferguson's classification which is outlined on page 15.

Clinical classification of the American College of Surgeons.

Class A. In this class, the carcinoma is limited more or less to the prostate; the lesion has not metastasized. In this survey, cases in which the clinical history did not indicate local extension of the disease were placed in Class A which comprised over one-half this series.

Class B. The cases in which there is invasion of the base of the bladder, seminal vesicles or contiguous tissue are placed in Class B. Metastases are not demonstrable.

Class C. Local and distant metastases are demonstrable in cases of Class C.

Class D. This class was added for the purposes of this study to list those cases which were diagnosed clinically as benign lesions of the prostate. Ordinarily the cases would be placed in Class A.

TABLE XV

DISTRIBUTION OF 80 CASES OF CARCINOMA OF THE PROSTATE, CLASSIFIED ACCORDING TO THE METHOD OF THE AMERICAN COLLEGE OF SURGEONS

	No. of patients	% of Series
Class A	52	65
Class B	13	16
Class C	8	10
Class D	5	6
No Record	2	2.5

As seen from the above table, Class A is the largest group. Such a finding is contrary to all the reported series in the literature. The fault is not in the classification itself, but in the number of inadequate clinical descriptions throughout the series. Since the distribution of the cases is obviously not correct, no correlation between this clinical classification and the microscopic classification was attempted.

Ferguson's classification. Ferguson's classification, which takes into consideration such factors as age, the duration and type of symptoms, and clinical findings, was found more easily adapted to the study of the present series. Approximately one half of the cases in the series were easily classified according to Ferguson's clinical method. Inadequate history added to the difficulty in some of the remainder and eleven cases were not classified for this reason. One

case, the youngest, did not fit into the classification and was left unclassified. The factor of age gave difficulty in some cases and was given less weight than the duration and nature of the symptoms. On the basis of this series, it appears that the classification is not entirely practical but may be useful as a clinical guide. The percentages of cases placed in each category are given in the table below and agree closely with Ferguson's figures. Similarly, the averages of the survivals after diagnosis agree with the figures given by Ferguson. While the averages of the time of survival from diagnosis until death are different for each class, the longest and shortest duration of life after diagnosis is practically the same for Classes A and B. Such a finding makes the classification difficult to apply to the clinical case on the ward. The following tables summarize the data obtained using the classification in the present series.

TABLE XVI

POST-OPERATIVE SURVIVALS OF 68 CASES OF CARCINOMA OF THE PROSTATE, CLASSIFIED ACCORDING TO THE CLINICAL METHOD OF FERGUSON

Time of survival (post-operative) in months	Class A (37 Cases)	Class B (20 Cases)	Class C (11 Cases)
More than 30 months	20	2	0
25 - 29 months	2	3	0
20 - 24 months	6	3	0
10 - 19 months	5	5	2
Less than 10 months	2	6	7
Post-operative deaths	2	1	2

TABLE XVII

SHOWING AVERAGE TIME OF SURVIVAL FROM DATE OF DIAGNOSIS
FOR EACH CLASS OF THIS SERIES (FERGUSON'S CLASSIFICATION)

Class	No. of cases	% of cases classified (68 cases)	Time, in months from date of diagnosis until death (Post-operative deaths are excluded)		
			Average	Longest	Shortest
A	37	54.4	43.1	144	2.5
B	20	29.4	25.2	141	4
C	11	16.1	5.1	13	1

Note: Number of cases not classified, insufficient records: 11 cases.
Not classified, sufficient record: 1 case.

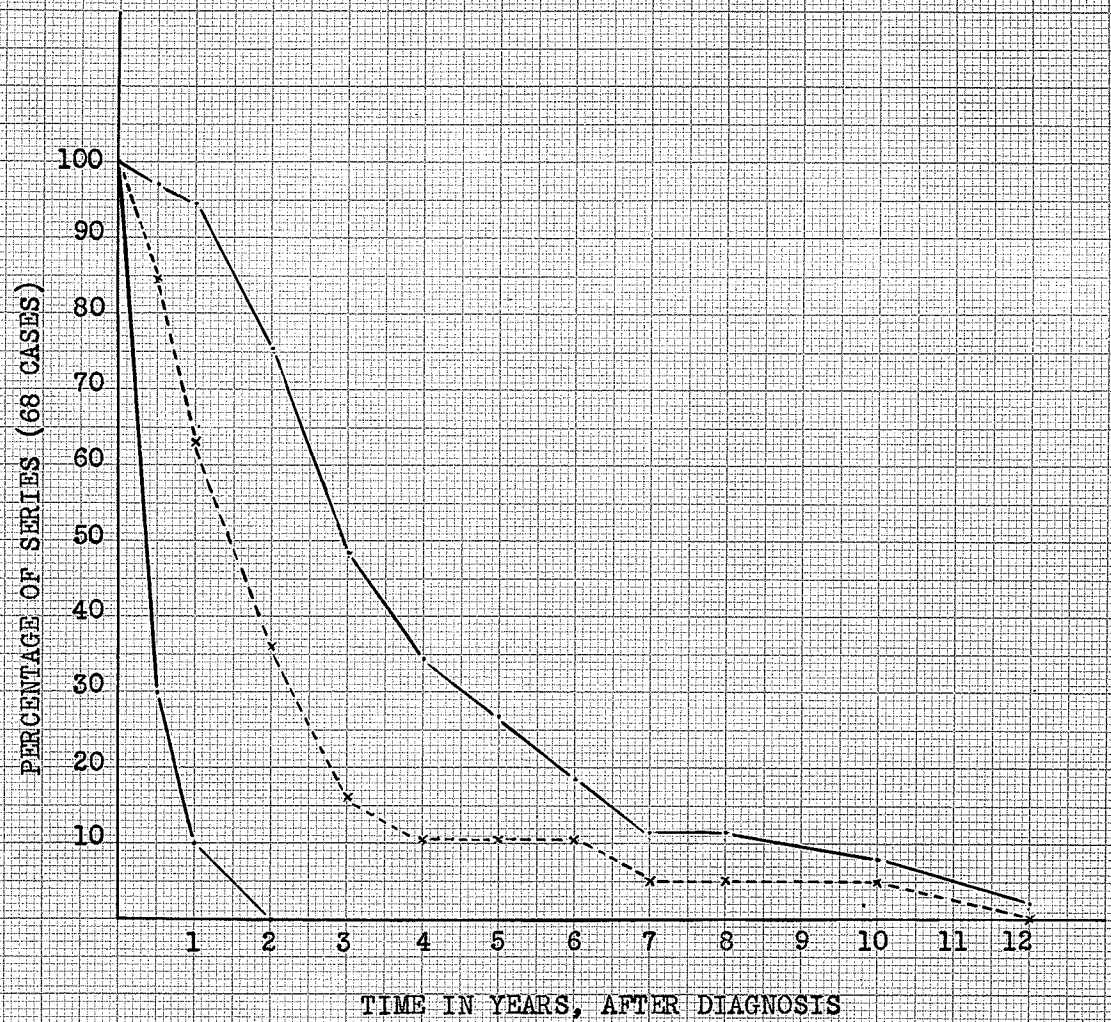
TABLE XVIII

THE SURVIVALS (IN PERCENTAGES) OF EACH CLINICAL CLASS
EXCLUDING POST-OPERATIVE DEATHS (68 CASES)

Class	% living 6 months or longer	1 year or longer	2 years or longer	3 years or longer	4 years or longer	5 years or longer	6 years or longer	7 years or longer	8 years or longer	10 years or longer	12 years or longer
A	97	94.5	75.5	48.6	34.8	27	18.9	11.7	11.7	8	2.7 (1 case) (144 months)
B	84.2	63.1	36.3	15.7	10.5	10.5	10.5	5	5	5	0
C	30	10	0	0	0	0	0	0	0	0	0

CHART 3

SURVIVAL RATES IN PERCENTAGE OF SIXTY-EIGHT CASES OF CARCINOMA OF THE PROSTATE, CLASSIFIED ACCORDING TO THE METHOD OF FERGUSON



CHAPTER VII

MICROSCOPIC CLASSIFICATION

The tissue sections of this series were classified according to the histological method of Edwards, whose classification is given in detail on page 27. Thirty-two cases or 40 per cent of the series showed only one type of carcinoma. All possible combinations were found in the remaining thirty-eight cases or 60 per cent of the series, as indicated in the following tables.

TABLE XIX

THE NUMBER AND PERCENTAGE OF THIS SERIES SHOWING ONE TYPE OF CARCINOMA (32 CASES OR 40% OF SERIES)

	No. of cases	% of 80 cases
Duct carcinoma only	10	12.5
Acinar carcinoma only	4	5
Anaplastic carcinoma only	17	21.5
Intratubular carcinoma only	1	1.2

TABLE XX

THE NUMBER AND PERCENTAGE OF THIS SERIES SHOWING A MIXED HISTOLOGICAL PICTURE (48 CASES OR 60% OF SERIES)

	No. of cases	% of 80 cases*
Duct features	32	40
Acinar features	18	22.5
Anaplastic features	38	47.5
Intratubular features	24	30

*Figures of this column total more than 100%, since the 48 cases had two or more features; thus, 28 cases showed two types, 17 cases showed three types and 4 cases had all four types of carcinoma.

The data obtained after microscopic classification. The duration of the symptoms prior to operation, the duration of the illness from the onset of symptoms until death and the time of survival after surgical treatment for each case in each classification are given in the tables following. In some instances, only the time of survival after the first surgical treatment is given. Only three classes are noteworthy, namely, the duct, acinar and anaplastic carcinomas which occurred as pure types. The duct and acinar carcinomas had the longest duration of symptoms and the longest survival after treatment of any of the groups, while the anaplastic carcinomas had a relatively short duration of symptoms and survival after treatment. Four cases of anaplastic carcinoma exceeded in duration of survival the shortest survival of the duct carcinomas, while only two cases exceeded the duration of survival of the shortest acinar carcinoma.

TABLE XXI

TABLE SHOWING THE DURATION OF SYMPTOMS AND THE PERIOD OF SURVIVAL AFTER OPERATIVE TREATMENT (TIME GIVEN IN MONTHS)

Type of carcinoma	Case	Duration of symptoms prior to operation	Duration of illness from onset to death	Time of survival after biopsy
Duct carcinoma	1	24	43	21
	2	61	90	29
	3	-	-	64
	4	3	78	75
	5	96	115	19
	6	-	-	127
	7	70	216	144
	8	140	190	50
	9	-	-	34
	10	1	45	44

TABLE XXI (CONTINUED)

TABLE SHOWING THE DURATION OF SYMPTOMS AND THE PERIOD OF SURVIVAL AFTER OPERATIVE TREATMENT (TIME GIVEN IN MONTHS)

Type of carcinoma	Case	Duration of symptoms prior to operation	Duration of illness from onset to death	Time of survival after biopsy
Acinar carcinoma	1	356	384	28
	2	127	192	75
	3	36	168	132
	4	72	132	60
Anaplastic carcinoma	1	-	-	1
	2	3.5	5	1.5
	3	8	23	15
	4	12.5	18	5.5
	5	-	-	4.5
	6	12	24	16
	7	1	13	12
	8	8	16	8
	9	12	26	14
	10	44	48	4
	11	12	35	23
	12	42	55	13
	13	5	24	19
	14	-	-	42
	15	72	84	12
	16	-	31	31
	17	-	-	16
Intratubular carcinoma	1	-	-	5
Four types mixed	1	13	18	5
	2	64	94	30
	3	20	36	16
Duct and Intratubular	1	35	72	37
	2	36	36	POD*
	3	16	24	8
Duct and Acinar	1	-	24	24
	2	22	156	134

* POD = Post Operative Death.

TABLE XXI (CONTINUED)

TABLE SHOWING THE DURATION OF SYMPTOMS AND THE PERIOD OF SURVIVAL AFTER OPERATIVE TREATMENT (TIME GIVEN IN MONTHS)

Type of carcinoma	Case	Duration of symptoms prior to operation	Duration of illness from onset to death	Time of survival after biopsy
Duct and Anaplastic	1	3.5	7	3.5
	2	9	20.5	11.5
	3	12	13	1
	4	27	47	20
	5	42	127	85
	6	5	54	49
	7	6	27	21
	8	36	144	108
	9	-	-	15
	10	-	-	23
Acinar and Intratubular		-	-	-
Acinar and Anaplastic	1	117.5	120	2.5
	2	-	-	65
	3	84	132	48
	4	12	36	24
Anaplastic and Intratubular	1	13	26	13
	2	23	24	1
	3	135	192	57
	4	13	15	2
	5	28	36	8
	6	6	12	6
	7	2	2.5	POD* .5
	8	-	2.25	2.25
Duct, Acinar, Intratubular	1	6	81	75
	2	13	18	5
	3	1	24	23
Duct, Acinar, Anaplastic	1	70	84	14
	2	20	99	79
	3	7	51	44
	4	-	-	8
	5	-	-	2
	6	.5	2	1.25

* POD = Post Operative Death

TABLE XXI (CONTINUED)

TABLE SHOWING THE DURATION OF SYMPTOMS AND THE PERIOD OF SURVIVAL AFTER OPERATIVE TREATMENT (TIME GIVEN IN MONTHS)

Type of carcinoma	Case	Duration of symptoms prior to operation	Duration of illness from onset to death	Time of survival after biopsy
Duct, Intratubular, Anaplastic	1	38	48	10
	2	2	30	28
	3	24	60	36
	4	23	48	25
	5	7	28	21
	6	12	40	28
Acinar, Intratubular, Anaplastic	1	48	84	36
	2	-	-	13

TABLE XXII

SURVIVALS, EXCLUDING POST-OPERATIVE DEATHS,
OF THOSE CASES WHICH SHOWED A PURE HISTOLOGICAL TYPE

Type of Carcinoma		% living 6 months or longer	1 year or longer	2 yrs. or longer	3 yrs. or longer	4 yrs. or longer	5 yrs. or longer	6 yrs. or longer	7 yrs. or longer	10 yrs. or longer	11 yrs. or longer	12 yrs. or longer
Duct	(10)	100	100	80	70	60	50	40	30	30	20	10*
Acinar	(4)	100	100	100	75	75	75	50	25	25	25	*
Anaplastic	(17)	70.5	47	11.7	5.8	0	0	0	0	0	0	0

* One case of duct carcinoma and one case of acinar carcinoma were still alive in July, 1950.

CHART 4

THE LENGTH OF SURVIVAL AFTER DIAGNOSIS OF THE DUCT, ACINAR AND ANAPLASTIC HISTOLOGICAL TYPES

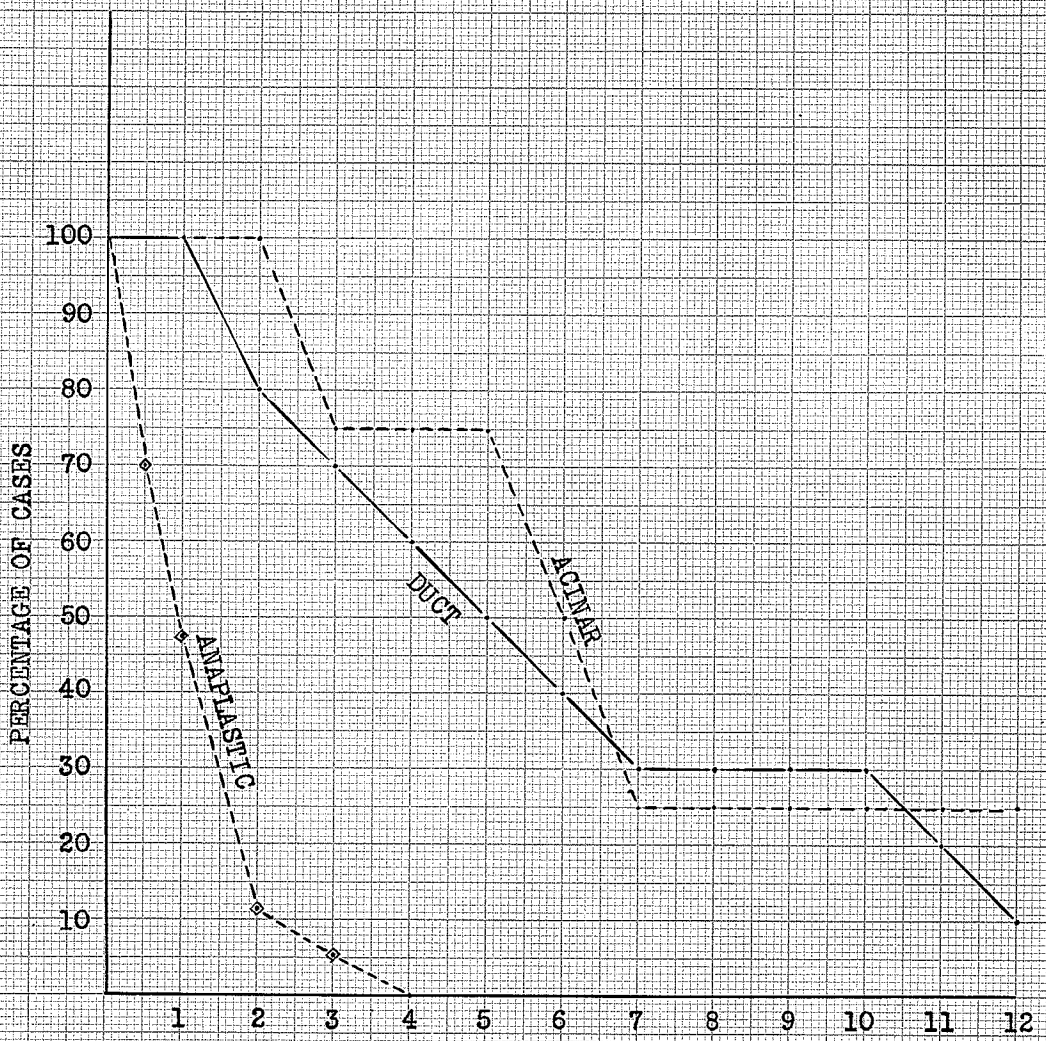


TABLE XXIII

SUMMARIZING DATA OF THE HISTOLOGICAL TYPES,
OF 80 CASES OF CARCINOMA OF THE PROSTATE

Type of Carcinoma	No. of cases	% of series	*Duration of symptoms prior to operation			*Duration of illness from onset to death			*Time of survival after first treatment		
			Aver.	Longest	Shortest	Aver.	Longest	Shortest	Aver.	Longest	Shortest
Duct	10	12.5	56.4	140	1	111	216	45	60.7	144#	19
Acinar	4	5	147	356	36	219	384	132	73.7	132#	28
Anaplastic	17	21.2	18.3	72	0/	31	84	5	13.9	42	1
Intratubular	1	1.2	-	-	-	-	-	-	-	-	-
All four types, mixed	3	3.9	32	64	13	47	94	18	17	30	5
Duct and intratubular	3	3.9	32	36	16	44	72	24	-	-	-
Duct and acinar	2	2.5	-	22	0	-	156	24	-	134	24
Duct and anaplastic	9	11.2	17.4	42	3.5	55	144	7	33.6	1.8	1
Acinar and anaplastic	4	5	71	117	12	97	132	36	34	65	2.5
Acinar and intratubular	1	1.2	-	-	-	-	-	-	-	-	-
Anaplastic and intratubular	8	10	31	135	2	38.5	192	2.25	11.2	57	1
Duct, acinar, intratubular	3	3.9	6.6	13	1	72	81	18	34.2	75	5
Duct, acinar, anaplastic	6	9.5	24.3	70	.5	59	99	2	24.6	79	2
Duct, intratubular, anaplastic	6	9.5	17.6	38	2	42.3	60	28	24.6	36	10
Acinar, intratubular, anaplastic	2	2.5	-	-	-	-	-	-	-	36	13

*Time in months.

/Acute retention.

#These cases were still alive in July, 1950.

CHAPTER VIII

COMPARISON OF FERGUSON'S CLINICAL CLASSIFICATION AND EDWARDS' HISTOLOGICAL CLASSIFICATION

Comparison of the cases classified according to the methods of Ferguson and Edwards is given in the Table below. Unfortunately, only inferences can be made, since the number of cases is small. It will be noted, however, that the two histological types of carcinoma with the best prognosis, that is, the duct and acinar types, are mostly in Class A, whereas those cases showing only anaplastic carcinoma and having the poorest prognosis are found mostly in Class B. The comparison does not hold when figures for the mixed types are considered, and on the basis of this small series, no relationship is apparent.

TABLE XXIV

COMPARING THE DISTRIBUTION OF CLINICAL CASES AND HISTOLOGICAL TYPES

Histological type	Ferguson's clinical classification Number of cases		
	A	B	C
Duct	7	2	0
Acinar	4	0	0
Anaplastic	4	9	2
Intratubular	0	0	0
All four types, mixed	0	2	1
Duct and Intratubular	3	0	0
Duct and Acinar	0	1	0
Duct and Anaplastic	5	0	2
Acinar and Intratubular	1	0	0
Acinar and Anaplastic	4	0	1
Anaplastic and Intratubular	1	2	2
Duct, Acinar and Intratubular	1	2	0
Duct, Acinar and Anaplastic	3	0	0
Acinar, Intratubular and Anaplastic	0	1	0
Duct, Intratubular and Anaplastic	4	1	2

TABLE XXV

COMPARING THOSE CASES SHOWING ONE HISTOLOGICAL TYPE OF CARCINOMA, FURTHER SUBCLASSIFIED BY FERGUSON'S CLINICAL METHOD

Histological type of carcinoma and the clinical classification of the case.	Age of the patient at the time of diagnosis.	Duration of the symptoms prior to operation. Time in months.	Duration of the illness from onset to death. Time in months.	Time of survival after biopsy. Time in months.	Remarks
Duct carcinoma	83	-	-	64	
Class A	67	3	78	75	
	76	96	115	19	
	70	-	-	127	
	68	70	216	144	Considered benign hypertrophy pre-operatively. Still alive (July, 1950). Section shows definite carcinoma.
	82	190	20 years	50	
	69	-	-	34	
Duct carcinoma	75	24	43	21)	Both of these cases had clinical
Class B	72	61	90	29)	evidence of metastases. Both cases had extravesicle pain. Both suffered hematuria.
Acinar carcinoma	71	32 years	-	28	(All cases have
Class A	73	127	192	75	(long duration of
	79	36	168	132	This case still (symptoms prior to
					alive in July/50.(first admission.
	71	72	132	60	(
Anaplastic	-	42	55	13	Diagnosed clinically as benign
Class A					prostatic hypertrophy.
	88	5	24	19	
	72	-	-	42	
	71	72	84	12	Died of carcinoma of the stomach.

TABLE XXV (CONTINUED)

COMPARING THOSE CASES SHOWING ONE HISTOLOGICAL TYPE OF CARCINOMA, FURTHER SUBCLASSIFIED BY FERGUSON'S CLINICAL METHOD

Histological type of carcinoma and the clinical classification of the case.	Age of the patient at the time of diagnosis.	Duration of the symptoms prior to operation. Time in months.	Duration of the illness from onset to death. Time in months.	Time of survival after biopsy. Time in months.	Remarks
Anaplastic carcinoma Class B	82	8	23	15	Most of the patients suffered extra-vesical pain, loss of weight. Their symptoms were of short duration and with one exception either close to the average age or younger than the average age of this series.
	69	$12\frac{1}{2}$	18	$5\frac{1}{2}$	
	50	-	-	$4\frac{1}{2}$	
	72	12	35	23	
	68	44	48	4	
	72	12	26	14	
	63	8	16	8	
	70	1	13	12	
	64	12	24	16	
Anaplastic carcinoma Class C	63	$1\frac{1}{2}$	5	$3\frac{1}{2}$	
	62	-	-	P.O.D.	Post-operative death.

CHAPTER IX

OBSERVATIONS, SUMMARY AND CONCLUSIONS

I. OBSERVATIONS

1. The arithmetic mean of the age at the time of diagnosis of 77 patients in this series of carcinoma of the prostate is 71.4 years. The youngest patient of the series was 48 years of age while the oldest patient was 88 years at the time of diagnosis.

2. A family history of cancer was recorded in six cases. There was no record of any relative having carcinoma of the prostate in this series.

3. In eleven cases a history of previous genito-urinary disease was recorded. Only one patient is known to have had a positive blood Wassermann reaction.

4. Entrance complaints were more numerous than initial complaints. Frequency of urination and nocturia were the two most common symptoms, either as initial complaints or as entrance complaints. Hematuria as an initial single symptom occurred in two cases, while complete urinary retention as the only initial complaint occurred in four cases. The duration of the symptoms before admission varied from less than one day to more than 190 months.

5. Approximately one third of the cases were considered to have good general health on their first admissions.

6. In more than 80 per cent of cases the gland was enlarged, hard and nodular as felt per rectum. Only one of the glands was considered

small in size. Only one case was described as soft in consistency.

7. The right lobe of the prostate was involved with carcinoma almost as often as the left lobe in this series.

8. Trabeculation of the urinary bladder was recorded in twenty cases of the series. Evidence of tumor invasion of the prostatic urethra or base of the bladder was recorded in twenty-two cases at the time of diagnosis.

9. Twenty-eight of the thirty-one plain roentgen films of the kidney, ureter and bladder revealed nothing pathological.

10. Lack of clinical description of the cases of the series precluded the use of the clinical classification of the American College of Surgeons.

11. Approximately one half of the cases of this series were easily classified according to Ferguson's clinical classification. Some of the cases did not fill the criteria of any group of the criteria of this classification. The factor of age gave most difficulty and was given less weight than the duration and type of symptoms. The average duration of survival and the relative percentage of the series for each group agree closely with the figures given by Ferguson. The average time of survival after diagnosis is different in each class of Ferguson's classification; however, the shortest and longest duration of survival are practically the same in Class A and Class B of this series. Such a finding decreases the clinical value of this classification.

12. Thirty-two cases or 40 per cent of the series showed only one histological type of carcinoma, after the sections were classified

according to the histological method of Edwards. Seventeen cases showed only anaplastic carcinoma, ten showed only duct carcinoma, while four showed only acinar carcinoma. Forty-eight cases or sixty per cent of this series had more than one histological type of carcinoma. Twenty-eight cases had two histological types of carcinoma, seventeen cases had three types, and four cases had all four types of Edwards' classification.

13. The average length of survival after diagnosis for the whole series is 31.4 months. The group of acinar carcinomas have an average survival of 73.7 months, while the group of duct carcinomas have an average of 60.7 months. Those cases with only anaplastic carcinoma have an average survival after diagnosis of 13.9 months. Of those cases which have more than one histological type of carcinoma, only two groups of this series are noteworthy. Those cases which have anaplastic and intratubular carcinoma have a survival of 11.2 months. Cases with all four histological types have an average survival of 17 months. The remaining groups with two or three histological types of carcinoma have average survivals for each group ranging between twenty-four and thirty-four months, and when these cases are grouped collectively, the average survival of 30.2 months is obtained.

14. Seventy-seven per cent of the duct and all of the acinar carcinomas were in Class A of the clinical classification while 69.3 per cent of the anaplastic carcinomas were in Class B. The following exceptions are noted: (a) Two cases of duct carcinoma placed in Class A lived only nineteen and thirty-four months after the date of diagnosis. (b) Two

cases of duct carcinoma lived only twenty-one and twenty-nine months after diagnosis (these cases were placed in Class B since both had extra-vesical pain). (c) One case of anaplastic carcinoma, in Class A, lived forty-two months while other cases of anaplastic carcinoma in Class A lived twelve, thirteen, and nineteen months respectively.

15. The relationship, if any, between the mixed histological types and the clinical classification is not apparent in this small series.

II. SUMMARY

One hundred and sixty-five cases of carcinoma of the prostate diagnosed clinically and confirmed by tissue section between 1930-1940 inclusive were reviewed and of these, histories, follow-ups and tissue sections were obtained in eighty-seven cases. On re-examination histological evidence of carcinoma was lacking or insufficient in seven cases, so that a series of eighty cases of carcinoma of the prostate was available for study.

The clinical histories of the cases were summarized and the results tabulated. The cases of the series were classified according to the clinical method of Ferguson and the clinical method used by the American College of Surgeons. The tissue sections were classified according to the histological classification of Edwards. A comparison of the two classifications has been made.

III. CONCLUSIONS

1. Forty per cent of this series of carcinoma of the prostate have, in tissue removed at operation, the pure histological types of acinar, duct, intratubular or anaplastic carcinoma of Edwards' classification, while sixty per cent have the histological types mixed in various proportions and combinations.

2. This study indicates a relationship between the length of survival after diagnosis and the histological types of duct, acinar, anaplastic and the combined form of anaplastic and intratubular carcinoma of the prostate.

3. In this series, those cases showing only duct or acinar carcinoma had the longest survival after diagnosis, while those cases showing only anaplastic carcinoma or the combined anaplastic and intratubular carcinoma had the shortest average duration of survival after diagnosis. The average duration of survival of the remaining cases showing mixed histological types is 30.2 months which is approximately equal to the average duration of the whole series (31.4 months) and the reported series of untreated cases in the literature.

4. Although Ferguson's classification is not applicable to every clinical case, it takes into consideration the factors which are known to influence prognosis. When Ferguson's clinical classification is used in conjunction with Edwards' histological classification, the prognosis most likely correct is the least favourable given by either classification.

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APPENDIX A

APPENDIX A

RECORDS OF SEVEN CASES WHERE REVIEW OF AVAILABLE TISSUE SHOWED EVIDENCE OF CARCINOMA EITHER LACKING OR INSUFFICIENT

Seven cases of the original material had been diagnosed as carcinoma of the prostate, but on review of the tissue available in the laboratory files, evidence of carcinoma was either lacking or insufficient so these cases were not included in the series. In order to record the seven cases for future reference, the history numbers, laboratory numbers and a brief summary of the history and findings from these sources are given below.

Case WGH 5219-40; OPD 46618; Pathology No. 2442-40

This patient, a white male, 65 years old, married, was admitted to hospital on August 10, 1940, complaining of difficulty and frequency of urination since January of 1940. The patient was small and thin, but had noticed no weight loss. The right lobe of the prostate was enlarged, hard, nodular and fixed. Trabeculation of the urinary bladder was recorded together with enlargement of the median and lateral lobes as seen on cystoscopic examination. The blood urea nitrogen was 14 milligrams per cent. Five grams of prostatic tissue were removed by transurethral resection on August 21, 1940 and the tissue was reported as adenocarcinoma, grade one. The patient died on April 25, 1941, in hospital. No autopsy was performed. The final diagnosis was carcinoma of the prostate.

No evidence of carcinoma is seen in the sections available for study.

Case WGH 6801-32; Pathology Nos. 1900-32, 1967-32, 2065-32

White male, married, 65 years of age, admitted on September 16, 1932. From 1917 to 1927 the patient had frequency and nocturia. Lower abdominal pain and difficulty began in 1927. On September 10, 1932, the patient had acute retention and was admitted on September 16, 1932. The prostate was enlarged and rather firm as felt per rectum. Two hundred pus cells were found per high power field in the centrifuged urinary sediment. Cystoscopic examination revealed trabeculation II, median lobe intravesical enlargement II, and median lobe intraurethral enlargement II; lateral lobe enlargement intravesical II. The blood urea nitrogen was 15 milligrams per cent. On September 20, 1932, 10.2 grams of tissue removed by transurethral resection were reported to show benign prostatic hyperplasia on microscopic examination (1900-32). A further resection was done on September 29, 1932 (1967-32) and this was reported as carcinoma, grade two, together with a very marked inflammatory reaction and much necrosis. On October 17, 1932 (2065-32) another resection was performed in which 19.8 grams of tissue were removed, and the microscopic report of this tissue, in summary, indicated a definite malignancy of low grade, similar to the intraduct carcinoma of the breast. The patient died of carcinoma of the prostate on September 19, 1945. No autopsy was performed.

The microscopic picture of 1967-32 is that of necrosis and

inflammatory reaction following a previous transurethral resection. Some intratubular proliferation and prostatitis are seen in 2065-32, but no definite evidence of malignancy is seen in the five sections available for study.

Case WGH 11268-38; Pathology Nos. 351-38, 510-38

White male, aged 72 years at the time of admission on January 14, 1938. The patient had symptoms of "mild prostatism" for a period from four to six years prior to admission. On December 24, 1937, acute retention required catheterization. On admission on January 14, 1938, entrance complaints were difficulty, dysuria, urgency, incontinence and retention. The patient was obese. Laboratory investigation included hemoglobin estimation (85%), blood urea nitrogen (100 mgms %), blood creatinine (8.1 mgms %). Plain films of the kidneys, ureters and the bladder revealed nothing of note, while an intravenous pyelogram showed a slight dilatation of both ureters. Eleven grams of tissue removed by transurethral resection on February 4, 1938 (351-38) were reported to show adenocarcinoma, grade two, on microscopic examination. A second resection on February 19, 1938, (510-38) was reported to show no evidence of carcinoma. The patient died in May, 1942. The cause of death is not known from the records available.

Five sections of two blocks of tissue are available for study. No evidence of carcinoma is seen in the sections. Benign prostatic hyperplasia, chronic prostatitis and calculi are present.

Case WGH 688-38; Pathology No. 1387-38

This sixty-four year old, white married male was admitted to hospital in May, 1938. In 1934, the patient began to have intermittent frequency and in the same year had prostatitis which was treated by massage. On admission, in May, 1938, the entrance complaints were frequency, difficulty, urgency and backache. On examination, the prostate was enlarged (2 plus) and a deeply situated, firm mass was felt in the middle portion of the gland. The residual urine was five ounces in which a few pus cells were found per high power field in the centrifuged sediment. Blood urea nitrogen was estimated to be 12 milligrams per cent. A pre-operative diagnosis of benign prostatic hypertrophy was made. A transurethral resection was done on May 11, 1938 and 5.5 grams of tissue removed. Microscopic sections were reported to show carcinoma in situ. The patient died on February 12, 1942, thirteen days after a gastric resection for carcinoma of the stomach. No autopsy was performed.

Two sections are available for study. Prostatitis, calculi and intratubular proliferation are the main features found. In some places the intratubular proliferation is seen as a collar of cells lining the inner circumference of a circular lumen. The basal layer is regular and no infiltration is found. Edwards stressed further examination of the tissue in such a case, and when this is done, definite evidence of malignancy is usually found.

Case WGH 6538-32; Pathology No. 1945-32.

This 65 year old, white, married male had frequency, difficulty, nocturia and dysuria since 1920. The symptoms gradually became more severe until the patient was admitted on September 7, 1932. The prostate was recorded as small in size; otherwise there was no description. Considerable pus was found in the urinary sediment (not recorded in numbers). Residual urine amounted to twelve ounces. Cystoscopic examination revealed hypertrophy of the lateral lobes and minimal trabeculation. The condition was diagnosed benign prostatic hypertrophy before operation. On September 26, 1932, a suprapubic prostatectomy was performed and a piece of prostatic tissue three centimetres in diameter was removed. The microscopic report of this tissue was adenocarcinoma of the prostate. The patient died on August 10, 1934 in hospital, of pyelonephritis. No autopsy was performed.

No carcinoma is seen in the sections available for study.

Case WGH 3549-37; Pathology No. 2061-37

White male, 75 years old, admitted to hospital in July, 1937. No history is recorded other than the patient suffered from frequency and nocturia for an unstated length of time. The general condition of the patient was considered to be good. No rectal examination was recorded. Six ounces of residual urine were obtained. On cystoscopic examination, the base of the bladder and the posterior urethra were ragged with tumor tissue. Seven and one-half grams of tissue were removed by transurethral resection on July 19, 1937, and the microscopic report was adenocarcinoma

grade two. The patient died on July 29, 1940 of carcinoma of the prostate. No autopsy was performed.

No definite evidence of carcinoma is seen in either of the two sections available for study.

Case WGH 4866-32; Pathology No. 1762-32

This white male, 65 years old, widower, pensioner, was admitted on August 10, 1932. In 1927, the patient had a single episode of acute retention which lasted only one day and did not require treatment. The patient had had frequency and difficulty for "years." On August 7, 1932, the patient had acute retention with overflow and was admitted on August 10, 1932, still with retention, incontinence and low back pain. No weight loss had been noticed by the patient whose general condition was considered to be good on admission. The prostate as felt per rectum was enlarged. The right lobe was stony hard and nodular. Tumor extended upwards into the right seminal vesicle. Cystoscopic examination revealed a median bar III, fixed posterior urethra and trabeculation I. The blood urea nitrogen was estimated to be 74 milligrams per cent and the blood creatinine to be 3.0 milligrams per cent. Plain films of the kidneys, ureters and bladder revealed no disease. Three and one-half grams of tissue removed by transurethral resection on April 30, 1932, were reported to show early carcinoma of the prostate on microscopic examination. The patient died on April 9, 1933. Autopsy examination (A 1641) disclosed pyonephrosis, multiple abscesses of the kidneys, metastases to abdominal lymph nodes, the lungs and the iliac bones. A

carcinoma of the stomach was found as well as the carcinoma of the prostate.

Each of the two sections of this case shows a small area of densely packed, darkly-staining cells with hyperchromatic, irregular nuclei. In the plane of section not more than 500 cells are seen in either area. There is some apparent infiltration. The lesions in these sections are probably carcinoma. Chronic prostatitis is also present.