

## REPRINTS AND REFLECTIONS

# On the frequency of occurrence of occult carcinoma of the prostate

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For a number of years the writer has been impressed by the frequency with which small carcinomata have been found in the prostate in the routine autopsy material of this Department. It seemed that these small tumours, which had attracted no attention clinically and which were brought to light unexpectedly at autopsy, were being encountered much more often than the usual estimates of the frequency of occurrence of prostatic carcinoma would have led on to expect. Impressions formed from unanalysed material are, of course, often misleading, and it was in the attempt to gain more precise information about the matter that the present study was undertaken. This study makes no pretensions to being an elaborate and complete examination of the question. It represents only a very simple and direct study of a limited amount of readily available material, the nature of which was such as to preclude any detailed analysis of various associated problems which suggest themselves. The results of the study are, nevertheless, sufficiently clear-cut and interesting to warrant being set forth in a brief report.

It is the practice in this Department to have histological preparations made from each organ of every body that comes to autopsy, regardless of whether the tissue appears normal or abnormal macroscopically, or of whether the clinical history does or does not provide a reason for suspecting the presence of microscopic lesions. Since this procedure involves the preparation of a large number of slides from each autopsy, it is only in the case of a special interest in a particular organ that more than one block is sectioned routinely from a macroscopically normal organ on which the clinical history casts no suspicion, or from one exhibiting only a very common and obvious lesion. In most cases, then, there was readily available for the present study only the routine single section of the prostate taken at the time of autopsy. It is important to point out, therefore, that although the frequency with which cancer was found in these sections is surprisingly high, the actual incidence of this condition is, in all probability, still higher; for the tumours with which this article deals are, for the most part, so small and so inconspicuous macroscopically that it was only a matter of chance that the routine section passed through them. Had numerous sections been made through various regions in each prostate there can be little doubt that similar minute early

carcinomata would have been found in some of the negative cases in the present series.

It must be particularly emphasized that in each instance recorded in this article the growth in question represents a true carcinoma. The writer is well aware that occasional forms of benign hypertrophy may be mistaken for carcinoma; that the prostatic acini may be so distorted by inflammatory lesions as to simulate carcinoma; and that when nodules of hypertrophy are present in a prostate, the previously normal tissue may be so compressed by the expanding nodules as to appear in the form of strands of cells which, when cut at various angles, may simulate strands of tumour cells on casual observation. These confusing conditions however, are readily distinguishable from 'frank' carcinoma on careful examination, and in the present series no cases regarded as questionable were included. In each instance, the tumour is composed of plump epithelial cells growing irregularly in strands and in acinar formation, and invading the neighbouring tissue in the manner characteristic of carcinoma. The illustrations are typical of the character of all the tumours in the group.

Since most of the tumours in this report represent the very early stages in the development of prostatic cancer, it is regrettable that the material was not of a nature which would have permitted a more satisfactory study of the question of the most common site of origin of the tumours. It is impossible in most cases to determine precisely the level at which the section containing the tumour was taken. However, although the exact level of the sections cannot be determined, it is perfectly clear that there is a decided tendency for the very early tumours to be situated either laterally or posteriorly in the tissue near the capsule of the gland, with the result that the capsule is not infrequently invaded before the prostate itself is appreciably enlarged by the growth of the tumour.

In the case of the late tumours involving practically the entire gland it was not possible to determine the co-existence of benign hypertrophy, but in the remainder of the cases, hypertrophy was present in addition to the carcinoma in 70%. When the tumours are very small, i.e. before widespread invasion has occurred, they are often situated either in normal tissue or in the glandular tissue which is compressed by nodules of hypertrophy. That cancer may arise also within the newly formed tissue of a nodule of hypertrophy there is no doubt, but the situation of the early tumours comprising the present series suggests that the non-hypertrophied senile tissue and the compressed atrophic glands outside the expanding nodules of hypertrophy are, perhaps, favourite sites of origin.

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**Table 1.** Forty-one cases of primary carcinoma of the prostate

Urological service				Surgical service				Medical service			
Autopsy number	Age	Race	Diagnosed clinically	Autopsy number	Age	Race	Diagnosed clinically	Autopsy number	Age	Race	Diagnosed clinically
12 076	67	W.	+	12 748	75	w.	0	12 606	60	C.	+
12 204	74	W.	+	12 791	73	c.	0	12 050	71	W.	0
12 363	76	W.	+	12 897	78	c.	0	12 134	66	W.	0
12 464	56	W.	+	12 969	66	w.	0	12 450	54	W.	0
12 494	71	W.	+	13 063	73	w.	0	12 661	54	W.	0
12 743	71	C.	+	13 257	57	w.	0	12 774	73	W.	0
12 863	80	W.	+	13 385	58	w.	0	12 941	71	W.	0
13 575	76	W.	+	12 483	50	c.	+	12 974	56	C.	0
13 619	69	W.	+					13 059	65	C.	0
13 628	90	W.	+					13 261	70	W.	0
13 637	60	W.	+					13 297	67	W.	0
13 902	65	W.	0					13 341	71	W.	0
12 053	70	C.	0					13 383	80	W.	0
12 074	52	C.	0					13 433	60	W.	0
12 493	75	W.	0					13 636	75	W.	0
13 713	80	W.	0					13 900	70	C.	0
13 785	68	W.	0								

**Table 2.**

Age	Number of males in 2000 autopsies	Cancer of prostate	Percent cancer
50-55	69	4	5.6
56-60	61	7	11.4
61-65	56	2	3.5
66-70	42	9	21.4
71-75	43	12	27.9
76-80	16	6	37.5
81-90	5	1	20.0
Total	292	41	14.0

**Table 3.** Age incidence and clinical recognition of 41 cases of cancer of prostate

Age	Number of cases	Percent of total number	Not recognized clinically	
			Number	Percent
50-55	4	9.7	3	75.0
56-60	7	17.0	4	57.1
61-65	2	4.8	1	50.0
66-70	9	21.9	7	77.7
71-75	12	29.2	9	75.0
76-80	6	14.6	3	50.0
81-90	1	2.4	0	0.0
Total	41		27	65.8

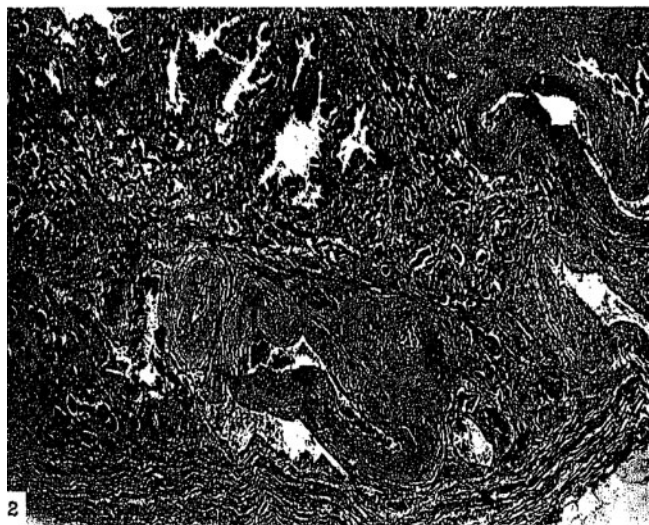
Serial sections of the tumours would, however, be necessary for the accurate determination of this point.

The present study was made from the material contained in 2000 consecutive autopsies performed in this Department during the past three years. Of these 2000 cases, 292 were males of 50 years or more in age, and it was this series of 292 cases, unselected except as regards age, which provided the material for the study (eighty-two of the 292 cases were from the Urological Service, the remaining 210 cases were from the Medical and the General Surgical Services). The sections of the prostates from all of these cases were carefully examined in the search for the tumours, with the results which are summarized in Tables 1, 2 and 3. These results were surprising to us even though the study had been begun with the impression that cancer of the prostate is more common than is ordinarily suspected.

It can be seen from the tables that primary carcinoma was found in the prostate in 41 (14.0%) of the 292 unselected males past the age of 50 who have died in this hospital from a wide variety of diseases during the past 3 years. In only 14 of the 41 cases was the presence of the carcinoma recognized clinically. In 12 of these 14 cases, the diagnosis was made on the Urological Service. In only one of the 16 cases from the Medical Service was the presence of the tumour recognized clinically, nor was it recognized in seven of the eight cases from the Surgical Service, nor in 5 of the 17 cases from the Urological Service. It must be emphasized that the failure to have recognized most of these tumours clinically cannot in any sense be construed as a slur upon the diagnostic ability of the clinicians in charge of these patients. The tumours which were

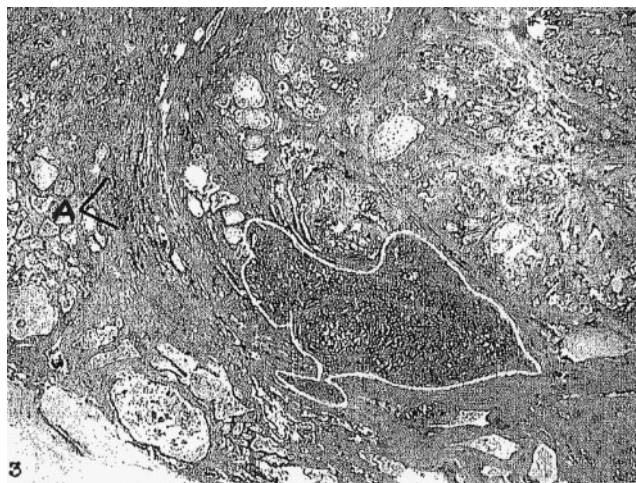


**Figure 1** Low power microphotograph of the tumour in case 12974, Table 1. A marks the urethra. The opposite lateral lobe is included in the section but not photographed. There is no tumour anywhere in the section outside the area enclosed in the white line at B. This area is only 4 mm. in diameter. See Figure 2.



**Figure 2** Higher magnification showing the invasion of the capsule by the tumour illustrated in Figure 1.

unrecognized clinically were in most cases so minute that they were neither seen nor felt even by the pathologist who was able to hold the dissected prostate in his hands and to examine the cut surface visually. I have seen several cases in which, after the microscopic study had revealed the presence of a cancer, a return to the gross specimen still failed to enable one to distinguish the tumour with any certainty even on the cut surface from which the block was taken for sectioning. Figures 1 and 3 will allow one to appreciate the minute size of some of these tumours, and others are even smaller than those illustrated. In several cases in which the gross specimens were available and in which the peri-capsular tissue was found microscopically to have been invaded by a very early carcinoma arising near the capsule, one could indeed, armed with the knowledge that the tumour was present, gain a faint suggestion of the existence of minute macroscopic strands of tumour which were overlooked at the time of autopsy. In two other cases the return to the gross material enabled one to detect on

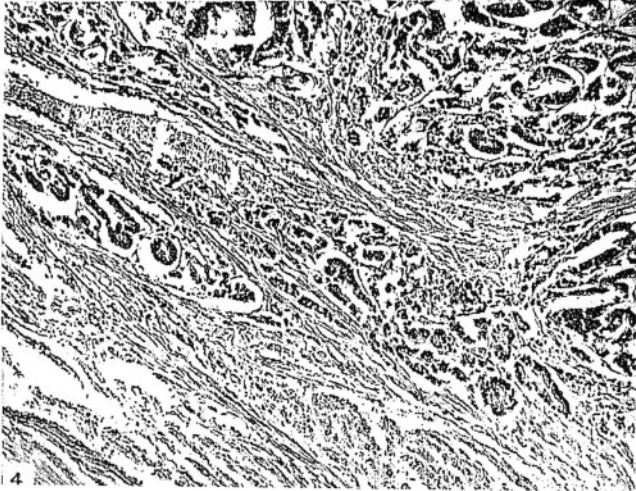


**Figure 3** Low power microphotograph of the tumour in case 12493, Table 1. There is no tumour anywhere in the section (which measures 3 cm  $\times$  2 cm) outside the area enclosed by the white line. This tumour measures only 5 mm. in diameter. The small adini seen at A are compressed, atrophic prostatic acini and not tumour. Another section 3  $\times$  2 cm. taken from a different region in this prostate contains no tumour. See Figure 4.

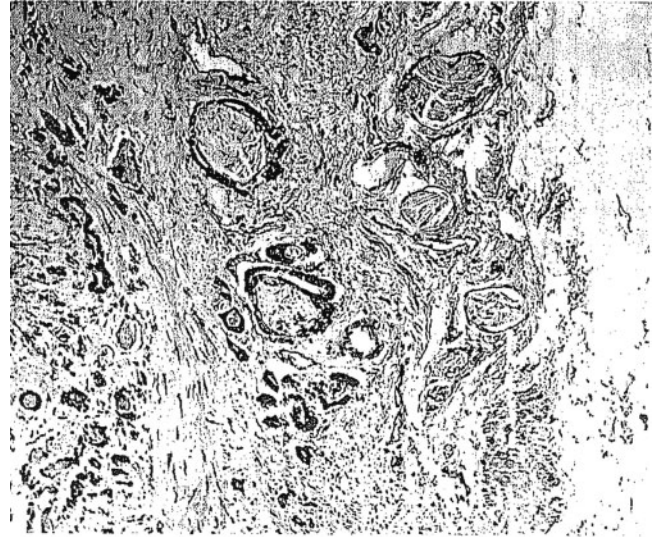
close examination definite though very delicate strands of tumour tissue, extending into the peri-capsular fat, which were not noticed by the pathologist at the time of autopsy; but even in these cases the tumours were exceedingly minute and would have required an exceptionally practised touch to have been palpated clinically if, indeed, their clinical recognition would have been possible at all.

I have made an attempt to determine whether these early cancers cause any constitutional effects which might lead to their clinical recognition before they attained a size large enough to be detected by palpation. This attempt, as might have been anticipated from the nature of the material, was a rather fruitless one for the reason that although anaemia and loss of weight are recorded not infrequently in the histories of the patients, since they were all dying of other diseases these effects could not be ascribed to the presence of the tumour in the prostate. Indeed, Young and Davis<sup>1</sup> have shown that anaemia and wasting rarely occurs before the tumour has reached a size large enough to cause urinary obstruction. Local pain, however, is not infrequently an early symptom, and this may well be due in some cases to the marked tendency of these tumours to invade the lymph spaces surrounding the nerves in and about the capsule of the gland, as illustrated in Figure 6. Considering the frequency with which the tumours are situated near the outer margins of the gland, and their tendency to invade the capsule even when quite small, it is perhaps surprising that pain is not more frequently an early warning symptom.

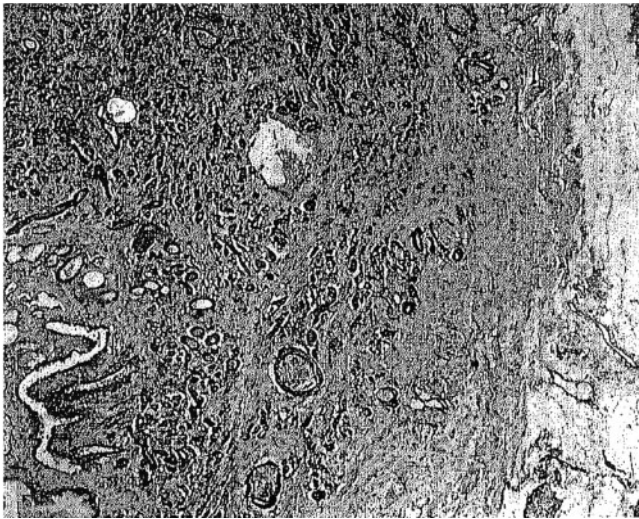
It is recognized that prostatic cancer is often a slowly growing tumour even after clinical symptoms have appeared, and this undoubtedly accounts for the fact that, since the tumour rarely occurs before the age of 50, many of those in whom it has made its appearance die of other diseases of this age period before the tumour causes their death by obstruction or metastasis.



**Figure 4** Higher magnification of the margin of the tumour illustrated in Figure 3.



**Figure 6** Higher magnification of the tumour illustrated in Figure 5, showing the invasion of the lymph spaces surrounding the nerves in the capsule. (Photographs by Mr. Milton Kougler.)



**Figure 5** Invasion of the capsule by the tumor in case 13261, Table 1. See Figure 6.

## Summary

In 292 consecutive autopsies on males 50 years or more in age dying from a wide variety of causes on the Medical, Surgical and Urological Services of the Johns Hopkins Hospital during

the past three years, frank carcinoma of the prostate was found in the routine microscopical section taken at autopsy in 41 cases (14.0%). There is little doubt that a thorough search throughout each gland would have brought to light an even greater number of these tumours, many of which were so small that they were not seen macroscopically at the time of autopsy. The number discovered, however, indicates plainly enough that cancer of the prostate is considerably more frequent than is ordinarily supposed.

In 65.8% of these 41 cases, the tumour was not recognized clinically, having been in most cases of a size too small to have produced symptoms or to have attracted attention on physical examination.

The tumours were most often found near the outer margins of the gland, and even when only a few millimetres in size, showed a tendency to invade the capsule.

## Reference

- <sup>1</sup> Young, HH, Davis, DM. *Young's Practice of Urology*. W.B. Saunders Co., 1927, i, 628.