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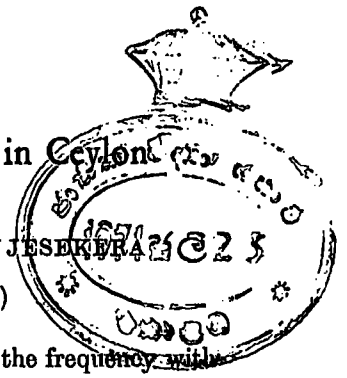

Some Observations on Prostatic Carcinoma in Ceylon

BY

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On account of its inaccessibility, it is not possible to estimate the frequency with which the prostate gland undergoes carcinomatous change. Clinically it is not always easy to distinguish between benign hyperplasia (' senile ' hypertrophy) and carcinoma and macroscopic examination of the gland at necropsies and after surgical removal cannot be relied upon in the differential diagnosis of the two conditions. Even histological distinction between highly differentiated carcinomas and benign hyperplasias is not always easy. Thus wide discrepancies are noted in the figures recorded by different workers who have attempted to estimate the incidence of carcinoma in prostates removed at autopsies or by surgical operations (Willis, 1948). Some of the difficulties in the histological diagnosis of prostatic carcinoma confronting the pathologist are discussed in this paper which is based on a study of 605 prostate glands removed surgically at the General Hospital, Colombo, during the seventeen year period 1936-1952. The prevalent histological types seen in this country are described and an attempt is made to co-relate these with the subsequent histories of some of the sufferers.

The incidence of carcinoma in surgically removed prostates. It will be seen from Table I that the number of prostates submitted for histological examination was comparatively few till 1947, when the addition of surgical staff to the General Hospital, Colombo, resulted in a larger number of prostatectomies and consequently more histological examinations. During the whole seventeen year period, 77 carcinomas were detected histologically in 605 prostate glands—an incidence of 13 per cent. The remaining 528 glands were considered to be cases of benign hyperplasia (' senile ' hypertrophy). This incidence of carcinoma in the whole group is not significantly different from the incidence viz. 15 per cent. and 12 per cent. respectively calculated for the two periods 1936-1946 when fewer prostatectomies were performed and 1947-1952 during which years a larger number of glands was surgically removed.

TABLE I

Years	*Total No. of Prostatectomies*	*Carcinomas*	*Benign Hyperplasia (' Senile ' Hypertrophy)*
1936 (9 Months)	13	2	11
1937	10	2	8
1938	15	4	11
1939	14	6	8
1940	19	4	15

TABLE I—*Contd.*

Years	*Total No. of Prostatectomies*	*Carcinomas*	*Benign Hyperplasia ('Senile' Hypertrophy)*
1941	20	2	18
1942	18	2	16
1943	20	0	20
1944	30	2	28
1945	21	3	18
1946	30	4	26
1947	55	5	50
1948	50	4	46
1949	65	3	62
1950	87	11	76
1951	109	17	92
1952 (3 Months)	29	6	23
Total	605	77	528

Incidence of carcinoma in surgically removed prostates.

Years	*Percentage*
1936-1952	13%
1936-1946	15%
1947-1952	12%

It is therefore reasonable to presume that the incidence of carcinoma in surgically removed prostates in this country appears to vary between 12 to 15 per cent. Swan (1923) and Barringer and Wildbolz (1932) in a comparable series found the proportion of carcinomatous glands to be 25.7 per cent. and 20.0 per cent. respectively. Such variations are partly due to the different histological standards used to assess malignancy in the prostate and partly to the fact that, unlike in Western countries, only a few men are to be found in the older age groups amongst our population who are more liable to develop prostatic carcinoma.

In 450 prostatectomies where the ages of the patients had been recorded it is seen that 20 per cent. and 57 per cent. of the glands were carcinomatous in the age groups 25-44 years and 85 to 104 years respectively whereas only 14 per cent. were carcinomatous between 45 and 84 years (Table II). As it would appear that a surgically removed gland is more likely to show carcinomatous change at these periods of life, several sections of the prostates of patients under 45 and over 85 should be submitted to a very careful histological examination before a definite opinion—whether carcinoma or benign hyperplasia—is expressed.

TABLE II

Age Group	*Prostatectomies*	*Carcinomas*	*% Carcinoma*
25-44 years	5	1	20
45-64 years	189	26	14
65-84 years	249	34	14
85-104 years	7	4	57
Total	450	65	14

Age incidence of prostatic carcinoma. Table III shows the age of onset of 65 carcinomas and 385 benign hyperplasias. The maximum number of carcinomas, viz. 38 per cent. occurred in the decade 65-74.

TABLE III

Age Groups	% *Cases of Carcinoma*	% *Cases of Benign Hyperplasia*
25-34 years	2	1
35-44 years	0	1
45-54 years	3	10
55-64 years	37	33
65-74 years	38	45
75-84 years	14	13
85-94 years	5	1
95-104 years	1	1

Although this finding is in agreement with that of workers in Western countries notably Willis (loc. cit.) a significant difference is that prostatic carcinoma occurs two decades later than carcinomas at other sites in this country. It has been observed that the cancer age for Ceylon based on a study of 1815 carcinomas occurring at 31 different sites is the decade 45-54 (Cooray, 1944) i.e. a decade earlier than in Western countries. It would therefore appear that such factors as a lower expectation of life in our population, differences in social customs, habits and usages which probably explain the earlier onset of carcinoma at other sites, do not operate in the causation of prostatic cancer.

The relationship between benign hyperplasia ('senile' hypertrophy) and carcinoma. The closely similar age incidence of these two conditions and their frequent co-existence have hinted at the possibility of a relationship between benign hyperplasia and carcinoma, and even Willis (loc. cit.) has remarked that it is difficult either to prove or disprove the claim that benign hyperplasia is a pre-cancerous condition. Our histological sections have shown the co-existence of the two conditions in 41 out of the 77 carcinomas i.e. 53 per cent. (Table IV) where the average age was 69.5 years, but in the remaining 36 carcinomas (i.e. 47 per cent.) no evidence of benign hyperplasia was found.

TABLE IV

Frequency of histological types and co-existence of benign hyperplasia in each histological type.

	Total	% *of total*	*No. of cases with co-existent benign hyperplasia*	%
Adenocarcinomas	50	65	32	64
Adenocarcinoma with Anaplasia	7	9	2	28
Trabecular Type	3	4	1	33
Anaplastic Type	17	22	6	35
Total	77	100	41	53

The absence of co-existent hyperplasia however cannot be regarded as evidence of a *de novo* origin from a non-hyperplastic gland because the average age of this group of cases was found to be 63·5 years, at which age the prostate gland is known to undergo hyperplasia. It is more likely that in these cases the carcinomatous picture predominated to such an extent as to completely obscure the hyperplastic process.

The limitations of clinical methods in the diagnosis of prostatic cancer. A careful survey of 29 case records has revealed that a prostatic carcinoma cannot be detected by a clinical examination. The naked eye appearances of the gland after removal are equally unreliable. Physical signs elicited at a clinical examination as well as operative findings such as adherence, fixity and difficulty of enucleation can only lead to a suspicion of malignancy, but no definite criteria other than histological, can be relied upon to differentiate between carcinoma and benign hyperplasia. Enlargement of the gland which was observed in 21 out of 29 cases of carcinoma is met with in benign enlargements too. Consistency of the gland is also not of diagnostic importance, for a hard gland is not necessarily carcinomatous. In those cases of benign hyperplasia where the over-growth is predominantly muscular the gland has been found to be hard. A soft gland is not always benign. Abnormalities in the urine are found in both carcinoma and benign hyperplasia and renal function tests are also valueless in the differentiation between these two conditions. Serum acid phosphatase had been estimated in 9 cases and the highest recorded was only 4·4.

In the absence of any reliable criteria, histological examination is the only means available to make a definite diagnosis of carcinoma and it is therefore imperative to make a histological examination of every gland removed surgically—especially in younger age groups—to exclude malignancy.

The difficulties confronting the pathologist. Although the differentiation between benign hyperplasia and the undifferentiated and anaplastic types of carcinoma can easily be made, difficulties arise in distinguishing an extreme degree of hyperplasia from a well differentiated adenocarcinoma. The differentiation between these two conditions is of considerable practical importance, because an erroneous diagnosis of carcinoma in a gland which is only the seat of an advanced hyperplastic process would result in unnecessary procedures such as orchidectomy and the administration of stiloebesterol. The following criteria are of considerable value in differentiating these two conditions (*a*) Although in both there is marked glandular proliferation, a low power view reveals a noticeable difference in gland size (Fig. 1). In the hyperplastic prostate, the glands are large and often cystic and abundant muscular stroma separates the glands from one another or a group of glands from a similar group. In the well differentiated adenocarcinoma the proliferating glands are often small and rudimentary and the stroma is scanty (Figs. 2 and 3); (*b*) The intra glandular epithelial projections in hyperplasia consist of well formed papillae with fine connective tissue cores (Figs. 1 and 8) which are lacking in carcinomas. The epithelial cells growing into the lumen in anastamosing strands giving rise to a 'cribriform' appearance (Fig. 4); (*c*) Corpora amylacae are more frequently seen in benign hyperplasia but are scanty or absent in adenocarcinomas; (*d*) Proliferation of cells beyond glandular basement membranes into the stroma is a feature in adenocarcinomas (Fig. 5). In hyperplasias the proliferating epithelial cells are confined to glandular

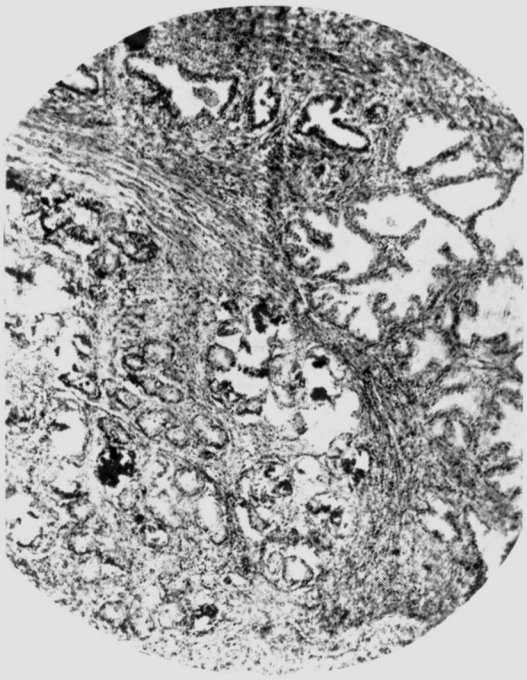

Fig. 1

Circumscribed carcinomatous nodule (bottom) and benign hyperplasia (top) showing noticeable reduction in gland size in the former. Also note well formed intra glandular papillae in the hyperplastic part. H & E × 60.

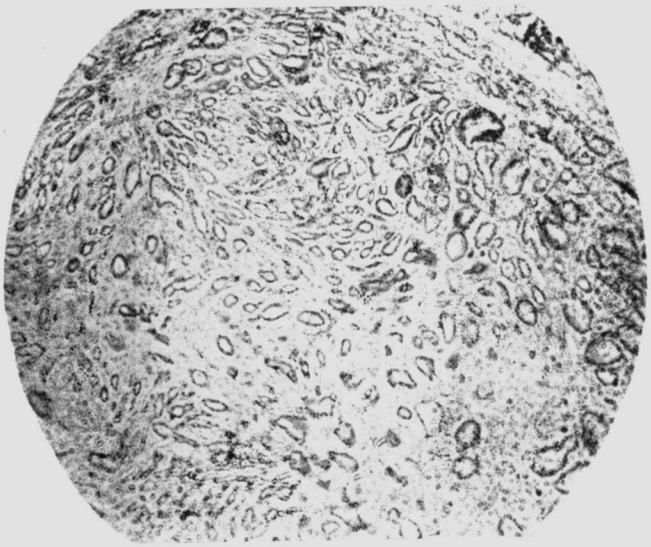

Fig. 2

Numerous small glands in an adeno-carcinoma. H & E ×60.

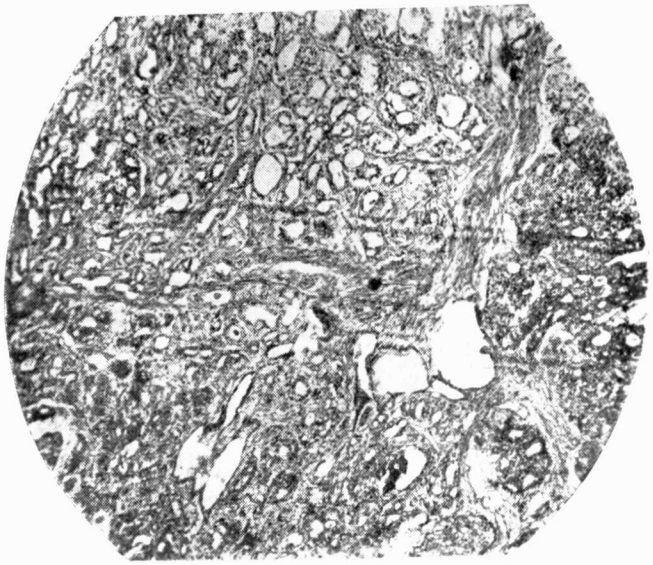

Fig. 3

Small rudimentary glands with scanty stroma.
H & E × 60.

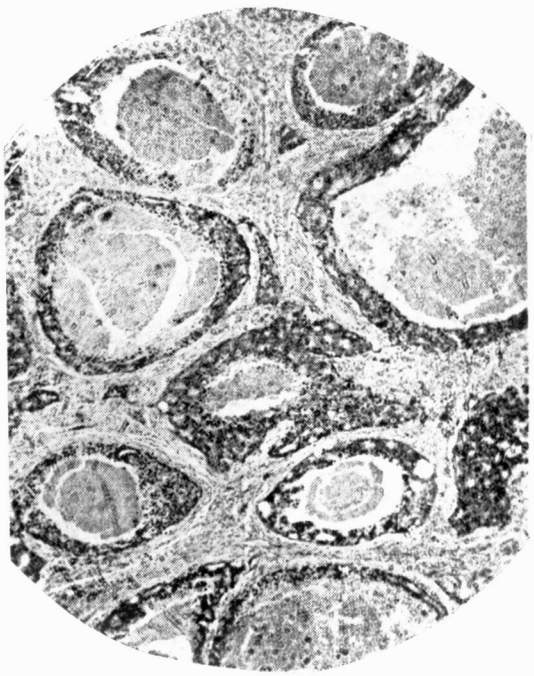

Fig. 4

'Cribriform' appearance in prostatic carcinoma.
H & E × 60.

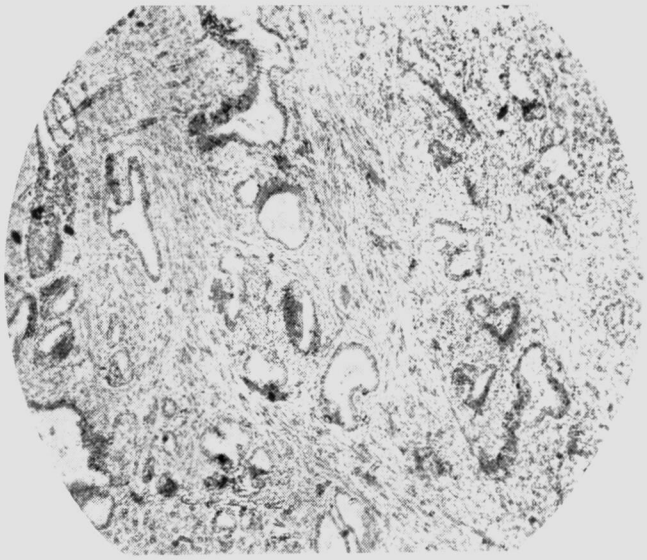

Fig. 5

Adeno-carcinoma showing cell proliferation beyond basement membrane (centre). H & E × 60.

Fig. 6

Perineural invasion—a prostatic acinus seen in a perineural space. H & E × 250.

lumina; (e) In a doubtful case the diagnosis of adenocarcinoma can be confirmed by examination of the peripheral part of the gland which yields evidence of neural invasion (Figs. 6 and 7).

Epithelial metaplasia in glandular acini is sometimes apt to be mistaken for carcinoma. Metaplastic epithelium composed of squamous, transitional and low columnar cells, is seen in hyperplastic nodules especially in old people (Fig. 8). An erroneous diagnosis of carcinoma is made unless the sections are examined very closely. The main features that distinguish epithelial metaplasia in the prostate gland from carcinoma are that in the former condition the cells show no anaplasia no hyperchromatism, no increased or abnormal mitotic activity and no evidence of stromal invasion.

Histology. Four histological types have been identified in this series of 77 carcinomas (Table IV) and after histories of 22 cases showed some degree of co-relation between each type and subsequent behaviour.

(1) *Adenocarcinoma* was the most prevalent type and 50 out of 77 carcinomas (65 per cent.) belonged to this category. Co-existence of benign hyperplasia was most frequently seen in the adenocarcinomas, (64 per cent. of the tumours showed a co-existent benign hyperplasia (Table IV)). Certain features of this type have already been described (page 194). The main characteristic however is the remarkable degree of differentiation (Figs. 1-5).

(2) *Adenocarcinoma with anaplasia.* Differentiation was not complete as in the previous type. There was a mixture of well formed as well as rudimentary glandular structures intermingled with undifferentiated and pleomorphic cellular areas (Figs. 9 and 10). These formed only 9 per cent. of carcinomas and evidence of co-existing benign hyperplasia was found in 28 per cent.

(3) *Trabecular type.* Only 3 cases (4 per cent.) belonged to this category. The main feature was the presence of several solid strands or alveoli of metaplastic epithelial cells (Fig. 11). The diagnosis of malignancy was confirmed by evidence of vascular or neural invasion.

(4) *Anaplastic type.* These formed 22 per cent. of the carcinomata being next in frequency to the adenocarcinomas. Co-existent benign hyperplasia was seen in 6 (35 per cent.). These were highly cellular tumours composed of pleomorphic cells showing several mitotic figures with but little or no stroma and containing few or no glands (Figs. 12-14). Excepting in those cases where there was co-existent benign hyperplasia, there was no histological evidence of a prostatic origin.

Subsequent histories of prostatic carcinoma. (Table V). These were available in 22 out of the 77 cases (i.e., 29 per cent.).

TABLE V

Subsequent histories of 22 cases of carcinoma.

Number of cases alive after prostatectomy 19.

Deaths (all anaplastic carcinomas) 3.

TABLE V—*Contd.*

Period of Survival	*Adenocarcinoma*	*Trabecular*	*Anaplastic*	*Total*
>5 years	2	—	—	2
>4 years <5 years	1	—	—	1
>2 years <3 years	2	—	—	2
>1 year <2 years	6	1	1	8
<1 year	4	2	—	6
Total	15	3	1	19

Three are dead and nineteen are alive. Two deaths occurred one week after and the other, 3 months after the operation and in all three the histological type was anaplastic carcinoma. Of the 19 survivors, 15 were adenocarcinomas, 3 trabecular and 1 anaplastic. Two patients with the adenocarcinomatous type have survived over 5 years while 3 with the anaplastic type are already dead. There appears to be a marked contrast in the death rates and periods of survival between the two most prevalent histological types, viz. the adenocarcinomatous and the anaplastic types. The available evidence suggests that the former have a reasonably good prognosis while, in the case of the latter, the prognosis is poor.

Summary and Conclusions

1. Histological evidence of carcinoma was found in 77 out of 605 prostate glands removed surgically during the period 1936-1952 an incidence of 13 per cent.

2. The likelihood of a surgically removed gland being carcinomatous is greater between the ages of 25 and 44 years and 85 and 104 years than between 45 and 84 years.

3. The largest number of carcinomata occurred in the decade 65-74, i.e. two decades later than carcinomas at other sites.

4. Co-existence of benign hyperplasia ('senile' hypertrophy) was seen in 41 out of the 77 carcinomas (i.e. 53 per cent.) where the average age was 69·5 years. The average age of the remaining 36 cases was 63·5 years. As the prostate gland undergoes hyperplastic changes at this time it is surmised that the carcinomatous picture predominated in sections of this group to such an extent as to completely obscure the hyperplastic process.

5. Two difficulties confronting the pathologist in histological diagnosis are discussed. Firstly the distinction between the fully differentiated adenocarcinomas and extreme forms of benign hyperplasia is difficult. Secondly the presence of metaplastic epithelium gives rise to confusion in the diagnosis.

6. Four histological types have been met with in this series (1) adenocarcinoma, 65 per cent. (2) adenocarcinoma with anaplasia, 9 per cent. (3) trabecular type, 4 per cent. (4) anaplastic type, 22 per cent.

7. The subsequent histories of 29 cases have shown that the prognosis in the case of adenocarcinomatous types was favourable whereas the anaplastic types are rapidly fatal.

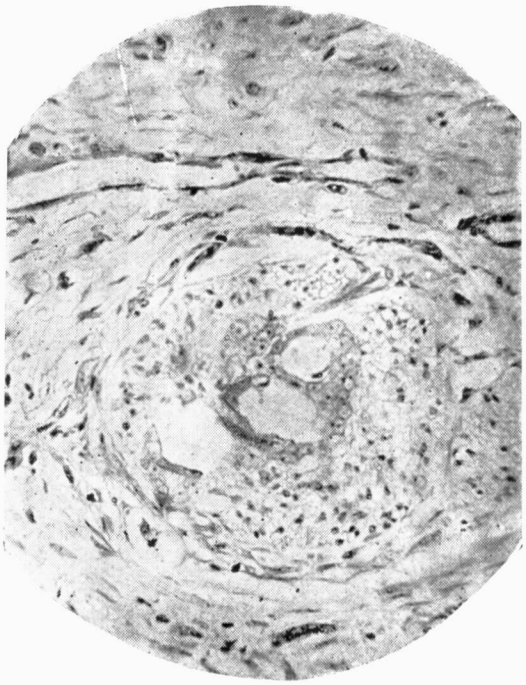

Fig. 7
Prostatic acini in the substance of a nerve.
H & E × 250.

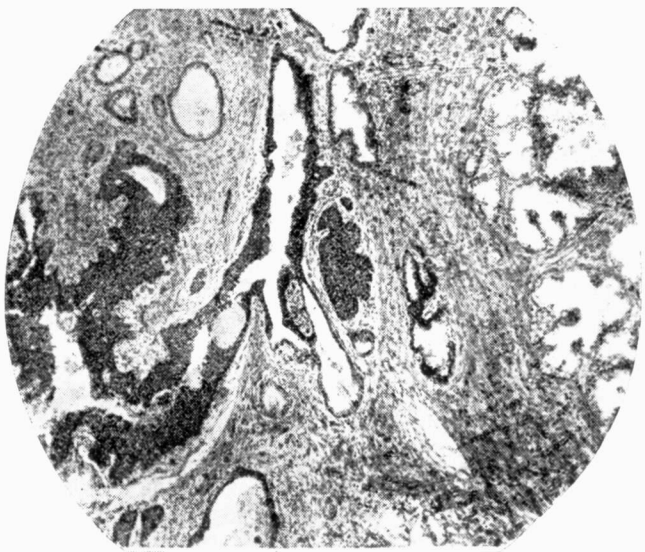

Fig. 8
Metaplastic epithelium. Typical appearance of glands in benign hyperplasia seen on right. H & E × 60.

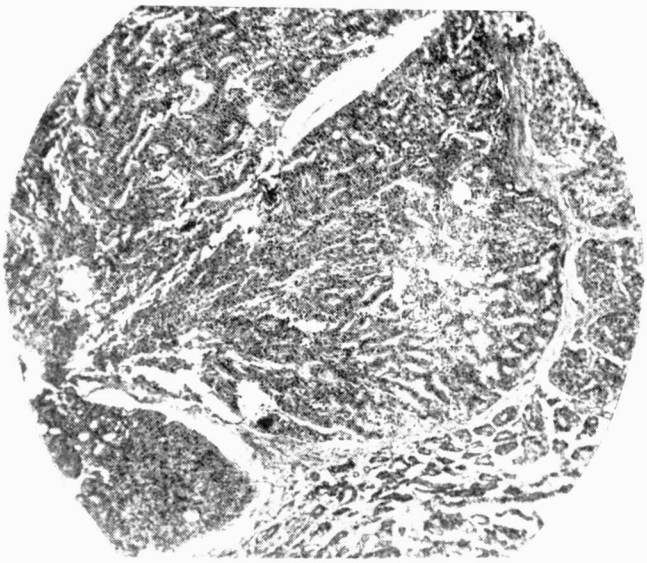

Fig. 9
Rudimentary glands— solid area of neoplastic cells in bottom left. H & E × 60.

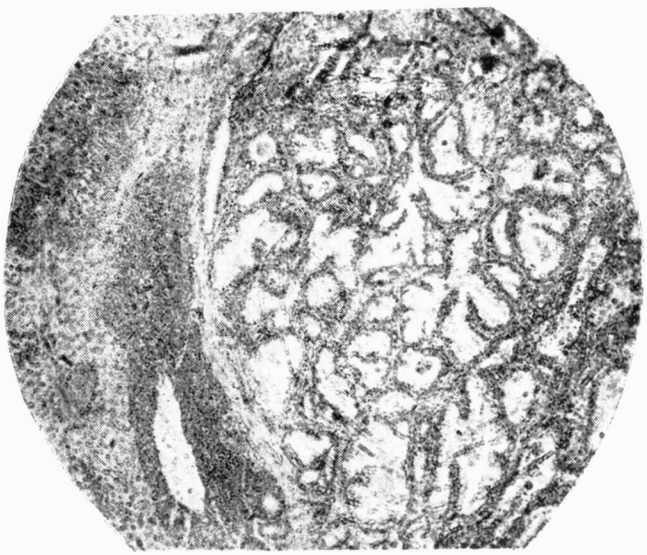

Fig. 10
Well differentiated adenocarcinoma (right) with solid carcinomatous masses (left). H & E × 60.

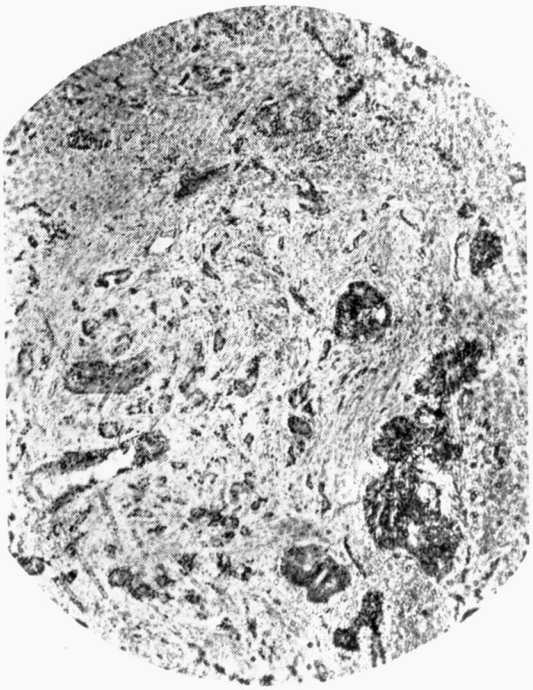

Fig. 11
Trabecular type of prostatic carcinoma.
H & E × 60.

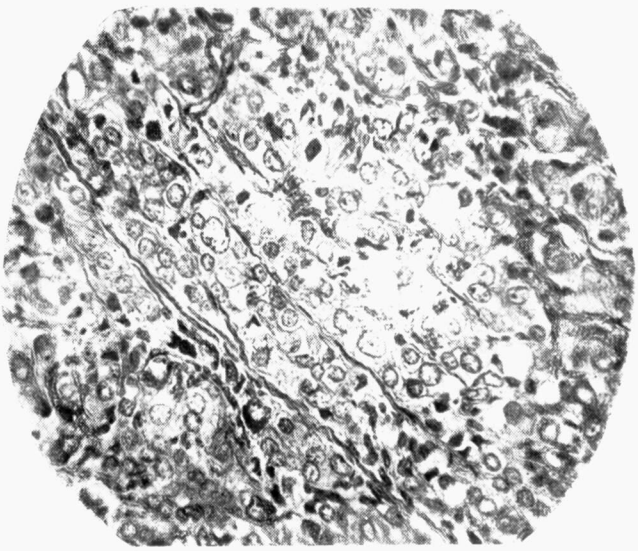

Fig. 12.
Anaplastic carcinoma showing absence of glands—pleomorphic cells with mitoses. H & E × 250.

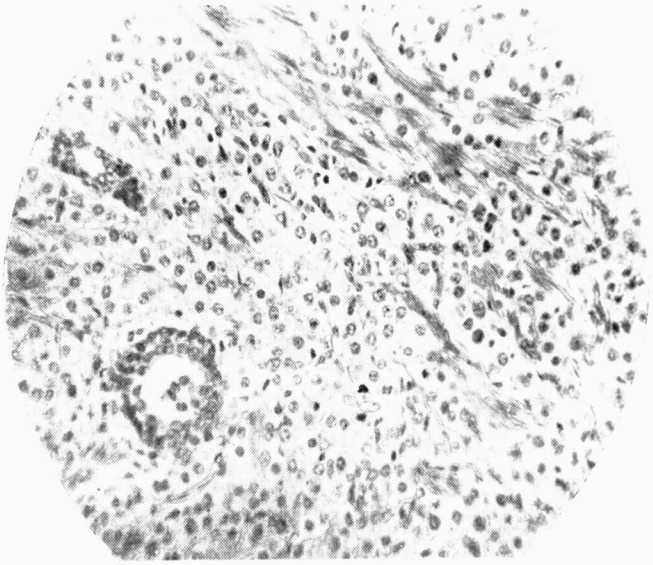

Fig. 13

Anaplastic carcinoma composed of round cells—a single gland lumen seen on bottom left and a few muscle strands on top right. H & E × 250.

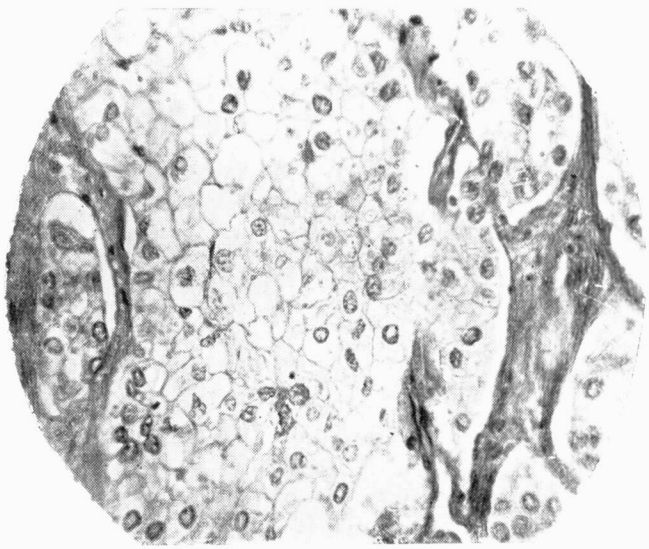

Fig. 14

Anaplastic carcinoma composed of clear cells without gland formation ('Hypernephromatoid' type). H & E × 250.

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