INTERNATIONAL HISTOLOGICAL
CLASSIFICATION OF TUMOURS
Nº 22

Histological Typing of Prostate Tumours

WORLD HEALTH ORGANIZATION
HISTOLOGICAL TYPEING
OF PROSTATE TUMOURS
LIST OF PARTICIPANTS

WHO Collaborating Centre for the Histological Classification of Male Urogenital Tract Tumours, Armed Forces Institute of Pathology, Washington, DC, USA

Head of Centre

DR F. K. MOSTOFI

Participants

DR G. DHOM, Department of Pathology, University of Saarland, Homburg-Saar, Federal Republic of Germany

DR V. V. BYALIK, Department of Pathology, Research Institute of Roentgen-Radiology and Oncology, Kiev, USSR

DR L. M. FRANKS, Imperial Cancer Research Fund Laboratories, Department of Cellular Pathology, Lincoln's Inn Fields, London, England

DR C. GOUYGOU, Service central d'Anatomie pathologique, Centre hospitalo-universitaire Henri Mondor, Créteil, France

DR P. KOSSEY, Oncological Institute for Slovakia, Bratislava, Czechoslovakia

DR V. J. MCGOVERN, Fairfax Institute of Pathology, Royal Prince Alfred Hospital, Camperdown, New South Wales, Australia

DR I. OLCHOVSKAYA, Department of Pathology, Cancer Research Centre of the USSR Academy of Medical Sciences, Moscow, USSR

DR L. H. SOBIN, Cancer, WHO, Geneva, Switzerland

DR H. D. TANDON, Department of Pathology, All India Institute of Medical Sciences, New Delhi, India

DR J. VARGAS DE LA CRUZ, Department of Pathology, General Hospital, La Raza Medical Centre, Mexico, D.F., Mexico

1 This centre deals with tumours of the urinary bladder, testis, prostate, and kidney. The participants listed here have dealt only with prostate tumours.

2 Deceased.
ALREADY PUBLISHED IN THIS SERIES:

No. 1. Histological typing of lung tumours (1967)
No. 2. Histological typing of breast tumours (1968)
No. 3. Histological typing of soft tissue tumours (1969)
No. 4. Histological typing of oral and oropharyngeal tumours (1971)
No. 5. Histological typing of odontogenic tumours, jaw cysts, and allied lesions (1971)
No. 6. Histological typing of bone tumours (1972)
No. 7. Histological typing of salivary gland tumours (1972)
No. 8. Nomenclature of cytology of the female genital tract (1973)
No. 9. Histological typing of ovarian tumours (1973)
No. 10. Histological typing of urinary bladder tumours (1973)
No. 11. Histological typing of thyroid tumours (1974)
No. 13. Histological typing of female genital tract tumours (1975)
No. 15. Histological typing of intestinal tumours (1976)
No. 16. Histological typing of testis tumours (1977)
No. 17. Cytology of non-gynaecological sites (1977)
No. 18. Histological typing of gastric and oesophageal tumours (1977)
No. 19. Histological typing of upper respiratory tract tumours (1978)
No. 20. Histological typing of tumours of the liver, biliary tract and pancreas (1978)
No. 21. Histological typing of tumours of the central nervous system (1979)
CONTENTS

General preface to the series ........................................... 9
Preface to Histological typing of prostate tumours .................. 11
Introduction ...................................................................... 13
Histological classification of prostate tumours ...................... 15
Histological classification of tumours of the seminal vesicle ..... 24
Index .............................................................................. 26

Colour Photomicrographs

The photomicrographs reproduced in this volume were taken by Mr B. B. Allen, Jr, and Mr L. Duckett, Armed Forces Institute of Pathology, Washington, DC, USA.
GENERAL PREFACE TO THE SERIES

Among the prerequisites for comparative studies of cancer are international agreement on histological criteria for the classification of cancer types and a standardized nomenclature. At present, pathologists use different terms for the same pathological entity, and furthermore the same term is sometimes applied to lesions of different types. An internationally agreed classification of tumours, acceptable alike to physicians, surgeons, radiologists, pathologists and statisticians, would enable cancer workers in all parts of the world to compare their findings and would facilitate collaboration among them.

In a report published in 1952,¹ a subcommittee of the WHO Expert Committee on Health Statistics discussed the general principles that should govern the statistical classification of tumours and agreed that, to ensure the necessary flexibility and ease in coding, three separate classifications were needed according to (1) anatomical site, (2) histological type, and (3) degree of malignancy. A classification according to anatomical site is available in the International Classification of Diseases.²

The question of establishing a universally accepted classification by histological type has received much attention during the last 20 years and a particularly valuable Atlas of Tumor Pathology—already numbering more than 40 volumes—is being published in the USA by the Armed Forces Institute of Pathology under the auspices of the National Research Council. An Illustrated Tumour Nomenclature in English, French, German, Latin, Russian and Spanish has also been published by the International Union Against Cancer (UICC).

In 1956 the WHO Executive Board passed a resolution³ requesting the Director-General to explore the possibility that WHO might organize centres in various parts of the world and arrange for the collection of human tissues and their histological classification. The main purpose of such centres would be to develop histological definitions of cancer types and to facilitate the wide adoption of a uniform nomenclature. This resolution was endorsed by the Tenth World Health Assembly in May 1957⁴ and the following month a Study Group on Histological Classification of Cancer Types met in Oslo to advise WHO on its implementation. The Group recommended criteria for selecting tumour sites

---

for study and suggested a procedure for the drafting of histological classifications and testing their validity. Briefly, the procedure is as follows:

For each tumour site, a tentative histopathological typing and classification is drawn up by a group of experts, consisting of up to ten pathologists working in the field in question. An international centre and a number of collaborating laboratories are then designated by WHO to evaluate the proposed classification. These laboratories exchange histological preparations, accompanied by clinical information. The histological typing is then made in accordance with the proposed classification. Subsequently, one or more technical meetings are called by WHO to facilitate an exchange of opinions and the classification is amended to take account of criticisms.

In addition to preparing the publication and the photomicrographs for it, the centre produces up to 100 sets of microscope slides showing the major histological types for distribution to national societies of pathology.

Since 1958, WHO has established 23 centres covering tumours of the lung; breast; soft tissues; oropharynx; bone; ovaries; salivary glands; thyroid; skin; male urogenital tract; jaws; female genital tract; stomach and oesophagus; intestines; central nervous system; liver, biliary tract and pancreas; upper respiratory tract; eye; and endocrine glands; as well as oral precancerous conditions; the leukaemias and lymphomas; comparative oncology; and exfoliative cytology. This work has involved more than 300 pathologists from over 50 countries. Most of these centres have completed their work, and their classifications have already been published (see page 6).

The World Health Organization is indebted to the many pathologists who have participated in this large undertaking. The pioneer work of many other international and national organizations in the field of histological classification of tumours has greatly facilitated the task undertaken by WHO. Particular gratitude is expressed to the National Cancer Institute, USA, which, through the National Research Council and the USA National Committee for the International Council of Societies of Pathology, is providing financial support to accelerate this work. Finally, WHO wishes to record its appreciation of the valuable help it has received from the International Council of Societies of Pathology (ICSP) in proposing participants and in undertaking to distribute copies of the classifications to national societies of pathology all over the world.
PREFACE TO HISTOLOGICAL TYING OF PROSTATE TUMOURS

The WHO Centre for the Histological Classification of Male Urogenital Tract Tumours was established at the Armed Forces Institute of Pathology, Washington, DC, USA.

The Centre prepared and distributed microscope specimens from selected cases of prostate tumours to the participants for histological typing according to a tentative classification. This was subsequently reviewed and modified in the light of the study.

It will, of course, be appreciated that the classification reflects the present state of knowledge, and modifications are almost certain to be needed as experience accumulates. Although the present classification has been adopted by the members of the group, it necessarily represents a view from which some pathologists may wish to dissent. It is nevertheless hoped that, in the interests of international cooperation, all pathologists will try to use the classification as put forward. Criticism and suggestions for its improvement will be welcomed; these should be sent to the World Health Organization, Geneva.

The publications in the series International Histological Classification of Tumours are not intended to serve as textbooks but rather to promote the adoption of a uniform terminology of tumours that will facilitate and improve communication among cancer workers. For this reason the literature references have intentionally been kept to a minimum and readers should refer to standard works on the subject for extensive bibliographies.
INTRODUCTION

This classification is based primarily on the microscopic characteristics of tumours and therefore is concerned with morphologically identifiable cell types and histological patterns as seen with conventional light microscopy.

The term tumour is used synonymously with neoplasm. The phrase tumour-like is applied to lesions which clinically or morphologically resemble neoplasms, but do not behave biologically in a neoplastic manner. They are included in this publication because they give rise to problems in differential diagnosis and because of the unclear borderline between neoplasms and certain non-neoplastic lesions.

Synonyms are listed only if they have been widely used, or if they are considered to be helpful for the understanding of the lesion. In such cases, the preferred term is given first, followed by the synonym in brackets.

Carcinoma of the prostate is commonly categorized as follows:

(a) Clinical carcinoma: Any case in which a diagnosis of prostatic carcinoma is made clinically and confirmed by microscopical examination.

(b) Occult carcinoma: Tumours which are manifested by their metastases before the primary site is detected.

(c) Incidental [subclinical] carcinoma: A carcinoma that is discovered on microscopical examination of prostatic tissue removed surgically for non-malignant disease. Such tumours can be extensive without clinical manifestations of cancer. Most carcinomas in this group are of small and large acinar varieties but tumours of any histological pattern may be found. It is important in these cases to assess the amount of tumour, the histological type and grade, whether or not the tumour is entirely surrounded by non-tumour tissue, and whether it extends beyond the limits of resection. The designation latent carcinoma has been used for tumours of the prostate found at autopsy in patients who had had no clinical evidence of prostatic cancer.

Prostatic abnormalities in the older age group are dominated by nodular hyperplasia and carcinoma. Since the outer part of the gland is the usual site of origin of carcinoma, biopsies from this area are more likely to contain cancer than tissue from transurethral resections. Other changes occur in the senescent prostate, such as atrophy, basal cell hyperplasia, and metaplasia, which may result in diagnostic difficulties. The histological appearance of
the epithelium may also be affected by involutional changes, inflammation and therapy. Furthermore, the assessment of pathological findings may present particular problems in biopsies because of the limited amount of material available for study and the occurrence of distortion.

*   *   *

The histological classifications which appear on pages 14–15 and 23 contain the appropriate morphology code numbers of the *International Classification of Diseases for Oncology* (ICD-O)\(^1\) for tumours, and of the *Systematized Nomenclature of Medicine* (SNOMED)\(^2\) for tumour-like lesions.


HISTOLOGICAL CLASSIFICATION OF PROSTATE TUMOURS

I. EPITHELIAL TUMOURS

A. BENIGN

B. MALIGNANT

1. Adenocarcinoma [carcinoma] 8140/3*
   a. small acinar
   b. large acinar
   c. cribriform
   d. solid/trabecular
   e. others
2. Transitional cell carcinoma 8120/3
3. Squamous cell carcinoma 8070/3
4. Undifferentiated carcinoma 8023/3

II. NON-EPITHELIAL TUMOURS

A. BENIGN

B. MALIGNANT

1. Rhabdomyosarcoma 8900/3
2. Leiomyosarcoma 8890/3
3. Others

III. MISCELLANEOUS TUMOURS

IV. SECONDARY TUMOURS ----/6*

* These numbers refer to the morphology coding of ICD-O and SNOMED.
  a Code specific type.
V. UNCLASSIFIED TUMOURS

VI. TUMOUR-LIKE LESIONS AND EPITHELIAL ABNORMALITIES

A. **NODULAR HYPERPLASIA**
   - 72030

B. **OTHER HYPERPLASIAS**
   1. Atrophy-associated hyperplasia [post-atrophic hyperplasia] 72425
   2. Focal intra-acinar hyperplasia [secondary hyperplasia] 72020
   3. Basal cell hyperplasia 72120

C. **ATROPHY**
   - 58000

D. **SQUAMOUS METAPLASIA**
   - 73220

E. **INFLAMMATION**
   1. Chronic prostatitis 43000
   2. Granulomatous prostatitis 44000
   3. Malakoplakia 43180

---

\(^{b}\) /0 for benign, /3 for malignant tumours.

\(^{c}\) 72425 is Atypical glandular hyperplasia.

\(^{d}\) 72020 is Secondary hyperplasia.
DEFINITIONS AND EXPLANATORY NOTES

I. EPITHELIAL TUMOURS

A. BENIGN

It is questionable whether true adenomas exist in the prostate. The commonly encountered benign adenoma-like proliferations are considered here to be hyperplastic rather than neoplastic (See VI.A, page 20).

_Papillary adenomas_ (Fig. 1) of prostatic acinar epithelium occur in the posterior urethral area. The distinction from the more common _papillary hyperplasia_ (Fig. 2) is based on the presence of stroma in the core of hyperplastic lesions. Prostatic acinar tissue in the urethra frequently has a papillary appearance.

B. MALIGNANT

1. _Adenocarcinoma [carcinoma]_ (Fig. 3–35): A malignant tumour of the prostatic glandular epithelium.

Adenocarcinoma of the prostate is commonly reported as _carcinoma_.

Architectural disturbance is an important criterion for the diagnosis of adenocarcinoma of the prostate since anaplasia is often not marked and invasion difficult to assess. In the normal organ, the glands radiate from the urethra, and the acini have a characteristic convoluted structure. In the hyperplastic prostate, there is a typical nodular pattern. The radiating arrangement of glands may be lost but their convoluted appearance is preserved. These features are absent in carcinoma. Groups of acini are either packed together or distributed in a haphazard fashion. The acini do not contain convolutions and appear to be growing out irregularly in all directions. This change in pattern is best seen at low magnification.

The acini of the normal and of the hyperplastic prostate are surrounded by a delicate basement membrane. There is often an elastic tissue network surrounding the acinus and the whole is invested by muscle strands. Malignant acini do not appear to have this orderly connective tissue framework, although special stains may show a periacinar basement membrane. The normal arrangement of elastic tissue is not seen in carcinomatous areas, and the tumour cells may penetrate and break up the muscle bundles, eventually replacing them. Malignant epithelium can lie in very close relationship to small blood vessels, and the connective tissue zone between the epithelium and the capillary endothelium is then thin or absent. This is rarely seen in the normal prostate.

Invasion of the stroma has been the subject of considerable discussion because, until electron microscopy confirmed its presence, there were doubts
that a basement membrane actually existed. Stromal invasion is best seen where there is outgrowth of the cells at the base of the acinus. Invasion of intraprostatic perineural spaces is an early and frequent occurrence. It is easily recognizable and is considered as unequivocal evidence of malignancy. Lymphatic and vascular invasion, on the other hand, may be difficult to detect.

Examination of the total prostate is desirable for the determination of capsular and pericapsular invasion and facilitates accurate pathological staging. Needle biopsy specimens may provide such information, particularly if tumour is seen in fibroadipose tissue. One criterion used frequently for capsular invasion in transurethral resections deserves comment. The presence of acini in skeletal muscle has been recognized as evidence par excellence of extraprostatic extension, but skeletal muscle occurs in the prostate proper and prostatic acini intermingled with such fibres should not be regarded as a sign of an invasive tumour unless other evidence is present.

Most carcinomas of the prostate form glands and show one or more of the following growth patterns:

(a) **Small acinar**: Simple glandular structures much smaller than normal, closely packed or isolated, and lined by a single layer of cuboidal cells.

(b) **Large acinar**: Glandular structures approximately the size of, or somewhat smaller than, normal acini but typically without convolutions, usually closely packed and lined by a single layer of cuboidal or columnar cells.

(c) **Cribriform**: Large acinar structures filled with epithelial cells forming multiple gland-like lumens without supporting stroma. This should be distinguished from those acinar growths in which closely packed glands appear to fuse.

(d) **Solid/trabecular**: Cells arranged in sheets and/or trabeculae. Frequently, more than one growth pattern is seen in an individual case. The components should be mentioned in the report.

Prostatic carcinoma can be categorized according to glandular differentiation. Well-differentiated tumours consist of simple glands, either small or large, or those with papillary structures. Moderately differentiated tumours are those with cribriform or fused glands. Poorly differentiated tumours have little or abortive gland formation. Those with no glandular elements should be considered as undifferentiated prostatic carcinomas.

Several types of cells are recognized in adenocarcinoma of the prostate by light microscopy: clear, dark and eosinophilic cells. The cytoplasm of the clear cell is foamy or diffusely pale pink; that of the dark cell is homogeneous and lightly basophilic. The eosinophilic cells have granular cytoplasm. Small acinar tumours are usually composed of dark cells; large acinar of clear cells; cribriform, solid and trabecular forms may have clear, dark or all cell types. The eosinophilic cells rarely, if ever, occur alone. The cells range from cuboidal to columnar and show varying degrees of anaplasia. Nuclear anaplasia can be categorized according to the deviation from the normal into: Grade I, slight; Grade II, moderate; Grade III, marked.
In addition to histological assessment, the clinical and histopathological staging of the extent of the tumour should be taken into account for treatment and prognosis. Such a system of staging has been developed by the International Union Against Cancer.\(^1\) The main histopathological categories regarding local spread are as follows:

- **pT1** Focal (single or multiple) carcinoma
- **pT2** Diffuse carcinoma with or without extension to the capsule
- **pT3** Carcinoma with invasion beyond the capsule and/or invasion of the seminal vesicles
- **pT4** Tumour with invasion of adjacent organs.

Small regular nucleoli may be seen in normal or hyperplastic cells. In many cancer cells, the nucleoli are large and deeply staining, often with blurred outlines. Occasionally, there may be more than one nucleolus.

Mitoses are infrequently seen in tumours with the small acinar pattern but may be numerous in the cribriform, solid and trabecular varieties.

Both normal and neoplastic tissue can have large amounts of prostatic acid phosphatase; carcinomas tend to contain diminishing amounts with decreasing differentiation. This histochemical determination is not usually helpful in the diagnosis of primary carcinoma of the prostate, but the presence of prostatic acid phosphatase in a metastatic tumour is diagnostic of adenocarcinoma of the prostate (Fig. 28–29).

**(e)** Other adenocarcinomas: Several rare variants of adenocarcinoma have been described. "Endometrioid" carcinoma (Fig. 30) has been the designation used by some authors for a papillary tumour of the utricle composed of columnar cells resembling those of endometrial carcinoma. This tumour has also been called papillary adenocarcinoma of the utricle. A papillary pattern (Fig. 31) may also occur in association with prostatic carcinomas of other forms. Rarely, the tumour may appear as a papillary cystadenocarcinoma. Many carcinomas of the prostate contain some mucin, but the term mucinous carcinoma (Fig. 32) should be reserved for tumours in which there are substantial amounts. It is important to exclude secondary mucinous adenocarcinoma of vesicle, intestinal or other origin. Adenoid cystic carcinoma (Fig. 33), as described in the salivary gland, rarely occurs in the prostate. The term should not be used for cribriform carcinomas, which superficially resemble it.

Treatment by hormones or radiation may alter the appearance of normal as well as neoplastic tissues (Fig. 34–35). Carcinoma cells can show pleomorphic vacuolated nuclei, pyknosis, karyorrhexis, loss of nucleoli, flattening or vacuolation of cytoplasm, and rupture of cell membranes. In tumours that are less responsive to therapy, these changes are less evident or absent. The normal glandular epithelium is often atrophic or may show squamous metaplasia after hormonal therapy and atypical basal cell hyperplasia after

---

irradiation. The stromal response to irradiation is similar to that seen in other organs.

2. *Transitional cell carcinoma* (Fig. 36): A prostatic tumour composed of cells which resemble those of transitional cell carcinoma of the urinary bladder.

Primary prostatic transitional cell carcinomas arise in the prostatic ducts. Occasionally, there is a coincidental prostatic adenocarcinoma. Transitional cell tumours may also arise in the prostatic urethra and/or bladder and extend into the prostate either by direct infiltration or along the ducts. Multicentric transitional cell tumours in the prostate, urethra and bladder do occur.

3. *Squamous cell carcinoma* (Fig. 37): An extremely rare tumour composed of cells with intercellular bridges and keratin.

Squamous cell metaplasia and carcinoma may occur in oestrogen-treated adenocarcinomas of the prostate. Squamous metaplasia commonly occurs adjacent to infarcts in nodular hyperplasia and may mimic squamous cell carcinoma.

4. *Undifferentiated carcinoma* (Fig. 38): A malignant tumour of epithelial structure that is too poorly differentiated to be placed in any of the other groups of carcinoma.

II. NON-EPITHELIAL TUMOURS

These are named and defined according to the WHO histological classification of soft tissue tumours.\(^1\)

A. BENIGN

It is questionable whether true leiomyomas and fibromas of the prostate exist. The commonly encountered circumscribed masses of smooth muscle and fibrous tissue are considered to be hyperplastic rather than neoplastic (see VI.A, page 20).

B. MALIGNANT

1. *Rhabdomyosarcoma* (Fig. 39)

This is most frequently found in the prostate of children, in which it is usually of embryonal type. In advanced cases, it is often not possible to determine whether the tumour has originated in the bladder or in the prostate.

2. *Leiomyosarcoma* (Fig. 40), although rare, is the most frequent sarcoma of the prostate in adults.

3. *Others*: Fibrosarcoma, malignant fibrous histiocytoma, and other sarcomas have been described in adults but are very uncommon.

III. MISCELLANEOUS TUMOURS

Primary carcinoid tumours (Fig. 41), sometimes functional, occur in the prostate and may be pure or combined with adenocarcinoma.

Carcinosarcomas (Fig. 42) have been described in the prostate. Spindle-shaped carcinoma cells, infiltrations of tumour from adjacent organs and stromal reactions following treatment may simulate carcinosarcoma.

Naevi (Fig. 43) and primary malignant melanoma (Fig. 44) very rarely occur in the prostate.

A lesion analogous to the phyllodes tumour (Fig. 45) of the breast may be seen in the prostate.

IV. SECONDARY TUMOURS

In this category are included metastatic tumours and tumours extending into the prostate from adjacent organs such as the bladder, the prostatic urethra, the rectum, the seminal vesicles, and the peri-urethral glands. The initial manifestation of leukaemia or lymphoma may be enlargement of the prostate. In lymphoma there is a massive infiltrate of cells which destroys the fibromuscular stroma, but glandular elements can still be recognized (Fig. 46). Leukaemic cells infiltrate the prostate in a similar manner, and in addition may be seen within the blood vessels.

V. UNCLASSIFIED TUMOURS

These are benign or malignant tumours that cannot be placed in any of the categories described above.

VI. TUMOUR-LIKE LESIONS AND EPITHELIAL ABNORMALITIES

The following lesions are described because they may give rise to problems in differential diagnosis or be related to the development of carcinoma.

A. NODULAR HYPERPLASIA (Fig. 47–49): A lesion in which there is hyperplasia of varying proportions of the glandular and stromal (muscular and fibrovascular) tissues of the prostate.

In this condition, there is uneven hyperplasia of all elements, and some grow at a greater rate than others, forming glandular and/or stromal nodules that characteristically compress adjacent structures. Eventually, the prostate becomes irregularly enlarged and nodular. Congestion, oedema, and infarction may occur.

In nodular hyperplasia an intra-acinar epithelial proliferation may assume a cribriform pattern simulating carcinoma. The presence of delicate fibrovascular cores and the absence of anaplasia favour the diagnosis of a benign lesion.
The term *lobular hyperplasia* (Fig. 50) has been used to designate a proliferation of acini of uniform appearance surrounding a duct or acinus.

**B. OTHER HYPERPLASIAS**

1. *Atrophy-associated hyperplasia [post-atrophic hyperplasia]* (Fig. 51): A proliferation of small irregularly shaped and distributed acini around a central atrophic duct. The acinar cells may show atypia.

   This type of hyperplasia occurs in the peripheral zones of the prostate and has been associated with carcinoma of small acinar type.

2. *Focal intra-acinar hyperplasia [secondary hyperplasia]* (Fig. 52): Focal intra-acinar proliferation of epithelium forming plaques and papillary projections in a cystic acinus otherwise lined by flattened involuted cells.

   This type of hyperplasia may occur in any part of the prostate. It is interpreted as representing renewed (secondary) hyperplastic activity after involution.

3. *Basal cell hyperplasia* (Fig. 53–54): An intra-acinar proliferation of small basophilic cells with ovoid nuclei and scant cytoplasm.

   The lumens may be obliterated. The surrounding stroma is frequently hyperplastic. This lesion can be focal or extensive.

**C. ATROPHY** (Fig. 55)

Focal atrophy in the prostate is often manifested as small darkly stained collapsed acini which can resemble carcinoma.

**D. SQUAMOUS METAPLASIA** (Fig. 56–57)

This may be associated with infarcts or occur following oestrogen therapy, surgery or the use of indwelling catheters, particularly in the presence of infection.

**E. INFLAMMATION**

Inflammation of the prostate may simulate cancer clinically and pathologically. Chronic inflammatory cells, particularly histiocytes, can be mistaken for diffusely infiltrating tumour. Regenerating ductal structures are often basophilic and distorted. The presence of neutrophilic and eosinophilic leukocytes, lymphocytes, degenerating corpora amylacea, and giant cells and the involvement of duct walls help to distinguish this from carcinoma.

1. *Chronic prostatitis* (Fig. 58)

   Many prostates contain lymphocytic infiltrates which, when dense, may mimic carcinoma or lymphoma. Carcinoma of the prostate is not usually associated with a lymphocytic infiltrate.

2. *Granulomatous prostatitis* (Fig. 59)

   This may be specific (e.g., tuberculous) or nonspecific. In nonspecific granulomatous prostatitis, there are collections of large histiocytes and epithelioid cells.
3. *Malakoplakia* (Fig. 60)

This is characterized by collections of large eosinophilic histiocytes containing Michaelis-Gutmann bodies.

* * *

* *

Cowper's glands may be included in specimens removed with the prostate and have been misinterpreted as carcinoma (Fig. 61).
HISTOLOGICAL CLASSIFICATION OF TUMOURS OF THE SEMINAL VESICLE

I. EPITHELIAL TUMOURS
   A. BENIGN
   B. MALIGNANT
      1. Adenocarcinoma 8140/3*

II. NON-EPITHELIAL TUMOURS
   A. BENIGN
      1. Fibroma 8810/0
      2. Leiomyoma 8890/0
   B. MALIGNANT

III. UNCLASSIFIED TUMOURS 8000/-a

IV. INVOLUTIONAL CHANGE 70800

* These numbers refer to the morphology coding of ICD-O and SNOMED.
  a /0 for benign, /3 for malignant tumours.
DEFINITIONS AND EXPLANATORY NOTES

I. EPITHELIAL TUMOURS

A. BENIGN

Hyperplasia and adenoma of the seminal vesicle may be papillary. Both are very rare.

B. MALIGNANT

*Adenocarcinoma* (Fig. 62): A very rare epithelial tumour, usually forming papillary glandular structures.

This diagnosis should be made only when it can be demonstrated, both grossly and microscopically, that the seminal vesicle is the principal site of involvement, and should there be tumour outside the gland, direct continuity with the seminal vesicles must be demonstrated.

Many tumours diagnosed as carcinoma of the seminal vesicles are carcinomas of the prostate, and tumours involving both the seminal vesicles and the prostate should be regarded as prostatic in origin unless proved otherwise. The presence alone of papillary structures or pigmentation in the tumour cells does not justify the diagnosis of carcinoma of the seminal vesicles.

Involutional changes in the seminal vesicles must not be mistaken for carcinoma.

II. NON-EPITHELIAL TUMOURS

These are defined according to the WHO histological classification of soft tissue tumours. Fibroma and leiomyoma are the most frequently encountered.

III. UNCLASSIFIED TUMOURS

IV. INVOLUTIONAL CHANGES (Fig. 63–64)

Involutional changes in the epithelium of the seminal vesicles are sometimes confused with carcinoma, the ductal structures being lined by bizarre large cells, often giant sized, with large hyperchromatic nuclei. However, the large cells are located in the superficial layers of the epithelium, have considerable cytoplasm, and do not show mitoses.

---

<table>
<thead>
<tr>
<th>Term</th>
<th>Page</th>
<th>Figures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenocarcinoma</td>
<td>17</td>
<td>3-35</td>
</tr>
<tr>
<td>Adenoid cystic carcinoma</td>
<td>19</td>
<td>33</td>
</tr>
<tr>
<td>Adenoma</td>
<td>17</td>
<td>1</td>
</tr>
<tr>
<td>Atrophy</td>
<td>22</td>
<td>55</td>
</tr>
<tr>
<td>Carcinoid tumour</td>
<td>21</td>
<td>41</td>
</tr>
<tr>
<td>Carcinoma</td>
<td>17</td>
<td>3-35</td>
</tr>
<tr>
<td>Carcinoma, clinical</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Carcinoma, incidental</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Carcinoma, latent</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Carcinoma, occult</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Carcinosarcoma</td>
<td>21</td>
<td>42</td>
</tr>
<tr>
<td>Cowper's glands</td>
<td>23</td>
<td>61</td>
</tr>
<tr>
<td>&quot;Endometrioid&quot; carcinoma</td>
<td>19</td>
<td>30</td>
</tr>
<tr>
<td>Hyperplasia, papillary</td>
<td>17</td>
<td>2</td>
</tr>
<tr>
<td>Hyperplasias</td>
<td>21</td>
<td>47-54</td>
</tr>
<tr>
<td>Involutinal change, seminal vesicle</td>
<td>25</td>
<td>63-64</td>
</tr>
<tr>
<td>Leiomyosarcoma</td>
<td>20</td>
<td>40</td>
</tr>
<tr>
<td>Malakoplakia</td>
<td>23</td>
<td>60</td>
</tr>
<tr>
<td>Melanoma, malignant</td>
<td>21</td>
<td>44</td>
</tr>
<tr>
<td>Metaplasia, squamous</td>
<td>20</td>
<td>56-57</td>
</tr>
<tr>
<td>Mucinous carcinoma</td>
<td>19</td>
<td>32</td>
</tr>
<tr>
<td>Naevus</td>
<td>21</td>
<td>43</td>
</tr>
<tr>
<td>Papillary cystadenocarcinoma</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Phyllodes tumour</td>
<td>21</td>
<td>45</td>
</tr>
<tr>
<td>Prostatitis, chronic</td>
<td>22</td>
<td>58</td>
</tr>
<tr>
<td>Prostatitis, granulomatous</td>
<td>22</td>
<td>59</td>
</tr>
<tr>
<td>Rhabdomyosarcoma</td>
<td>20</td>
<td>39</td>
</tr>
<tr>
<td>Seminal vesicle, tumours of</td>
<td>25</td>
<td>62</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>20</td>
<td>37</td>
</tr>
<tr>
<td>Transitional cell carcinoma</td>
<td>20</td>
<td>36</td>
</tr>
<tr>
<td>Undifferentiated carcinoma</td>
<td>20</td>
<td>38</td>
</tr>
</tbody>
</table>

Unless otherwise stated, all the preparations shown in the photomicrographs reproduced on the following pages were stained with haematoxylin-eosin.
Fig. 1. Papillary adenoma
Lesion in posterior urethra with prostatic acinar epithelium and delicate stroma. × 100

Fig. 2. Papillary hyperplasia
Prominent fibrovascular stroma covered by prostatic acinar epithelium. Located in posterior urethra. × 100
Fig. 3. Adenocarcinoma
Focus of carcinoma in posterior lateral region. Remainder of gland shows some hyperplasia. × 2.5

Fig. 4. Adenocarcinoma
Haphazardly arranged small acini intermingled with hyperplastic glands. Well-differentiated tumour with slight anaplasia. × 60
Fig. 5. Adenocarcinoma
Small acini invade muscle bundles. Well-differentiated tumour with moderate anaplasia. × 150

Fig. 6. Adenocarcinoma
Perineural invasion. × 250
Fig. 7. Adenocarcinoma
Lymphatic invasion. × 115

Fig. 8. Adenocarcinoma
Venous invasion. × 100
Fig. 9. Adenocarcinoma
Invasion of periprostatic fat. × 60

Fig. 10. Adenocarcinoma
Extension of tumour to bladder neck. Poorly differentiated tumour with moderate anaplasia. ×160
Fig. 11. Adenocarcinoma
Extension of tumour to seminal vesicle. × 100

Fig. 12. Adenocarcinoma
Small acinar pattern in a well-differentiated tumour. Moderate anaplasia. × 160
Fig. 13. Adenocarcinoma
Large acinar pattern in a well-differentiated tumour. Slight anaplasia. × 100

Fig. 14. Adenocarcinoma
Large acinar pattern in a well-differentiated tumour. Papillary infolding of epithelium. Slight anaplasia. × 100
Fig. 15. Adenocarcinoma
Cribriform pattern in a moderately differentiated tumour. Moderate anaplasia. $\times 100$

Fig. 16. Adenocarcinoma
Small acinar pattern with fusion of glands in a moderately differentiated tumour. Moderate anaplasia. $\times 150$
Fig. 17. Adenocarcinoma
Solid growth pattern in a poorly differentiated tumour. Moderate anaplasia. × 100

Fig. 18. Adenocarcinoma
Trabecular pattern in a poorly differentiated tumour. Moderate anaplasia. Abundant stroma. × 100
Fig. 19. Adenocarcinoma
Trabecular pattern in a poorly differentiated tumour. Moderate anaplasia. × 250

Fig. 20. Adenocarcinoma
Solid pattern. Moderate anaplasia. × 150
Fig. 21. Adenocarcinoma
Mixture of cribriform and acinar patterns. Moderate anaplasia. × 60

Fig. 22. Adenocarcinoma
Small acinar pattern with clear cells in a well-differentiated tumour. Slight anaplasia. × 160
Fig. 23. Adenocarcinoma
Mixture of clear and dark cells. Moderate anaplasia. × 100

Fig. 24. Adenocarcinoma
Mixture of eosinophilic and dark cells. Moderate anaplasia. × 250
Fig. 25. Adenocarcinoma
Slight anaplasia in a well-differentiated clear-cell small acinar tumour. × 250

Fig. 26. Adenocarcinoma
Moderate anaplasia in a small acinar tumour. Dark cells. × 250
Fig. 27. Adenocarcinoma
Marked anaplasia in a poorly differentiated tumour. × 250

Fig. 28. Metastatic adenocarcinoma
From a supracleivicular lymph node. × 160
Fig. 29. Metastatic adenocarcinoma
Same field as in Fig. 28, showing prostatic acid phosphatase activity. Immunoperoxidase stain. × 160

Fig. 30. "Endometrioid" carcinoma. × 60
Fig. 31. Papillary adenocarcinoma. $\times 60$

Fig. 32. Mucinous adenocarcinoma. $\times 100$
Fig. 33. Adenoid cystic carcinoma. x 160

Fig. 34. Adenocarcinoma
Vacuolation of cytoplasm, pyknotic nuclei of tumour cells and squamous metaplasia following oestrogen treatment. x 160
Fig. 35. Adenocarcinoma
Following ionizing radiation. × 160

Fig. 36. Transitional cell carcinoma
Primary prostatic tumour. Grade II. × 100
Fig. 37. Squamous cell carcinoma
Primary prostatic tumour. Grade II. × 100

Fig. 38. Undifferentiated carcinoma. × 250
Fig. 39. Rhabdomyosarcoma
Primary prostatic tumour in a child. × 100

Fig. 40. Leiomyosarcoma
Primary prostatic tumour. × 160
Fig. 41. Carcinoid tumour
Tumour cells were argyrophilic with special stains. Adenocarcinoma also present. × 150.

Fig. 42. Carcinosarcoma
Adenocarcinomatous area adjacent to chondrosarcoma. × 100.
Fig. 43. Naevus. \( \times 50 \)

Fig. 44. Malignant melanoma. \( \times 110 \)
Fig. 45. Phyllodes tumour. × 100

Fig. 46. Malignant lymphoma. × 100
Fig. 47. Nodular hyperplasia
Glandular proliferation. $\times 60$

Fig. 48. Nodular hyperplasia
Stromal proliferation. $\times 60$
Fig. 49. Nodular hyperplasia
Intra-acinar proliferation simulating cribriform pattern of carcinoma. x 60

Fig. 50. Lobular hyperplasia
Orderly proliferation of acini around a duct. x 60
Fig. 51. Atrophy-associated hyperplasia
Atrophic lobule with peripheral proliferated acini. × 60

Fig. 52. Focal intra-acinar hyperplasia
Dilated acini with short papillary projections. Atrophic epithelium in some acini. × 60
Fig. 53. Basal cell hyperplasia
Focal maturation to secretory epithelium. × 110

Fig. 54. Basal cell hyperplasia
Focal maturation to secretory epithelium. × 160
Fig. 55. Atrophy
Small collapsed acini with dark cells. × 100

Fig. 56. Squamous metaplasia
Clear cytoplasm typical of oestrogen effect. Resembles vaginal epithelium. × 100
Fig. 57. Squamous metaplasia
Distortion and haemorrhage at periphery of infarct. × 150

Fig. 58. Chronic prostatitis
Reactive epithelial proliferation and cells with clear spaces simulate carcinoma. × 150
Fig. 59. **Granulomatous prostatitis**

Granuloma at periphery of a dilated duct containing inflammatory exudate. × 100

Fig. 60. **Malakoplakia**

Large eosinophilic histiocytes. × 250
Fig. 61. Cowper's gland
Normal appearance of mucus-containing acini associated with ducts. \( \times 130 \)

Fig. 62. Adenocarcinoma, seminal vesicle. \( \times 120 \)
Fig. 63. Involutional change, seminal vesicle
Cross section of peripheral portion of gland with a cribiform appearance. Nuclear atypia. × 140

Fig. 64. Involutional change, seminal vesicle
Pronounced nuclear atypia of luminal cells. × 150