

# XIX. Tumours of the prostate and penis

WILLIAM C. HALL,<sup>1</sup> SVEND W. NIELSEN,<sup>2</sup> & KENNETH McENTEE<sup>3</sup>

*Tumours of the male genital tract, excluding the testes, are relatively rare in the six major domestic animals. The most important tumours are prostate carcinoma and transmissible venereal tumour of the penis in dogs, fibropapilloma of the penis in bulls, squamous papilloma and squamous cell carcinoma in horses, and squamous papilloma in pigs. Four histological types of canine prostate carcinoma exist: alveolar papillary, acinar, organoid, and poorly differentiated. The biological behaviour of prostate carcinomas is similar to that in man, with frequent metastasis to the regional pelvic nodes, bones, and lungs. There appears to be no relationship between the common diffuse glandular hyperplasia and carcinoma in the prostate of dogs. A unique lesion of dogs is squamous metaplasia of the prostate related to estrogen-producing Sertoli cell tumours of the testis. Three different transmissible tumours of the penis occur in domestic animals. The canine venereal tumours can be transmitted only by intact tumour cells during licking and coital contact, whereas bovine fibropapillomas and porcine squamous papillomas can be transmitted by cell-free material. In cattle, the fibropapillomas are caused by the same virus that produces cutaneous papillomatosis. All three tumours are benign and usually regress spontaneously.*

Neoplasms of the prostate are extremely rare in domestic animals except the dog. No cases were found in bulls, stallions, boars, or rams, and only one was found in a cat. Owing to the limited number of specimens available for study, this classification should be considered valid only for the dog, and should be taken as provisional for the other species until more tumours can be examined.

Neoplasms of the penis, including the mucous membranes of the prepuce, are more common than prostate tumours, but are much less common than testicular tumours. The three most common tumours of the penis are fibropapilloma of bulls, squamous cell carcinoma of horses, and transmissible venereal tumour of dogs. It is of interest that, in addition to the canine venereal tumour, the bovine fibropapilloma and the porcine papilloma are transmissible; in the latter two species, transmission can occur by means of cell-free material.

Organs of the male genital system apart from the testis, prostate, and penis are so rarely sites of

tumour formation in domestic animals that an attempt to present a morphological classification would be pretentious. Two tumours of the canine epididymis were seen and we feel certain that tumours of the seminal vesicles and of the bulbourethral (Cowper's) gland have been recorded by pathologists. However, their classification must await studies on additional cases.

Tumours of the cutaneous side of the prepuce are essentially the same as those of other areas of hair-bearing skin and have been described elsewhere.<sup>a</sup>

The material used in this classification consisted of sections of biopsy and necropsy specimens provided by veterinary institutions in Europe, Canada, and the USA, in addition to cases studied in the Department of Pathobiology, University of Connecticut, Storrs and the New York State College of Veterinary Medicine, Ithaca, New York, USA. The following contributors were especially helpful: Dr I. Leav, Angell Memorial Animal Hospital, Boston, USA; Dr E. Weiss, University of Giessen, Federal Republic of Germany; Dr H. Casey, Armed Forces Institute of Pathology, Washington, DC, USA; Dr A. Koestner, Ohio State University, Columbus, USA; and Dr B. Schiefer, University of Saskatchewan, Canada.

<sup>1</sup> Veterinary Pathologist, United States Army Medical Research Institute for Infectious Diseases, Fort Detrick, MD 21701, USA.

<sup>2</sup> Professor of Pathology and Director of the Northeastern Research Center for Wildlife Diseases, University of Connecticut, Storrs, CT 06268, USA.

<sup>3</sup> Professor, New York State College of Veterinary Medicine, Cornell University, Ithaca, NY 14853, USA.

<sup>a</sup> WEISS, E. & FRESE, K. *Bulletin of the World Health Organization*, 50: 79-100 (1974).

## HISTOLOGICAL CLASSIFICATION AND NOMENCLATURE OF TUMOURS OF THE PROSTATE AND PENIS

### *Tumours of the prostate*

#### I. ADENOCARCINOMA

- A. ALVEOLAR PAPILLARY TYPE
- B. ACINAR TYPE
- C. ORGANOID (ROSETTE) TYPE

#### II. POORLY DIFFERENTIATED CARCINOMA

#### III. BENIGN MESENCHYMAL NEOPLASMS

- A. LEIOMYOMA
- B. FIBROMA

#### IV. SARCOMA

#### V. UNCLASSIFIED TUMOURS

#### VI. SECONDARY TUMOURS

#### VII. TUMOUR-LIKE LESIONS

- A. ACINAR HYPERPLASIA

#### B. SQUAMOUS METAPLASIA

#### C. CYSTS

### *Tumours of the penis*

#### I. EPITHELIAL TUMOURS

- A. SQUAMOUS PAPILLOMA
- B. SQUAMOUS CELL CARCINOMA

#### II. FIBROPAPILLOMA (FIBROMA)

#### III. TRANSMISSIBLE VENEREAL TUMOUR

#### IV. OTHER MESENCHYMAL TUMOURS

- A. FIBROSARCOMA
- B. LYMPHOSARCOMA
- C. VASCULAR TUMOURS

#### V. UNCLASSIFIED TUMOURS

#### VI. TUMOUR-LIKE LESIONS

## DESCRIPTION OF TUMOURS

### *Tumours of the prostate*

Tumours of the canine prostate are uncommon. There is no particular breed predisposition and the mean age of dogs with prostate carcinomas of all types is 10 years, with a range of from 6 to 15 years.

Information from available case histories indicates that certain characteristic clinical signs exist in the dog, reflecting the biological behaviour of the tumour. The most frequent signs are weakness of the hind legs, emaciation, and difficult urination and defaecation. Rectal palpation and radiography are

often helpful in detecting a tumorous mass of the prostate. Metastasis occurs in about 70–80% of cases and the most frequent sites are the iliac nodes, followed in order by lung, urinary bladder, mesentery, rectum, and bone (especially of the pelvis, femur, and posterior vertebrae). Neoplasms of the prostate probably metastasize to the lungs both via the iliac lymph nodes and by means of the vertebral venous system. Direct extension, with adhesion between the prostate and the bladder, rectum, and lower colon, is frequently observed. The high frequency of metastasis to bone by prostate carcinomas and the

appearance of the metastatic bone lesions, both radiographically and histologically, is similar to the disease in man.

Only slides or paraffin blocks were available to us, which precluded the examination of tissues for lipids and acid phosphatase. However, one of the contributors (Dr Leav) has demonstrated intense staining of signet-ring cells in prostatic adenocarcinomas with oil-red-O, Sudan black B, and PAS stains; acid phosphatase activity was demonstrated in the cytoplasm of fresh tissue from two adenocarcinomas. The diagnostic importance of acid phosphatase in the serum of dogs with prostate tumours has not yet been evaluated.

### I. ADENOCARCINOMA

The epithelium in this group of neoplasms forms ducts or acini. Individual cells vary from small to very large, with open-faced nuclei and multiple nucleoli. Signet-ring cells can be seen in neoplastic prostatic epithelium of most of the adenocarcinomas; they are found with great frequency in some but are rare in others. Usually 2-5 mitoses are found per high-power field but the frequency may range from 0 to 20. Sclerosis and fibromuscular hyperplasia of the stroma occur in all neoplastic patterns but are most often associated with the acinar type. Metastasis to the lymphatics occurs with all types. Plasma cells and lymphocytes, and occasionally germinal centres, are found throughout the stroma of some neoplasms. Haemorrhage and necrosis are common.

A few neoplasms appeared to be mixtures of alveolar papillary, acinar, and organoid types. Mucin was usually most abundant in acinar structures, whereas the alveolar papillary and organoid rosette types had only sparse amounts of mucin.

#### A. Alveolar papillary type (Fig. 1-4)

These tumours consist of papillary ribbons of epithelial cells projecting into round or oval, cystic, alveolar-like spaces bounded by connective tissue, which is frequently invaded by the neoplastic cells. The cytoplasm of the neoplastic cells is abundant, often granular, and brightly eosinophilic. In most of the tumours, the cytoplasm of individual cells is frequently enlarged in a bulb-like manner; this displaces the nucleus and forms a signet-ring cell that contains material positive to alcian blue and PAS stains. Individual eosinophilic protein droplets, which may be as large as the nucleus, are often

found in the cytoplasm of some cells. Nuclei are round-to-oval, are often pyknotic with condensed chromatin, and generally contain one or two nucleoli. There is often a high degree of anaplasia but this varies from neoplasm to neoplasm. Polymorphonuclear leukocytes are frequently found in the lumens. Brown isotropic pigments are occasionally found in macrophages.

#### B. Acinar type (Fig. 5-8)

The neoplastic epithelium forms acini of various sizes throughout the stroma. Severe fibromuscular hyperplasia accompanies the neoplastic cells, giving the tumours a scirrhous appearance. Cells in acini are usually small and differ in the degree of anaplasia. Signet-ring cells are rarely observed. Papillary infoldings of the epithelium are rare but may be found. The epithelium is usually only one or two cells deep. Individual neoplastic cells are occasionally observed in the stroma. Varying amounts of mucin are found in the acinar lumens of most neoplasms of this type.

#### C. Organoid (rosette) type (Fig. 9-10)

An alveolar pattern is evident, with stromal invasion by tumour cells in some areas. Each alveolus is filled with solid masses or strands of tumour cells that form small rosettes with nuclei situated at the periphery. Occasionally, a lumen can be demonstrated in the central portion of the rosette. The cells are usually small and cuboidal-to-columnar in appearance, the cytoplasmic borders are often distinct, and an oval, large or medium-sized nucleus with one or two prominent nucleoli is found at the peripheral portion of each cell.

Necrosis is frequently observed in the central portion of tumour masses. In contrast to other types of prostatic carcinoma, connective tissue proliferation and sclerosis are not marked.

### II. POORLY DIFFERENTIATED CARCINOMA

This designation is used for malignant epithelial tumours that lack a glandular appearance and lumen formation. The neoplastic epithelium is diffusely scattered throughout the fibromuscular stroma as individual cells, as syncytia, as solid islands, or as strands. The tumour cells may be spindle-shaped with a sarcomatous appearance or they may be round cells with either small hyperchromatic or large vesicular nuclei. Neoplastic giant cells, mitoses, and tumorous invasion of lymphatics, venules, and perineural sheaths frequently occur.

### III. BENIGN MESENCHYMAL NEOPLASMS

#### A. *Leiomyoma*

Leiomyomas are rarely observed but are the most common benign tumours. Their histological characteristics do not differ from those of leiomyomas occurring elsewhere in the body.

#### B. *Fibroma*

This is a rare tumour with the same features as those of fibromas occurring at other sites.

### IV. SARCOMA

Sarcomas have been described in the literature and a few were examined by us. They were poorly differentiated spindle cell sarcomas of either fibroblast or smooth muscle cell origin, but there was insufficient history and descriptive documentation to warrant further classification.

### V. UNCLASSIFIED TUMOURS

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

### VI. SECONDARY TUMOURS

Metastasis to the prostate is rare; however, infiltration by lymphosarcomas can occur in cattle, dogs, and cats, and invasion of the prostate by carcinomas of the neck of the urinary bladder has been seen in several species.

### VII. TUMOUR-LIKE LESIONS

#### A. *Acinar hyperplasia*

Hyperplastic acinar epithelium with exaggerated infolding of the basement membrane increases with age and occurs frequently in old dogs. It is usually a bilateral process that may produce great enlargement and cause difficulties in defaecation and/or urination. The former is probably more common than the latter because of the narrow pelvic cavity in some breeds of dog.

Acinar hyperplasia frequently accompanies carcinoma of the prostate in the dog, but at present there is no basis for considering hyperplasia to be a preneoplastic process in dogs. The cause of acinar hyperplasia is not known, but it is believed to be related to hormonal imbalance associated with aging.

If only a small biopsy sample is available, it can be difficult to distinguish between acinar hyperplasia and early adenocarcinoma and a careful search for atypia, mitoses, and invasion must be made.

#### B. *Squamous metaplasia*

This lesion is most frequently seen in dogs with a functioning Sertoli cell tumour of the testis. It also occurs occasionally in cattle that have eaten plants with estrogenic potency, such as subterranean clover, or are suffering from vitamin A deficiency or chlorinated naphthalene poisoning. Squamous metaplasia occurs in both acinar and ductal epithelium and is frequently associated with cystic dilatation of acini and subsequent enlargement of the prostate. It is important not to confuse this benign lesion with a squamous cell tumour.

#### C. *Cysts*

Cyst formation occurs frequently in old dogs, often together with chronic inflammation and acinar hyperplasia. Cysts probably arise from dilated acini that, owing to scar tissue formation, have lost their communication with ducts and the urethral lumen.

## *Tumours of the penis*

### I. EPITHELIAL TUMOURS

#### A. *Squamous papilloma*

This is a benign, keratinizing, epithelial, papilliform tumour with scant fibrous stroma. The papilloma is usually small, but can reach a large size, frequently with areas of necrosis. Lymphoplasmacytic infiltration is frequent at the base of the tumour. It occurs most frequently in the horse, but may be seen in other species. In the pig, a virus-induced papilloma occurs, which is venereally transmitted.

#### B. *Squamous cell carcinoma* (Fig. 11, 12)

Squamous cell carcinoma of the penis is usually well differentiated, being made up of large epithelial cells showing intercellular bridges and keratin pearls; single cell keratinization occurs in less well differentiated carcinomas. Squamous cell carcinoma is the malignant counterpart of squamous papilloma. It occurs most frequently in the horse, followed by the dog and the bull. It mainly affects old horses and appears to occur with equal frequency in cas-

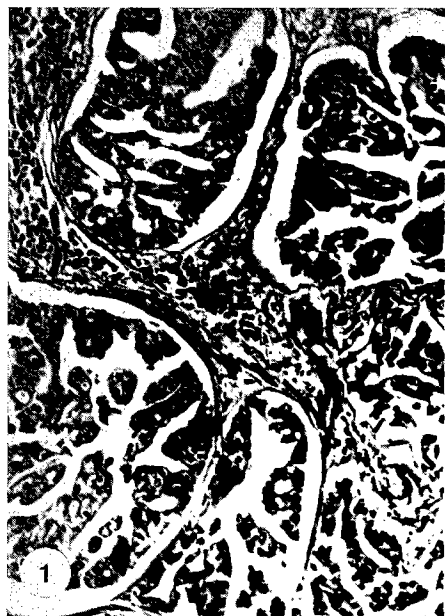


Fig. 1-4. Alveolar papillary prostatic carcinoma (dog). Alveolar structures are filled with papillary projections of tumour cells in which cytoplasmic vacuoles, frequently containing proteinaceous droplets and mucoid material, may be seen.



Fig. 5-8. Acinar prostatic carcinoma (dog). Scattered acinar and tubular structures are found in the scirrhous, fibromuscular stroma.

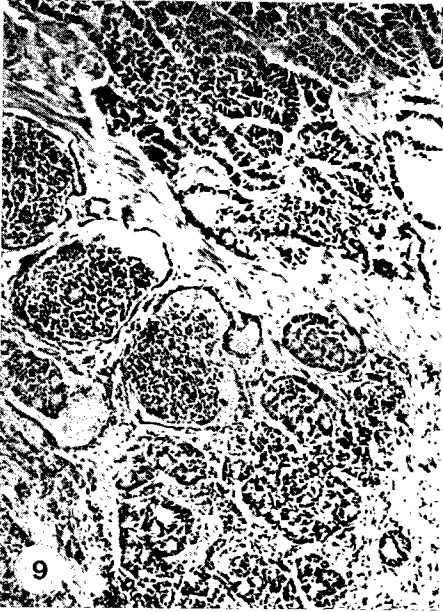


Fig. 9 and 10. Organoid (rosette) prostatic carcinoma (dog). Lobules of tumour cells are seen in the lower left corner and normal prostate acini in the upper right of Fig. 9. The rosette formation is readily apparent in Fig. 10.

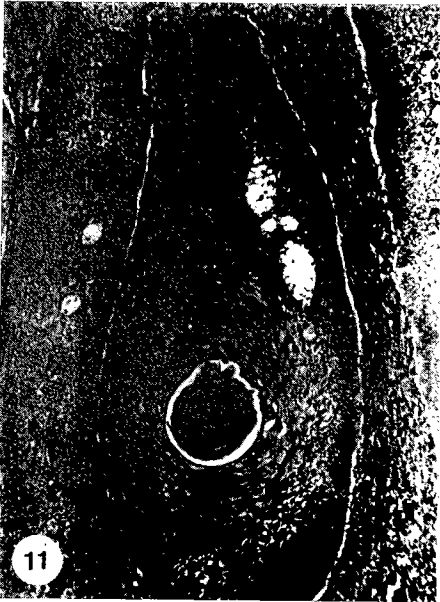


Fig. 11 and 12. Squamous cell carcinoma of the penis showing invasion and keratin pearls (horse).

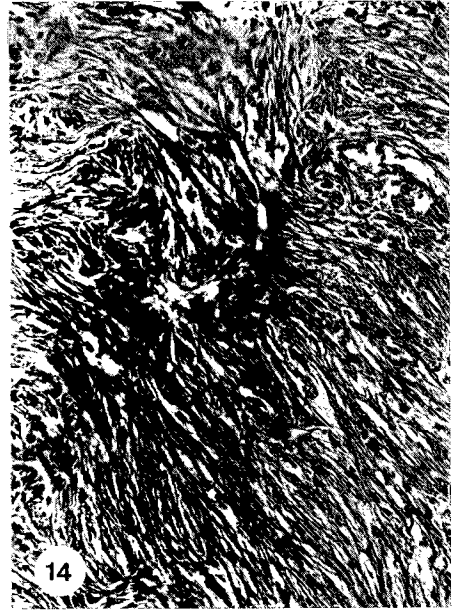
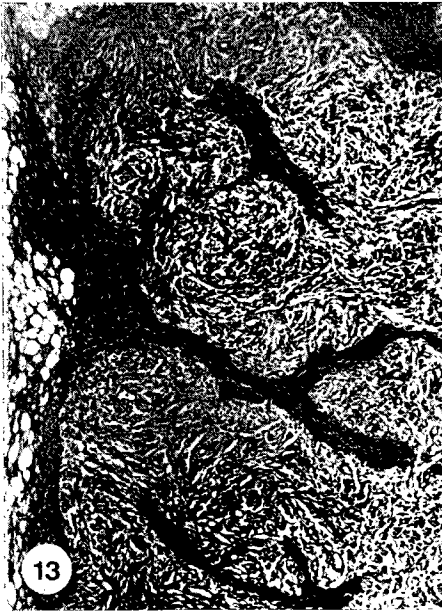


Fig. 13 and 14. Fibropapilloma of the penis (bull). Epithelial fronds from the surface of the neoplasm extend into a matrix composed of intertwining fascicles of fibroblasts.



Fig. 16 and 15. Transmissible venereal tumour of the penis (dog).

trated horses and stallions. Its etiology has been associated with smegma accumulations in the horse. The tumour has great propensity for invasion but metastasizes infrequently to the superficial and deep inguinal lymph nodes and rarely to distant sites. If only limited biopsy material is available, it can be extremely difficult to distinguish squamous papillomas from squamous cell carcinomas.

## II. FIBROPAPILLOMA (FIBROMA) (Fig. 13, 14)

This is a benign tumour of bulls that is mainly composed of fibroblasts. It is associated with marked epithelial proliferation; this occurs not only on the surface but also deep into the fibromatous centre, and is similar to the pseudoepitheliomatous hyperplasia seen in some forms of epulis. Fibroblasts are arranged in intertwining fascicles and the amount of collagen present varies. If biopsy material is limited, rapidly growing fibropapillomas may have the appearance of fibrosarcomas. The two most frequent sites are the junction of the glans penis and sheath, and the craniodorsal part of the penis, which is prone to trauma. The tumour is often fungoid and it may be attached by either a broad base or by a long pedicle, allowing some of the tumour to protrude from the preputial orifice. The tumours are usually less than 3 cm across but they are sometimes larger. Their presence may seriously impede copulation because of pain or mechanical interference. Ulceration and haemorrhage are frequent, particularly in large tumours. Spontaneous regression is common.

Fibropapillomas can be transmitted experimentally with cell-free material to the penile or vaginal mucosa. The causative virus appears to be the same as that causing bovine cutaneous warts (*verruca vulgaris*). Susceptibility varies with age, young calves being easier to infect than older cattle, indicating that immunity may be acquired.

## III. TRANSMISSIBLE VENEREAL TUMOUR (Fig. 15, 16)

This neoplasm of dogs is composed of tumour cells forming diffuse masses or sheets of cells beneath the mucosa of the penis or prepuce, and extending up to the stratum germinativum of the mucosa. The surface epithelium is frequently hyperplastic and occasionally ulcerated. Delicate fibrous connective tissue trabeculae, containing blood vessels, traverse the neoplastic masses in an irregular fashion and provide a supporting framework for the tumour. The vessels are frequently congested. For the most part,

the tumour cells are in close apposition to one another so that cell borders are difficult to discern; in areas where the cell population is less dense, cytoplasmic borders are distinct. The neoplastic cells have abundant, darkly eosinophilic cytoplasm with a finely reticulated, often foamy appearance, and large round-to-oval and occasionally U-shaped nuclei. The chromatin is finely stippled and one prominent nucleolus is usually visible in each nucleus. Mitoses are generally frequent. Lymphocytes, plasma cells, and a few eosinophils may be seen in some neoplasms. Although infrequent, metastases may be found in regional nodes and rarely in visceral organs; these appear similar to the primary lesion. Spontaneous regression is frequent and usually occurs within two months.

This tumour was first described over 100 years ago in Europe. It has a world-wide distribution at the present time; there are enzootic areas in Central America and South-East Asia, whereas in the northern USA, in Canada, and in northern Europe few dogs are affected. The tumour is transmitted by intact cells by licking, by coitus, or by experimental injection. The modal number of chromosomes in the tumour cells is fairly consistent even in different geographic areas, and is less than that of normal somatic canine cells (59 as against 78).

## IV. OTHER MESENCHYMAL TUMOURS

### A. *Fibrosarcoma*

This is a rare tumour in most species of domestic animal with only a few cases recorded in bulls, horses, and dogs. Fibrosarcomas of the penis have the same morphological features as those of other fibrosarcomas described previously.<sup>a</sup>

### B. *Lymphosarcoma*

Although lymphomas occur very frequently in bulls, dogs, boars, and cats, they are only rarely observed in the penis. The morphological features of this neoplasm are described in the classification of neoplastic diseases of the haematopoietic and lymphoid tissues.<sup>b</sup>

### C. *Vascular tumours*

Haemangiomas and malignant haemangioendotheliomas (angiosarcomas) are rare and of the same

<sup>a</sup> WEISS, E. *Bulletin of the World Health Organization*, 50: 101-110 (1974).

<sup>b</sup> JARRETT, W. F. & MACKEY, L. J. *Bulletin of the World Health Organization*, 50: 21-34 (1974).

morphological appearance as those described previously.<sup>a</sup>

#### V. UNCLASSIFIED TUMOURS

These are tumours that cannot be placed in any of the above categories.

---

<sup>a</sup> WEISS, E. *Bulletin of the World Health Organization*, **50**: 101-110 (1974).

#### VI. TUMOUR-LIKE LESIONS

Parasitic granulomas caused by *Habronema* larvae may result in irregular red nodules near the urethral process of the stallion. Microscopically, the lesion is characterized by central caseation necrosis surrounded by eosinophil, histiocyte, and lymphocyte infiltration, and peripheral fibrosis. *Habronema* larvae may be present in early lesions.

---