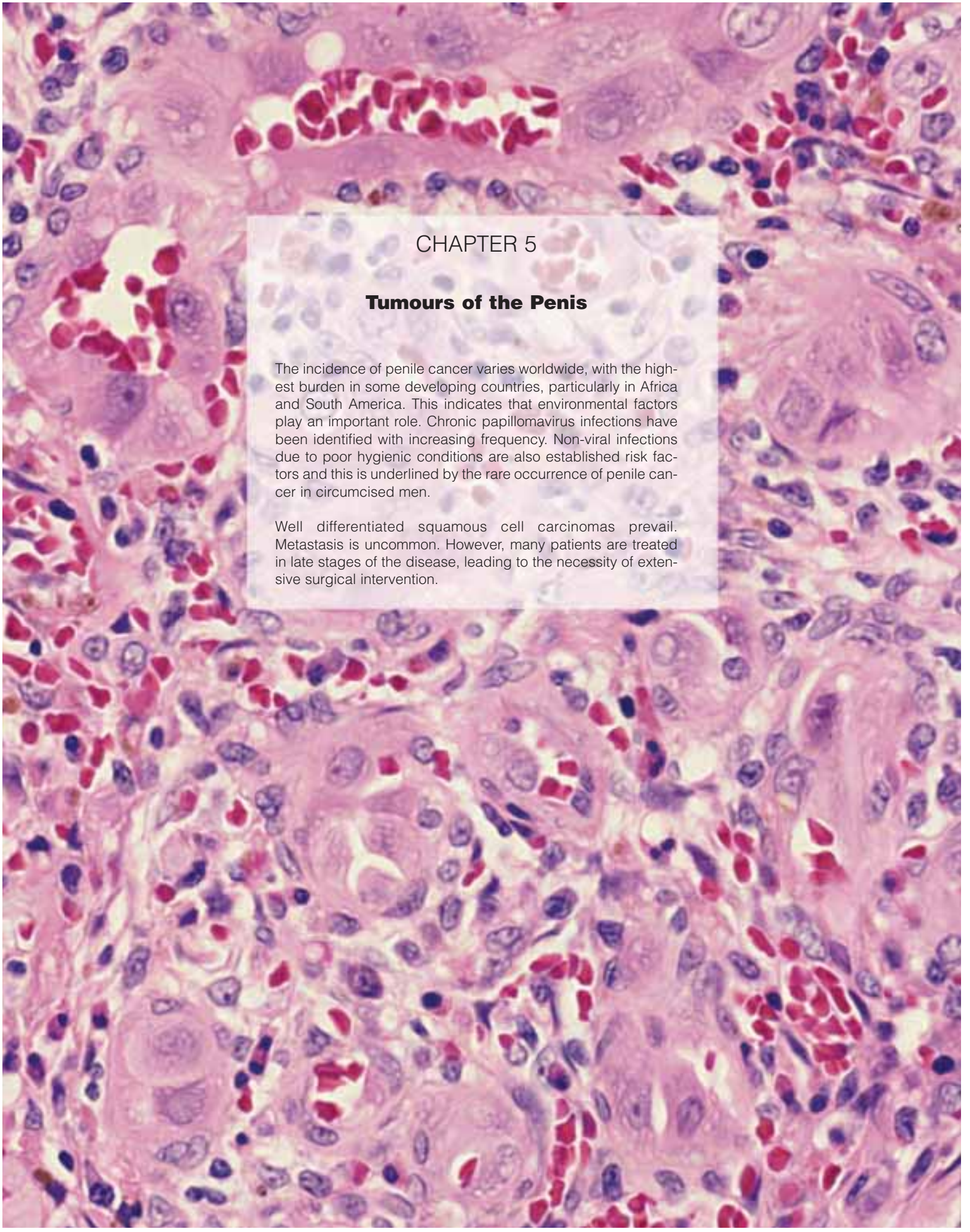

CHAPTER 5

Tumours of the Penis

The incidence of penile cancer varies worldwide, with the highest burden in some developing countries, particularly in Africa and South America. This indicates that environmental factors play an important role. Chronic papillomavirus infections have been identified with increasing frequency. Non-viral infections due to poor hygienic conditions are also established risk factors and this is underlined by the rare occurrence of penile cancer in circumcised men.

Well differentiated squamous cell carcinomas prevail. Metastasis is uncommon. However, many patients are treated in late stages of the disease, leading to the necessity of extensive surgical intervention.

WHO histological classification of tumours of the penis

Malignant epithelial tumours of the penis	
Squamous cell carcinoma	8070/3[1]
Basaloid carcinoma	8083/3
Warty (condylomatous) carcinoma	8051/3
Verrucous carcinoma	8051/3
Papillary carcinoma, NOS	8050/3
Sarcomatous carcinoma	8074/3
Mixed carcinomas	
Adenosquamous carcinoma	8560/3
Merkel cell carcinoma	8247/3
Small cell carcinoma of neuroendocrine type	8041/3
Sebaceous carcinoma	8410/3
Clear cell carcinoma	8310/3
Basal cell carcinoma	8090/3

Precursor lesions	
Intraepithelial neoplasia grade III	8077/2
Bowen disease	8081/2
Erythroplasia of Queyrat	8080/2
Paget disease	8542/3
Melanocytic tumours	
Melanocytic nevi	8720/0
Melanoma	8720/3
Mesenchymal tumours	
Haematopoietic tumours	
Secondary tumours	

[1] Morphology code of the International Classification of Diseases for Oncology (ICD-O) {808} and the Systematized Nomenclature of Medicine (http://snomed.org). Behaviour is coded /0 for benign tumours, /2 for in situ carcinomas and grade III intraepithelial neoplasia, /3 for malignant tumours, and /1 for borderline or uncertain behaviour.

TNM classification of carcinomas of the penis

TNM classification[1,2]

T – Primary tumour

TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Tis	Carcinoma in situ
Ta	Non-invasive verrucous carcinoma
T1	Tumour invades subepithelial connective tissue
T2	Tumour invades corpus spongiosum or cavernosum
T3	Tumour invades urethra or prostate
T4	Tumour invades other adjacent structures

N – Regional lymph nodes

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single superficial inguinal lymph node
N2	Metastasis in multiple or bilateral superficial inguinal lymph nodes
N3	Metastasis in deep inguinal or pelvic lymph node(s), unilateral or bilateral

M – Distant metastasis

MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

Stage grouping

Stage 0	Tis	N0	M0
	Ta	N0	M0
Stage I	T1	N0	M0
Stage II	T1	N1	M0
	T2	N0,N1	M0
Stage III	T1, T2	N2	M0
	T3	N0, N1, N2	M0
Stage IV	T4	Any N	M0
	Any T	N3	M0
	Any T	Any N	M1

[1] {344,2662}.
[2] A help desk for specific questions about the TNM classification is available at http://www.uicc.org/tnm/

Malignant epithelial tumours

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Introduction

The vast majority of malignant tumours are squamous cell carcinomas (SCC) and they occur chiefly in the squamous epithelium of the glans, coronal sulcus and foreskin {2905}. SCC of the skin of the shaft are less frequent {695} than melanomas or Paget disease. Benign and malignant soft tissue tumours are unusual, but a large variety occurs in the penis. Whereas carcinomas affect mainly the distal penis or glans, sarcomas (excluding Kaposi sarcoma) prefer the corpora. Tumours of pendulous urethra are discussed under urothelial neoplasms.

Topographic definition of penile mucosa and anatomical levels

Penile mucosa includes the inner surface of the foreskin, coronal sulcus and glans, from the preputial orifice to the fossa navicularis. The lamina propria (LP) is similar for all sites but deeper anatomical levels are different: in the glans there are the corpus spongiosum (CS), tunica albuginea (TA) and corpus cavernosum (CC) and in the foreskin the dartos, dermis and epidermis. The penile fascia covers the shaft and inserts into the lamina propria of the coronal sulcus {171}. The fossa navicularis represents the 5-6 mm of the distal penile urethra but its squamous lining is continuous with that of the perimeatal glans.

Incidence

The incidence rates of penile cancer vary among different populations, with the highest cumulative rates (1% by age 75) seen in parts of Uganda and the lowest, 300-fold less, found among Israeli Jews. Age standardized incidence rates in the Western world are in the range of 0.3-1.0/100.000 {2016}. The incidence of penile cancer is highly correlated to the incidence of cervical cancer {280}. There is a continuous increase with advancing age. An earlier age at onset and a higher proportion of younger patients are seen in high incidence areas. The incidence rates have been slowly declining in some countries since the fifties {1607}, a decline commonly speculated to be due to improved personal hygiene.

Etiology

Etiological factors associated with penile cancer are phimosis, chronic inflammatory conditions, especially lichen sclerosus, smoking, ultraviolet irradiation, history of warts, or condylomas and lack of circumcision {620,1058,1069,1187,1590, 1871,2507}.

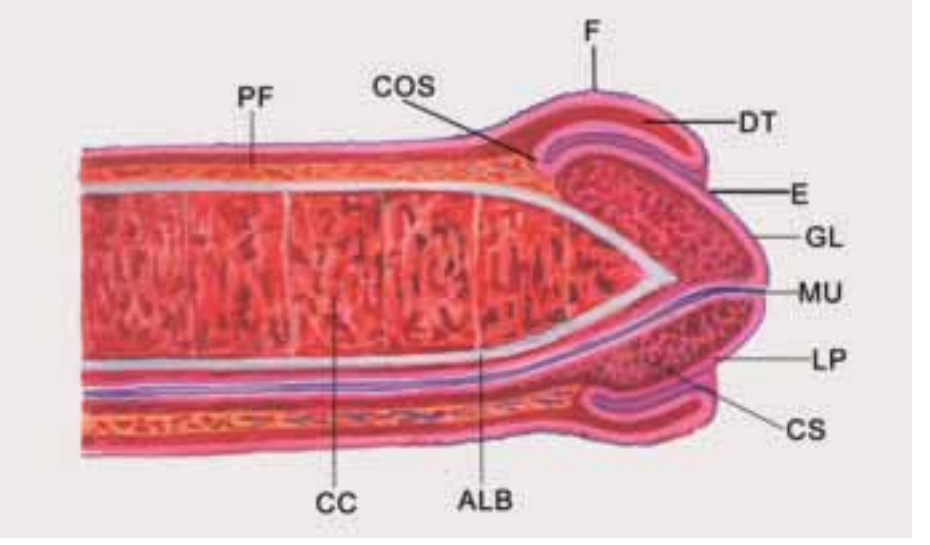

Fig. 5.01 Anatomy of the penile structures. Anatomical features: cut surface view of a partial penectomy showing anatomical sites, F= foreskin, GL= glans and COS= coronal sulcus. The anatomical levels in the glans are E= epithelium, LP= lamina propria, CS= Corpus Spongiosum and CC= corpus cavernosum. The tunica albuginea (ALB) separates CS from CC. In the foreskin additional levels are DT= dartos and F= skin. Penile fascia (PF) encases CC. The urethra is ventral and distally shows the meatus urethralis (MU).

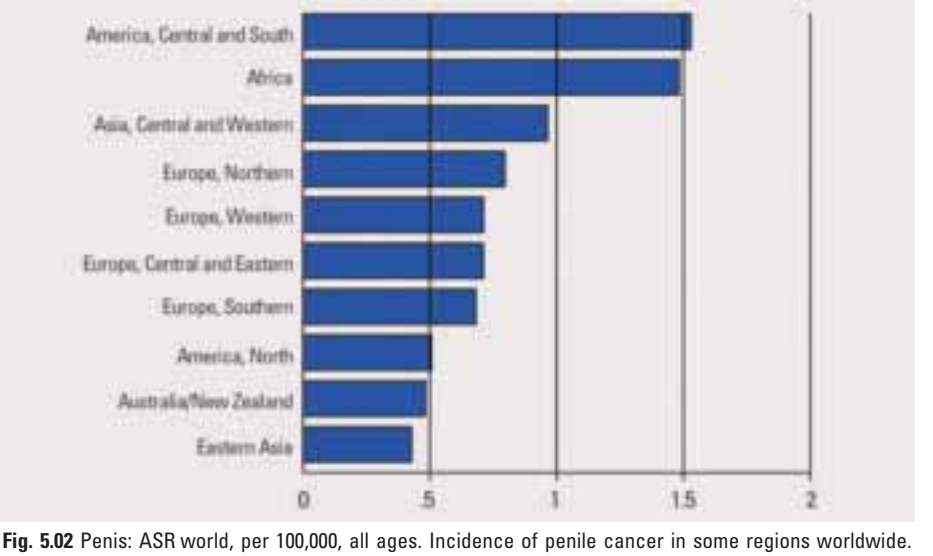

Fig. 5.02 Penis: ASR world, per 100,000, all ages. Incidence of penile cancer in some regions worldwide. From D. M. Parkin et al. {2016}.

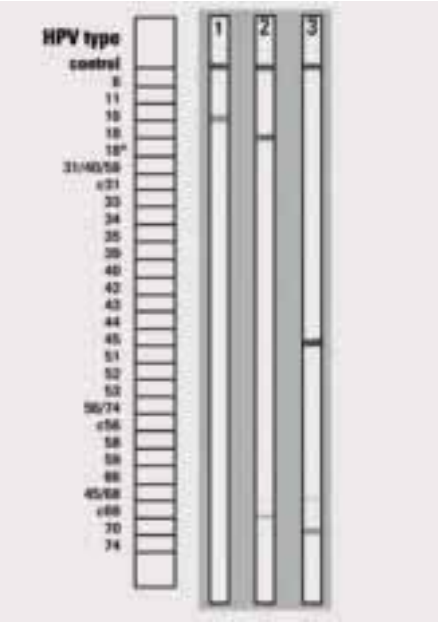

Fig. 5.03 HPV-typing in penile cancers. Identification of HPV genotypes using a linear probe assay. LiPA strips with hybridization bands indicating a single HPV type infection: lane 1: HPV 16; lane 2: HPV 18; and a multiple HPV type infection: lane 3: HPV 45 and 70. Note: HPV 18 is reactive with two probes, 18 and c68, and HPV 45 with probes 45 and 45/68. Reprinted with permission from M.A. Rubin et al. {2258}.

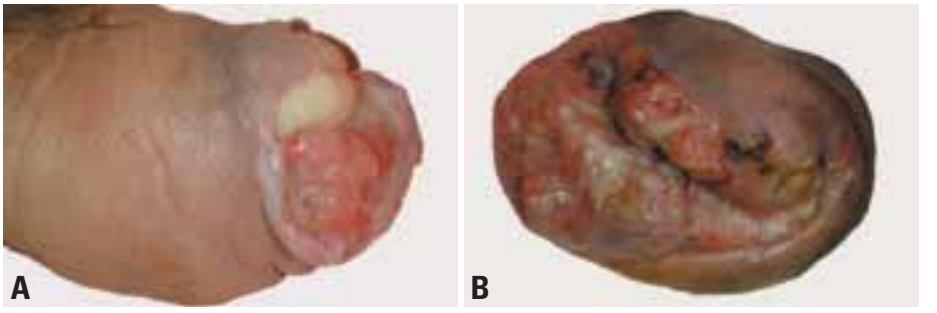

Fig. 5.04 A, B Squamous cell carcinoma of the usual type. Exophytic growth pattern.

Human papillomavirus (HPV) infection

HPV is present in a subset of penile SCC, with HPV 16 as the most frequent type {945,1153}. HPV DNA is preferentially found in cancers with either basaloid and/or warty features, and only weakly correlated with typically keratinizing SCC {945,2258}. Penile intraepithelial neoplasia (IN), a recognized precursor, is consistently HPV DNA positive in 70-100% of investigated cases {1153}. A possible explanation is that the HPV-negative invasive cancers do not arise from the HPV-positive IN, but from unrecognized HPV-negative precursor lesions.

Clinical features

Signs and symptoms

Mean age of presentation is 60 years {517,2905} and patients may present with an exophytic or flat ulcerative mass in the glans, a recurrent tumour in the surgical stump or a large primary tumour with inguinal nodal and skin metastases. Occasionally the lesions may be subtle, such as a blemish or an area of erythema. In patients with long foreskin and phimosis the tumour may be concealed and an inguinal metastasis be the presenting sign.

Imaging

Imaging, until very recently, has played a minimal role in the staging and direction of treatment options. A recent study compared the accuracy of physical examination, ultrasound investigation and magnetic resonance imaging (MRI) {1535} and found physical examination as the most accurate method to determine tumour site and extent of corpus spongiosum infiltration. Because of the possibility of imaging in various planes and because of the ability to visualize other structures of the penis, MRI can be useful to determine the true proximal extent of the tumour.

Recently the concept of sentinel node {356} has been explored again in penile cancer {2579}. Imaging by lymphoscintigraphy with a radioactive tracer is considered as one of the prerequisites to determine the individual drainage pattern in order to find the sentinel node. Lymphoscintigraphy visualized at least 1 sentinel node in 98% of the patients.

Tumour spread

Penile carcinoma has a fairly predictable dissemination pattern, initially to superficial lymph nodes, then to deep groin and pelvic nodes and lastly to retroperitoneal nodes. The first metastatic site is usually a superficial inguinal lymph node located in the groin upper inner quadrant (sentinel node). This pattern presents in about 70 % of the cases. Some tumours metastasize directly to deep inguinal nodes. Skip inguinal nodal metastases

Table 5.01
HPV DNA detection in penile condyloma, dysplasia and carcinoma. From Rubin et al. {2258}.

		HPV-positive		Low risk HPV		High risk HPV		Multiple HPV	
Diagnosis	**n**	**n**	**%**	**n**	**%***	**n**	**%***	**n**	**%***
Condyloma	12	12	100.0	11	91.7	1	8.3	0	0
Dysplasia	30	27	90.0	5	18.5	16	59.3	6	22.2
All benign cases	42	39	92.8	16	41.0	17	43.6	6	15.4
Keratinizing SCC	106	37	34.9	0	0	23	62.1	8	21.6
Verrucous SCC	12	4	33.3	1	25.0	2	50.0	0	0
Basaloid SCC	15	12	80.0	0	0	11	91.7	1	8.3
Warty SCC	5	5	100.0	0	0	4	80.0	1	20.0
Clear cell SCC	2	1	50.0	0	0	1	100.0	0	0
Sarcomatoid SCC	1	0	0.0	0	0	0	0	0	0
Metastatic SCC	1	1	100.0	0	0	1	100.0	0	0
All cancer cases	**142**	**60**	**42.2**	**1**	**1.6**	**42**	**70.0**	**10**	**16.6**

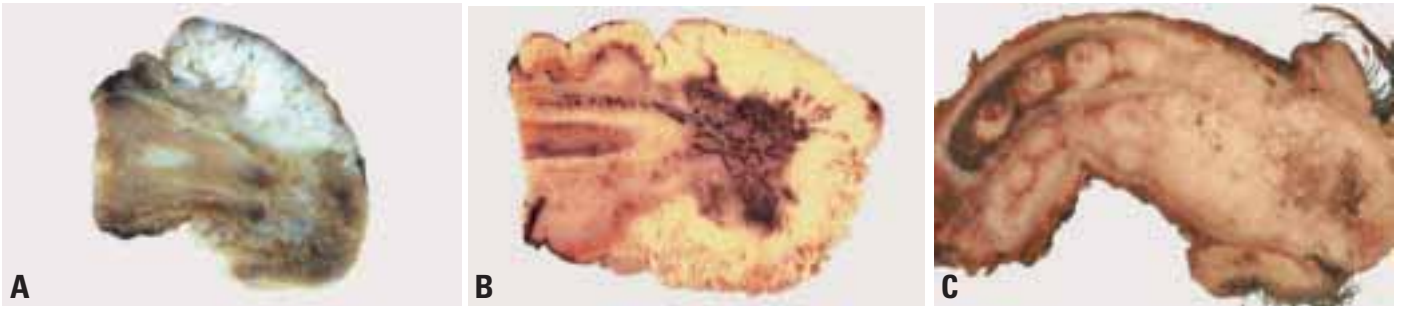

Fig. 5.05 A Well differentiated squamous cell carcinoma with invasion of corpus spongiosum. **B** Squamous cell carcinoma. Large neoplasm replacing glans surface. **C** Squamous cell carcinoma. Massive replacement of penile corpus spongiosum and cavernosum by a white neoplasm.

(primary tumour to pelvic inguinal nodes) are extremely unusual. Systemic blood borne dissemination occurs late. Common general sites of metastatic involvement are liver, heart, lungs and bone {2905}.

Prognosis

Pathologic factors related to prognosis of penile carcinomas are site of primary tumour, pattern of growth, tumour size, histological type, grade, depth and vascular invasion. Tumours exclusively in the foreskin, carry a better prognosis {1933} because of low grade and frequent superficially invasive growth {514}. The incidence of metastasis in verruciform tumours is minimal. Mortality in patients with superficially spreading carcinomas is 10% compared with 67% for patients with vertical growth pattern {521}. The 3 most important pathological factors to predict final outcome are histological grade, depth of invasion and vascular invasion especially the combination of grade and depth. There is no consensus regarding method of grading {1121, 1608,2438}. The depths of invasion should be evaluated on penectomy specimens {2719}. Measurement of depth of invasion in mm should be performed from the basement membrane of adjacent squamous epithelium to deepest point of invasion {693}. The large destructive lesions or bulky exophytic tumours especially those of the verruciform group should be measured from the nonkeratinizing surface of the tumour to the deepest point of invasion. Evaluation of the anatomical levels of tumour invasion is limited by the variation in thickness of the corpus spongiosum. The threshold for penile metastasis is about 4-6 mm invasion into the corpus spongiosum {520}. When possible, more than one method should be utilized. A combination of histologic grade and depth is thought to better predict metastasis and mortality, including micrometastasis {1672,2458}. One system utilizes a prognostic index from 1 to 6, combining numerical values for histologic grade (1-3) and anatomical level of invasion (1-3, LP, CS and CC in glans and LP, dartos and skin in the foreskin). Low indices (1-3) are associated with no mortality. Metastatic and mortality rates are high in patients with indexes 5 and 6 {519}. Molecular markers have been studied as prognostic predictors. Ploidy was not found to be useful as a predictor of prognosis {1002}. P53, however, appeared to be an independent risk factor for nodal metastasis, progression of disease and survival in 2 studies {1546,1640}. HPV was not found to be prognostically important {236}. Tissue associated eosinophilia has been linked with improved survival in patients with penile cancer {1961}.

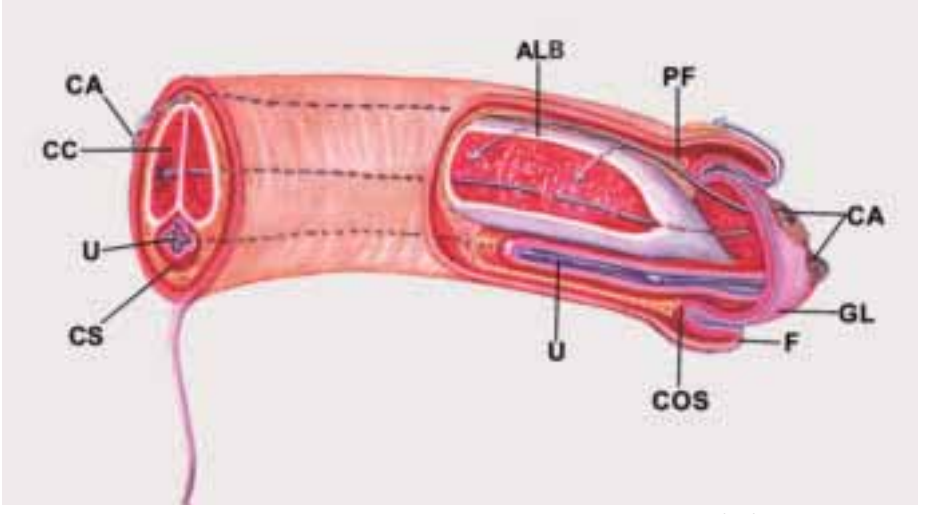

Fig. 5.06 Routes of local spread: Lines and arrows depict pathways of local tumour (CA) progression, from distal glans (GL), foreskin (F) and coronal sulcus (COS) to proximal corpus spongiosum (CS), corpora cavernosa (CC), penile fascia (PF), skin and urethra (U). (ALB) tunica albuginea.

Squamous cell carcinoma

Definition

A malignant epithelial neoplasm with squamous differentiation.

ICD-O codes

Squamous cell carcinoma	8070/3
Basaloid carcinoma	8083/3
Warty (condylomatous) carcinoma	8051/3
Verrucous carcinoma	8051/3
Papillary carcinoma (NOS)	8050/3
Sarcomatoid (spindle cell) carcinoma	8074/3
Adenosquamous carcinoma	8560/3

Macroscopy

Average tumour size varies from 3 to 4 cm. Three main growth patterns are noted: *superficially spreading* with horizontal growth and superficial invasion,

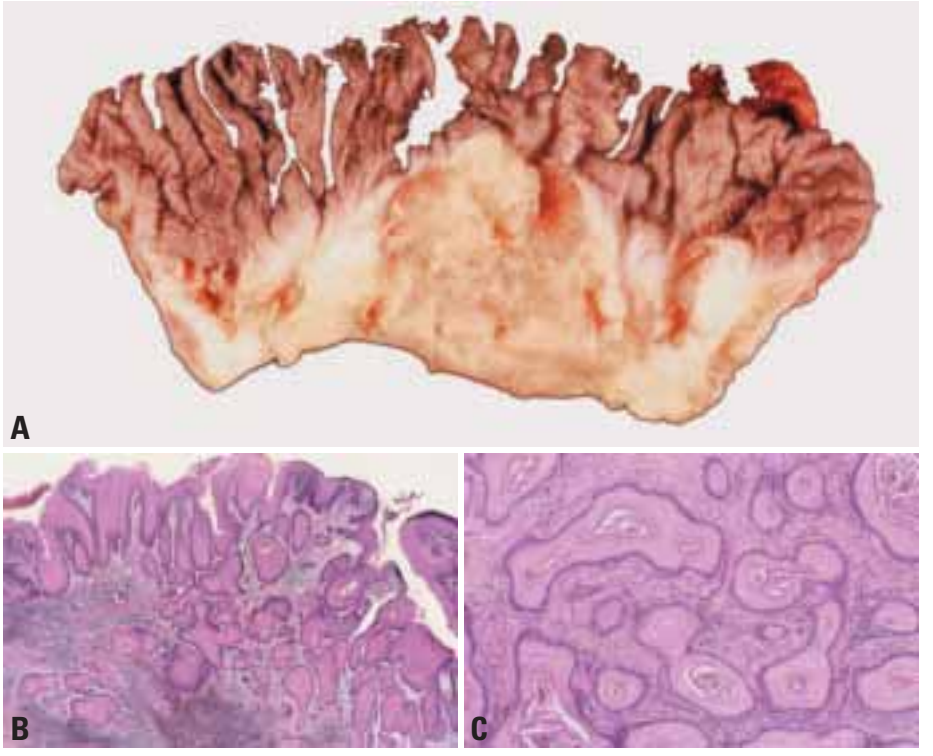

Fig. 5.07 Squamous cell carcinoma. **A** An irregular granular flat neoplasm involving the mucosal aspect of the foreskin. **B** Well differentiated SCC with irregular infiltrating borders. **C** Well differentiated keratinizing SCC.

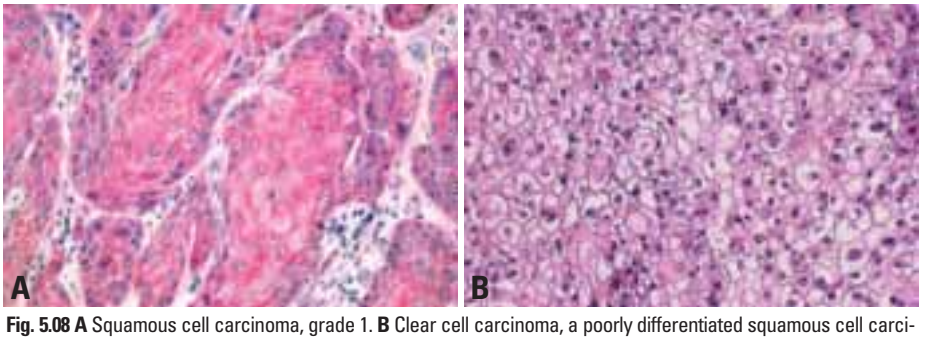

Fig. 5.08 A Squamous cell carcinoma, grade 1. **B** Clear cell carcinoma, a poorly differentiated squamous cell carcinoma with cytoplasmic clearing.

Fig. 5.09 Squamous cell carcinoma of the penis. **A** Squamous cell carcinoma infiltrating urethra. **B** Squamous cell carcinoma infiltrating periurethral glands.

vertical growth deeply invasive and *multicentric*. Any combination may occur {517}. Multicentric carcinomas are more frequent in the foreskin {1933}. The tumours are usually white, grey, granular irregular masses partially or totally replacing the glans or foreskin. The glans surface may be flat, ulcerated or deformed by an exophytic mass. In some patients the foreskin is abutted by underlying tumour and may show skin ulcerations. The contrast between the pale invasive tumour and the dark red colour of CS or CC permits determination of the deepest point of invasion, which is prognostically important {520}. Adjacent hyperplastic or precancerous lesions often can be visualized as a marble white 1-2 mm thickening. Mixed tumours should be suspected when different growth patterns are present.

Local spread

Penile tumours may spread from one mucosal compartment to the other. Typically, foreskin carcinomas spread to coronal sulcus or glans and carcinomas originating in the glans may spread to the foreskin. Penile SCC may spread horizontally and externally to skin of the shaft and internally to proximal urethral margin of resection. This is the characteristic spread of superficially spreading carcinomas. The vertical spread may progress from surface to deep areas {517}. An important, under recognized route of spread is the penile fascia, a common site of positive surgical margin of resection. The fascial involvement in tumours of the glans is usually through the coronal sulcus. Tumour in the fascia may secondarily penetrate into corpus cavernosum via nutritional vessels and adipose tissue traversing the tunica albugina. It is not unusual to find "satellite nodules", frequently associated with regional metastasis. Multiple urethral sites may be involved at the resection margins {2720}. Pagetoid intraepithelial spread may simulate carcinoma in situ or Paget disease. In more advanced cases penile carcinomas may spread directly to inguinal, pubic or scrotal skin.

Histopathology

There is a variable spectrum of differentiation from well to poorly differentiated. Most frequently there is keratinization and a moderate degree of differentiation. Very well differentiated and solid nonkeratinizing poorly differentiated carcinomas are unusual. Invasion can be as individual cells, small irregular nests of atypical cells, cords or large cohesive sheets present in the lamina propria or corpus spongiosum. Infrequently (about a fourth of cases) the corpus cavernosum is affected. The boundaries

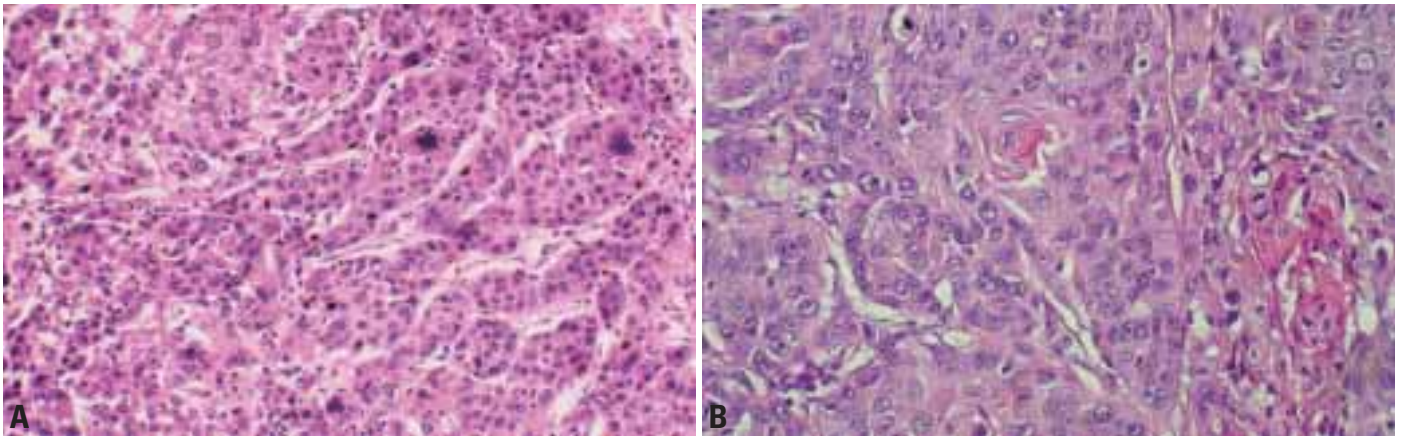

Fig. 5.10 Squamous cell carcinoma. **A** Poorly differentiated keratinizing SCC. **B** Squamous cell carcinoma of the penis, grade 3.

between stroma and tumour are irregular or finger like. Broadly based margins are unusual. Superficially invasive tumours tend to be well differentiated and deeper tumours poorly differentiated. Deeply invasive carcinomas may focally show spindle, pleomorphic, acantholytic, giant, basaloid or clear cells. In poorly differentiated tumours individual cell necrosis or comedo-like necrosis may be found as well as numerous mitotic figures {521,2905}.

Differential diagnosis

Superficial and differentiated invasive lesions should be distinguished from pseudoepitheliomatous hyperplasia. In SCC the nests detached from overlying epithelium are disorderly, show keratinization, are more eosinophilic and nucleoli are prominent. Stromal or desmoplastic reaction may be present in both conditions but is more frequent in carcinomas. Hyperplastic nests do not involve the dartos or corpus spongiosum.

Variants of squamous cell carcinoma

Basaloid carcinoma

Basaloid carcinoma is an HPV related aggressive variant, which accounts for 5-10% of penile cancers {518,522,945}. Median age at presentation is in the sixth decade. Most commonly it arises in the glans. Grossly, it presents as a flat, ulcerated and irregular mass, which is firm, tan and infiltrative. Microscopically, it is composed of packed nests of tumour cells, often associated with comedo-type necrosis. The cells are small with scant cytoplasm and oval to round, hyperchromatic nuclei and inconspicuous nucleoli. Mitotic rate is usually brisk. Palisading at the periphery of the nest and abrupt central keratinization is occasionally seen. They tend to infiltrate deeply into adjacent tissues, including corpora cavernosa. Spread to inguinal lymph nodes is common and the mortality rate is high.

Warty (condylomatous) carcinoma

This variant corresponds to 20% of "verruciform" neoplasms {235,521,523,945}. Median age is in the fifth decade. Grossly, it is a white to tan, cauliflower-like lesion that may involve glans, coronal sulcus or foreskin. Tumours as large as 5.0 cm have been described. Microscopically, it has a hyper-parakeratotic arborizing papillomatous growth. The papillae have thin fibrovascular cores and the tips are variably round or tapered. The tumour cells have low to intermediate grade cytology. Koilocytotic atypia is con-

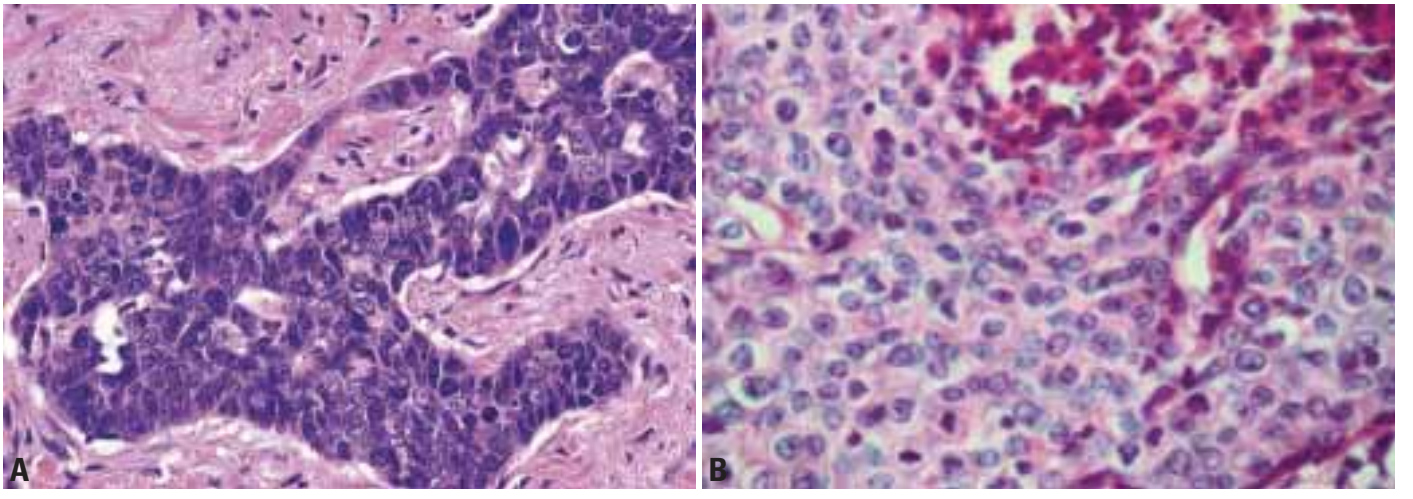

Fig. 5.11 A Basaloid carcinoma of the penis. **B** Basaloid carcinoma of the penis with comedo necrosis, upper right.

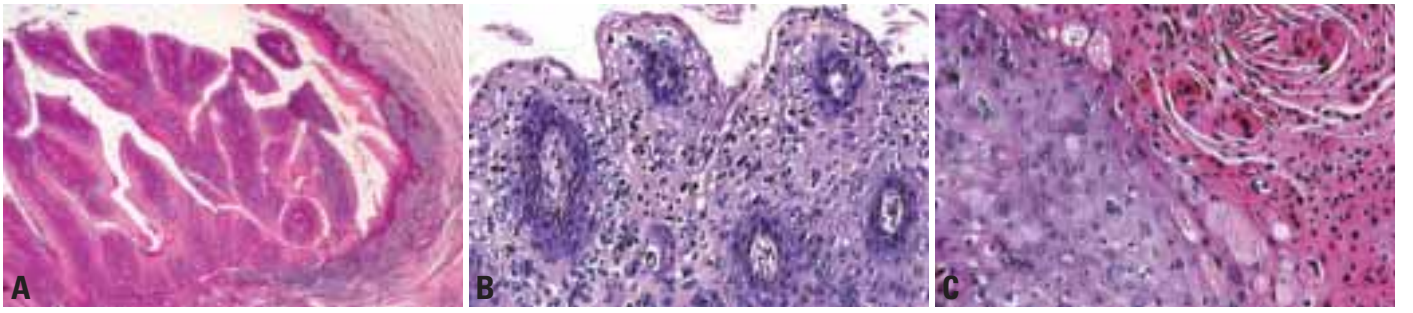

Fig. 5.12 A Warty (condylomatous) carcinoma of the penis. Note papillary growth. **B,C** Warty squamous cell carcinoma.

spicous. Nuclei may be large, hyperchromatic and wrinkled and binucleation is common. Tumours may infiltrate deeply and the interface of tumour with stroma is usually irregular. HPV DNA testing has demonstrated HPV 16 and 6 in some cases. Some have metastasized to regional lymph nodes, usually associated with deeply invasive lesions.

Verrucous carcinoma

This variant usually involves the glans or foreskin {1232,1643}. Grossly, it measures about 3.5 cm and appears as an exophytic, grey-white mass. Microscopically, it is a very well differentiated papillary neoplasm with acanthosis and hyperkeratosis. The papillations are of variable length and fibrovascular cores are inconspicuous. The nuclei are bland, round or vesicular, although slightly more atypical nuclei may be seen at the basal cell layer. Koilocytotic changes are not evident. Tumours may extend into the underlying stroma with a broad based, pushing border, making determination of invasion difficult. Verrucous carcinoma is considered not to be HPV-related. This is a slow growing tumour that may recur locally but metastasis does not occur in typical cases.

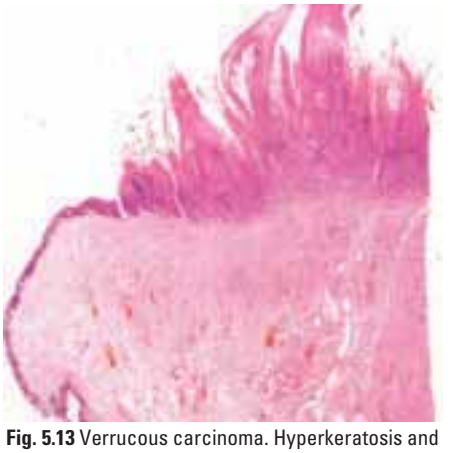

Fig. 5.13 Verrucous carcinoma. Hyperkeratosis and papillomatosis.

Papillary carcinoma, not otherwise specified (NOS)

This variant occurs mainly in the fifth and sixth decades {521}. Grossly, it is exophytic, grey-white and firm. The median size in one series was reported as 3.0 cm although cases as large as 14.0 cm have been reported. Microscopically, these are well differentiated, hyperkeratotic lesions with irregular, complex papillae, with or without fibrovascular cores. The interface with the underlying stroma is infiltrative and irregular. These tumours are not HPV-related. Despite the fact that invasion into the corpus cavernosum and spongiosum has been documented, regional lymph node involvement has not been seen in the relatively few cases reported.

Sarcomatoid (spindle cell) carcinoma

Squamous cell carcinoma with a spindle cell component arises de novo, after a recurrence, or following radiation therapy {821}. The glans is a frequent site {2838} but they may occur in the foreskin as well. Grossly, they are 5-7 cm irregular white grey mixed exophytic and endophytic masses. On cut surface, corpus spongiosum and cavernosum are invariably involved. Histologically, there are atypical spindle cells with features similar to fibrosarcoma, malignant fibrous histiocytoma or leiomyosarcoma. These cells have the potential to differentiate into muscle, bone and cartilage, benign or malignant {103}. Differentiated carcinoma in situ or invasive carcinoma is usually found. Electron microscopy and immunohistochemistry are useful to rule out sarcomas and spindle cell

Fig. 5.14 Verrucous carcinoma. The tumour pushes into corpus spongiosum with focal involvement of tunica albuginea.

Fig. 5.15 Mixed verrucous-squamous cell carcinoma. Predominantly papillomatous appearence except in the lower central area where the neoplasm is solid.

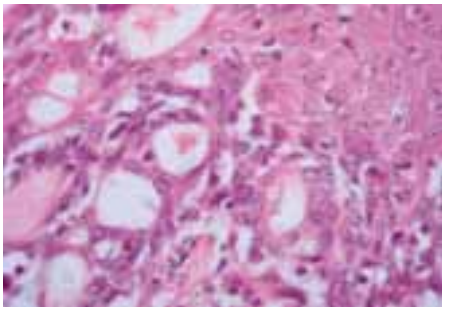

Fig. 5.16 Adenosquamous carcinoma.

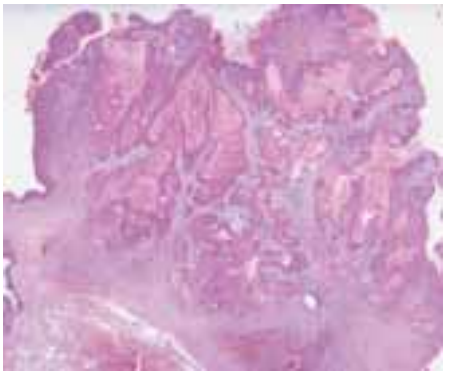

Fig. 5.17 Low grade papillary carcinoma affecting the foreskin.

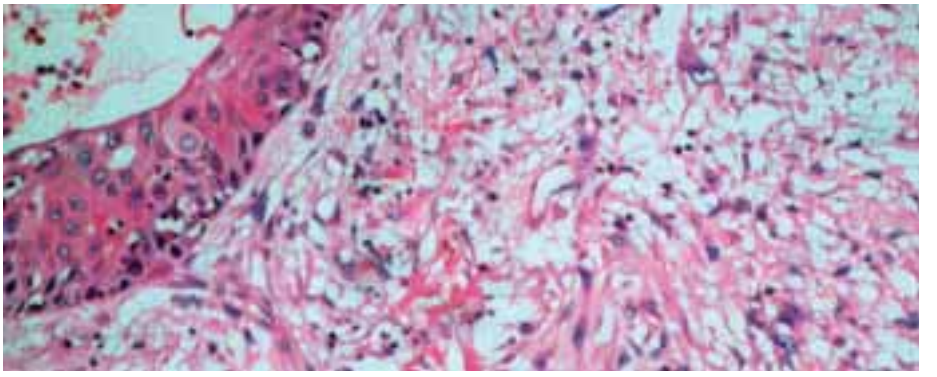

Fig. 5.18 Sarcomatoid (spindle cell) carcinoma of the penis.

melanomas {1613}. Sarcomatoid carcinomas are associated with a high rate of regional nodal metastases {521}.

Mixed carcinomas

About a fourth of penile carcinomas consist of a mixture of various types. A moderate to high grade squamous cell carcinoma in an otherwise typical verrucous carcinoma (so called 'hybridverrucous') shows metastatic potential {473,1232}. The warty-basaloid carcinoma has a high incidence of groin metastasis {2574}. Other recognized combinations include adenocarcinoma and basaloid {515} (adenobasaloid) and squamous and neuroendocrine carcinoma.

Adenosquamous carcinoma

Squamous cell carcinoma with mucinous glandular differentiation arises from surface epithelium. The origin may be related to misplaced or metaplastic mucinous glands {516,1208,1642}. Grossly, it is a firm white grey irregular mass involving the glans. Microscopically, the squamous predominates over the glandular component. The glands stain positive for CEA. Adenocarcinomas and mucoepidermoid carcinomas of the penis have also been reported {810,1455,2702}.

Other rare pure primary carcinomas

ICD-O codes

Merkel cell carcinoma	8247/3
Small cell carcinoma of neuroendocrine type	8041/3
Sebaceous carcinoma	8410/3
Clear cell carcinoma	8310/3

A small number of unusual primary penile neoplasms include the Merkel cell carcinoma {2625}, small cell carcinoma of neuroendocrine type {830}, sebaceous carcinoma {1967}, clear cell carcinoma {2905}, and well differentiated squamous cell carcinoma with pseudohyperplastic features (pseudohyperplastic carcinoma) {524}. Another rare lesion is the papillary basaloid carcinoma consisting of an exophytic growth, with papillae composed of small poorly differentiated cells similar to the cells seen in invasive basaloid carcinomas {515}.

Basal cell carcinoma

ICD-O code 8090/3

Basal cell carcinoma (BCC) is a rare indolent neoplasm of the penis identical to BCC of other sites {794,1425,2041}. They may be uni- or multicentric {2041}. The localization is on the shaft and rarely on the glans {872,1674}. Of 51 BCC of regions not exposed to sun, 2 were in the penis {1244}. BCCs are differentiated and usually superficial with minimal metastatic potential {1317}. It is impor-

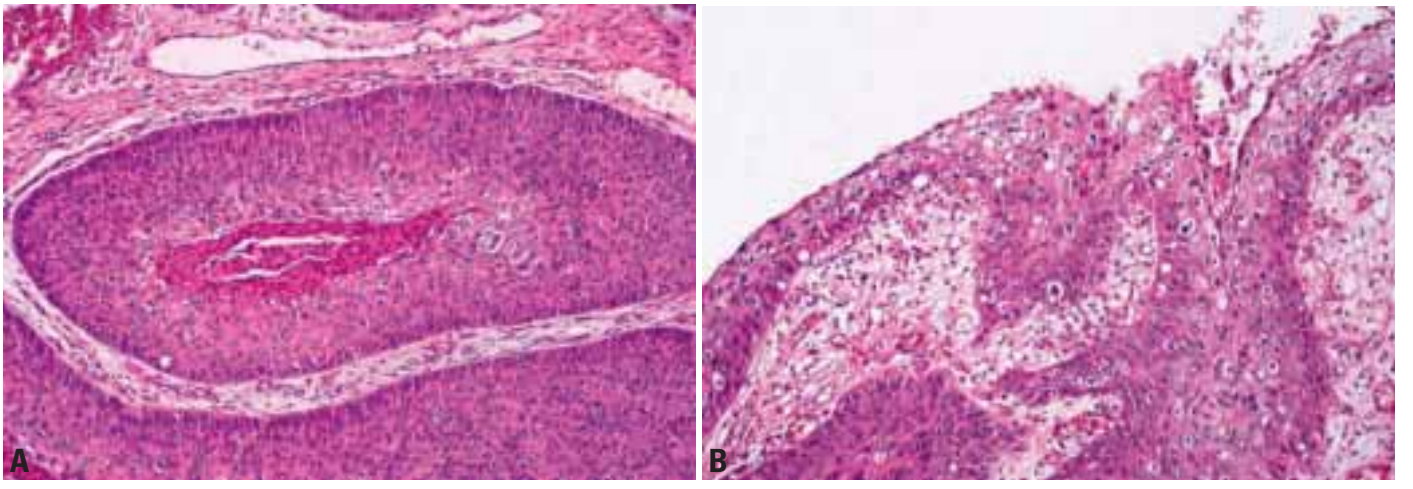

Fig. 5.19 Warty-basaloid carcinoma. **A** Invasive nests. **B** Surface appearance.

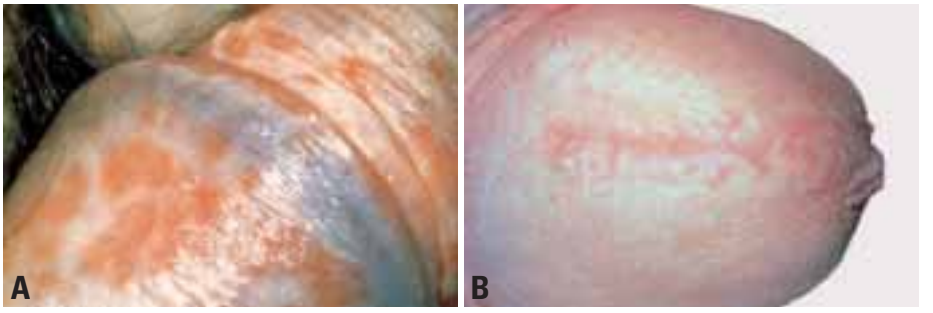

Fig. 5.20 Bowenoid papulosis. **A, B** Clinically, two types exist; macular and papular (right). The lesions may be multiple or solitary and the diameter varies from 2-10 mm.

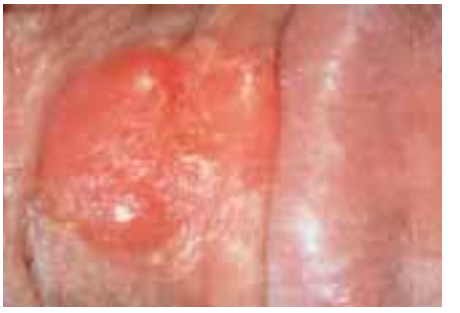

Fig. 5.21 Penile Bowen disease. Bowen disease appearing as a well demarcated reddish plaque on the inner aspect of the foreskin.

tant to distinguish them from the aggressive basaloid squamous cell carcinoma, which invades deeply, has abrupt keratinization, comedo necrosis and high mitotic rates.

Precursor lesions

HPV and penile intraepithelial neoplasia

ICD-O code

Intraepithelial neoplasia
Grade III 8077/2

Human papillomaviruses (HPV) are the most heterogeneous of human viruses {574}. About 30 sexually transmittable genotypes exist that are further classified into "low" and "high risk" types according to oncogenic potential {574,619}. Generally, overt genital warts ("condylomas") are associated with "low risk" HPVs - including types 6 and 11. The "high risk" HPVs - most commonly types 16 and 18 - are predominantly associated with subclinical lesions {2756}. Mucosal infections mainly are transient in young people {670}. Longitudinal studies demonstrate that patients who cannot clear high risk HPV infections within about a year are at risk for malignant transformation. SCC is thought to develop via HPV-associated precursor lesions (intraepithelial neoplasia; IN) that are graded I-III in proportion to the epithelial thickness occupied by transformed basaloid cells. These vary in size and shape, with the nuclei being pleomorphic and hyperchromatic. They are accompanied by loss of polarity. In grade I, the IN occupies the lower one third, in grade II the lower two thirds, and in grade III the full epithelial thickness ("Bowen atypia"; in situ SCC). Concurrent infection with low and high risk types is common. Condylomas and IN sometimes coexist as part of a morphological continuum.

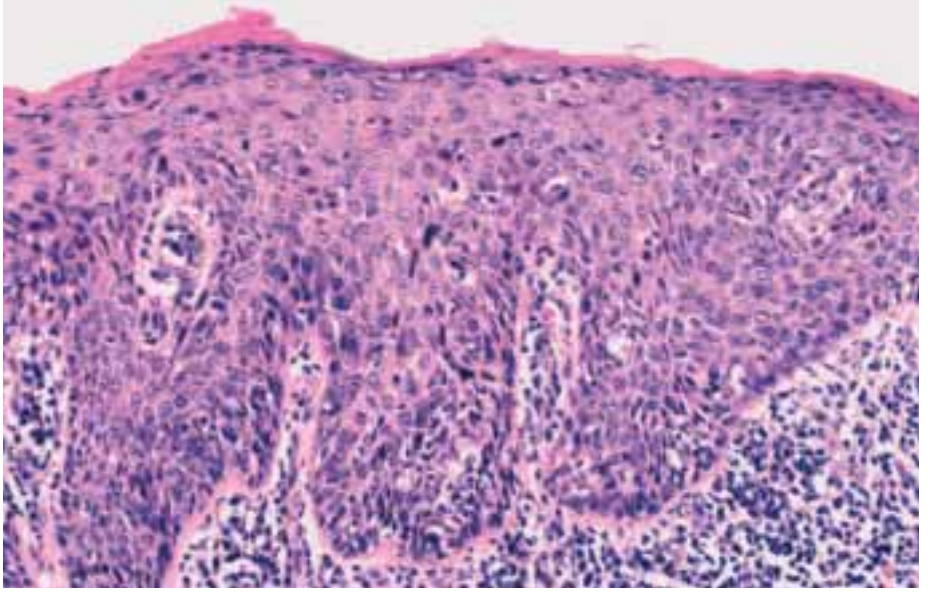

Fig. 5.22 High grade squamous intraepithelial lesion (SIL), squamous.

Studies of HPV and penile cancer are limited because of the scarce occurrence and the peculiar geographical distribution of this malignancy, being rare in the USA and Europe but fairly common in many developing countries {619,2756}. The predominant HPV that is found in penile SCC is type 16, followed by type 18. HPV types 6/11 have been detected in anecdotal cases.

Most patients with IN lack physical symptoms, but itching, tenderness, pain, bleeding, crusting, scaling and difficulty in retracting the foreskin may develop {2756}. Chronic inflammation, phimosis and poor hygiene may be important contributing factors {670,2754-2756}. A pathogenic role of chronic lichen sclerosus and verrucous carcinoma has been discussed, while oncogenic HPVs have been linked more strongly to warty/basaloid carcinomas {945}.

The following comments summarize clinical features of three penile conditions presumed to be precancerous: *Giant condyloma, Bowenoid papulosis* and *Bowen disease*. Due to clinical overlap and differential diagnostic problems, a vigilant approach to diagnostic biopsy sampling cannot be overly stressed.

Giant condyloma

"Giant condyloma" (Buschke-Löwenstein) is a rare (about 100 cases published) and peculiar condyloma variant {968,2756} generally arising due to poor hygiene of uncircumcized men (range 18-86 years of age). It is characterized by a semi-malignant slowly growing condylomatous growth often larger than

5 cm in diameter. The term has been used for various lesions namely: true giant condylomas, verrucous carcinoma and warty carcinoma. In some cases a complex histological pattern exists, with areas of benign condyloma intermixed with foci of atypical epithelial cells or even well differentiated in situ carcinoma. Moreover, mixed tumours have been observed in which unequivocal features of benign condyloma, warty carcinoma and either basaloid or typical squamous cell carcinoma occur adjacent to one another {2756}. It is currently believed that the giant condyloma and verrucous SCC are separate pathological lesions. The accurate diagnosis may require multiple biopsies.

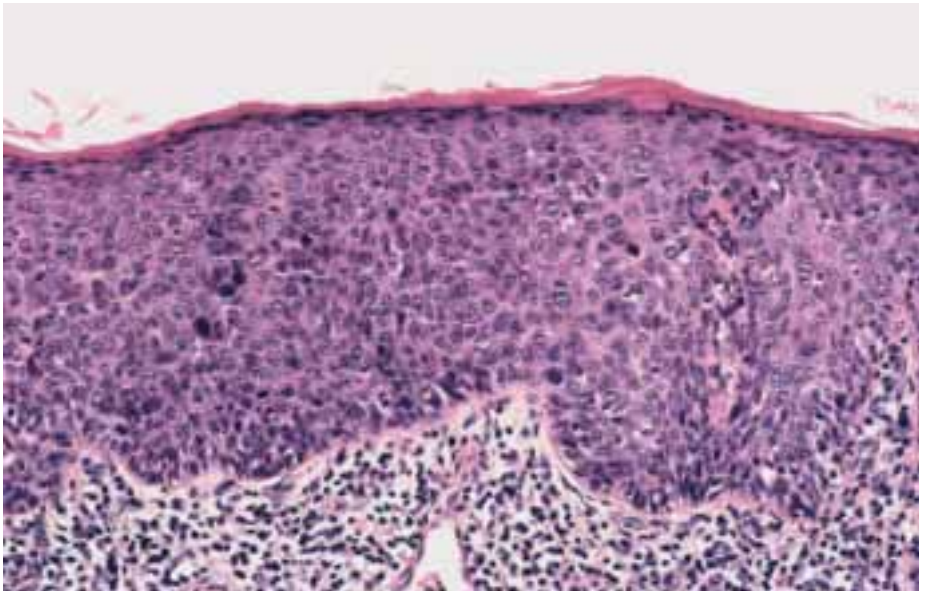

Fig. 5.23 High grade squamous intraepithelial lesion (SIL), basaloid.

Bowenoid papulosis and Bowen disease

ICD-O codes

Bowen disease	8081/2
Erythroplasia of Queyrat	8080/2

Genital Bowenoid papulosis (BP) is the term used for lesions in young sexually active people16-35 (mean 28) years of age that display histological features of IN III. The sharp border between the epidermis and the dermis is preserved. The histopathological presentation cannot be distinguished from that of Bowen disease (BD) although focal accumulations of uniformly round nuclei and perinuclear vacuoles in the horny layer is more common in BP {968}. Oncogenic HPV DNA, most commonly is type 16, but types 18 and/or 33-35 have repeatedly been discovered.

Reddish-brown and pigmented colour tones are more common than in benign condylomas. Typical IN III lesions tend to be small (2-10 mm), multicentric smooth velvety maculopapular reddish-brown, salmon-red, greyish-white lesions in the preputial cavity, most commonly the glans. Thicker epithelial lesions may be ashen-grey or brownish-black. BP may also be solitary or coalesce into plaques, when the clinical presentation overlaps with that of BD. Both conditions sometimes resemble lichen sclerosus, psoriasis and eczema {2756}.

BP is predominantly transient, self limiting and clinically benign in young people; spontaneous regression within a year has been reported in immunocompetent individuals below the age of 30 years. However, these lesions often show recalcitrance after surgical intervention. Possibly, some cases of persistent BP may progress to BD and invasive cancer.

Bowen disease (BD) has long been considered a premalignant lesion. If left untreated, documented transformation to SCC has been reported in the range of 5-33% in uncircumcized men {2756}. Usually, the clinical appearance is that of a single, well demarcated reddish plane and/or bright red scaly papule or plaques, ranging in diameter from a 2-35 mm. When located on the glans penis it is by tradition named erythroplasia of Queyrat (EQ). Lesions on dry penile skin are brownish-red or pigmented. Occasionally they are ulcerative or may be covered by a pronounced hyperkeratosis that may appear as a "cutaneous horn" {2756}. The most important clinical hallmark in the differential diagnosis versus BP is the age. The average age on diagnosis of BD/QE is 61 years. Review of 100 cases of QE revealed that 90% of cases were white men with a median age of 51 years. From the records of 87 men with BD, 84 were uncircumcized and

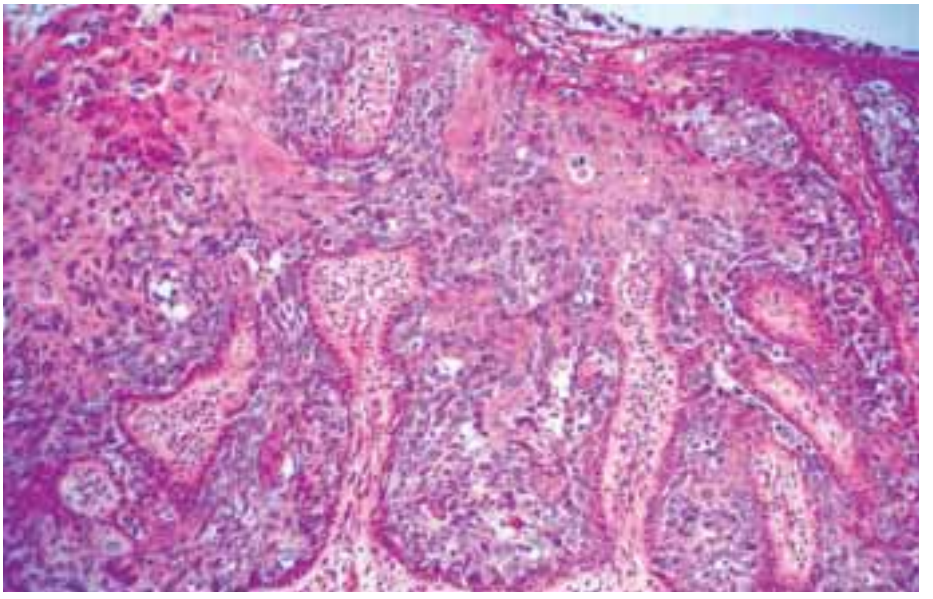

Fig. 5.24 Paget disease. Typical spread of atypical cells in the epithelium.

three had been circumcized by 9 years of age, the median age of patients with BD is 51 years {2756}.

Prognosis and follow-up of IN

It is clinically impossible to determine which individual will develop pernicious HPV infection and progress from IN III to invasive cancer. Therefore we advocate that in persons older than 40 years, as well as in immunosuppressed individuals at earlier ages (including HIV infected people and allograft recipients), lesions should always be considered as premalignant and treated surgically. In younger men, a year or so of watchful waiting may be justified.

Treatment failure may be related to indistinct margins (marginal recurrences), extension of IN down hair follicles and unrecognized foci of invasive tumour. A variety of treatments have been used. Following treatment, the duration of follow-up is uncertain, but a clinical follow-up at 3 and 12 months seems reasonable to confirm clearance and healing. Patients remain at risk after penis sparing therapy and should be instructed to come back as soon as possible in case of suspected recurrence including the experience of a "lump", or the occurrence of local symptoms.

Paget disease

ICD-O code 8542/3

This is a form of intraepidermal adenocarcinoma, primary in the epidermis or spread from an adenocarcinoma {1067, 1401,1417}. The skin of the shaft is usually involved as part of a scrotal, inguinal, perineal or perianal tumour, but exclusive penile lesions occur {1586}. Patients are in the six or seventh decades and present with thickened red to pale plaques with scaling or oozing. Microscopically, there is an intraepithelial proliferation of atypical cells with a pale granular or vacuolated cytoplasm. Nuclei are vesicular and nucleoli prominent. Invasion into the dermis may result in metastasis to groin or widespread dissemination {1744}. Paget disease (PD) should be distinguished from pagetoid spread of penile or urothelial carcinomas {2624}, Bowen disease and melanomas. Clear cell papulosis {422} pagetoid dyskeratosis {2685} or mucinous metaplasia {2684} should also be ruled out. Frequently positive stains in PD are mucins, CEA, low molecular weight cytokeratins, EMA, gross cystic disease fluid protein and MUC 5 AC {1401}.

Melanocytic lesions

A.G. Ayala
P. Tamboli

Definition
Melanocytic lesions of the penis identical to those in other sites.

Incidence
Malignant melanocytic lesions of the penis are rare, with just over 100 cases of malignant melanoma reported since their first description by Muchison in 1859 {1229,1439,1614,1950}. Other melanocytic lesions include penile melanosis, genital lentiginosis, atypical lentiginous hyperplasia, melanocytic nevi, and atypical melanocytic nevi of the acral/genital type.

ICD-O codes

Melanocytic nevi	8720/0
Melanoma	8720/3

Epidemiology and etiology
Penile melanoma affects white men, between the ages of 50 and 70 years. Risk factors include pre-existing nevi, exposure to ultraviolet radiation, and a history of melanoma.

Localization
Sixty to eighty percent of melanomas arise on the glans penis, less than 10% affect the prepuce, and the remainder arises from the skin of the shaft.

Macroscopy
Grossly, the lesion has been described as an ulcer, papule, or nodule that is blue, brown, or red.

Histopathology
Reported histologic subtypes include nodular, superficial spreading, and mucosal lentiginous. The Breslow level (depth of invasion) is an important determinant of overall survival.

Prognosis and predictive factors
Management is similar to melanomas of other regions.

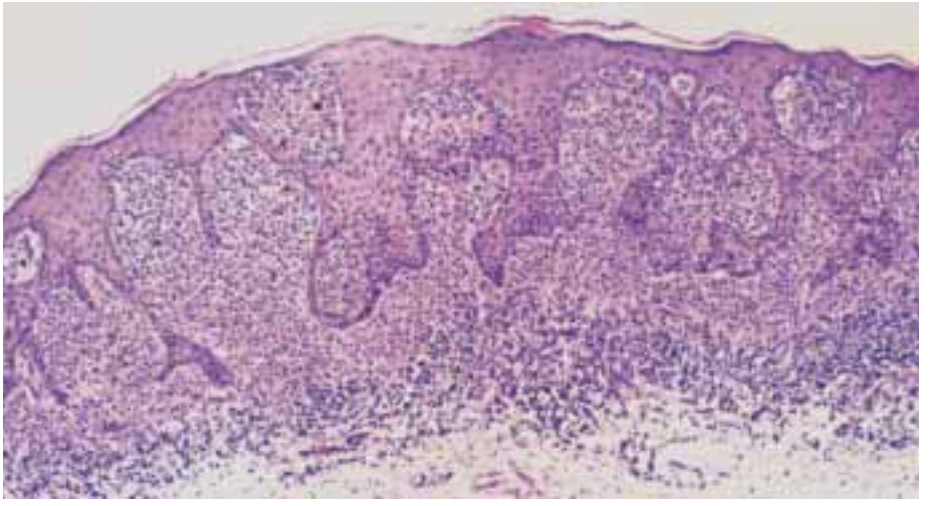

Fig. 5.25 Invasive melanoma. Perspective view of the atypical junctional component.

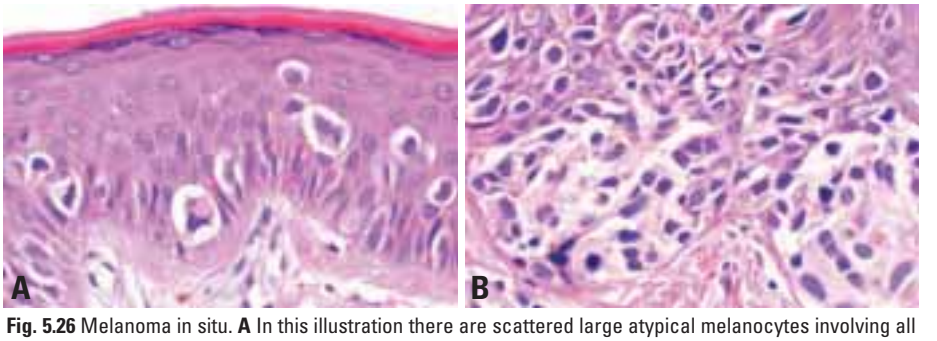

Fig. 5.26 Melanoma in situ. **A** In this illustration there are scattered large atypical melanocytes involving all layers of the epithelium. **B** This lesion shows an atypical junctional melanocytic proliferation associated with melanocytic cells that are present in the upper layers of the epithelium. Although the low power suggests a dysplastic nevus, the presence of atypical melanocytes migrating to different levels of the epithelium makes it a melanoma in situ.

Mesenchymal tumours

J.F. Fetsch
M. Miettinen

Definition

Tumours derived from the mesenchymal cells that are similar to those occuring at other sites.

Incidence

Mesenchymal tumours are very uncommon in the penis. The most frequently encountered benign mesenchymal tumours of the penis are vascular related. The most common malignant mesenchymal tumours are Kaposi sarcoma and leiomyosarcoma. With the exception of myointimoma, all of the listed tumours conform to definitions provided in other WHO fascicles (i.e., soft tissue, dermatopathology, and neuropathology fascicles). Myointimoma is a benign vascular related tumefaction with a myoid phenotype; this process is intimately associated with, and appears to be derived from, the vascular intima.

ICD-O codes

Benign	
Haemangioma variants	9120/0
Lymphangioma variants	9170/0
Neurofibroma	9540/0
Schwannoma (neurilemoma)	9560/0
Granular cell tumour	9580/0
Myointimoma	
Leiomyoma	8890/0
Glomus tumour	8711/0
Fibrous histiocytoma	8830/0
Juvenile xanthogranuloma	
Intermediate Biologic Potential	
Giant cell fibroblastoma	8834/1
Dermatofibrosarcoma protuberans	8832/3
Malignant	
Kaposi sarcoma	9140/3
Epithelioid haemangioendothelioma	9133/3
Angiosarcoma	9120/3
Leiomyosarcoma	8890/3
Malignant fibrous histiocytoma (including myxofibrosarcoma)	8830/3
Rhabdomyosarcoma	8900/3
Epithelioid sarcoma	8804/3
Synovial sarcoma	9040/3
Clear cell sarcoma	9044/3
Malignant peripheral nerve sheath tumour	9540/3
Peripheral primitive neuroectodermal tumour	9364/3
Ewing sarcoma	9260/3
Extraskeletal osteosarcoma	9180/3

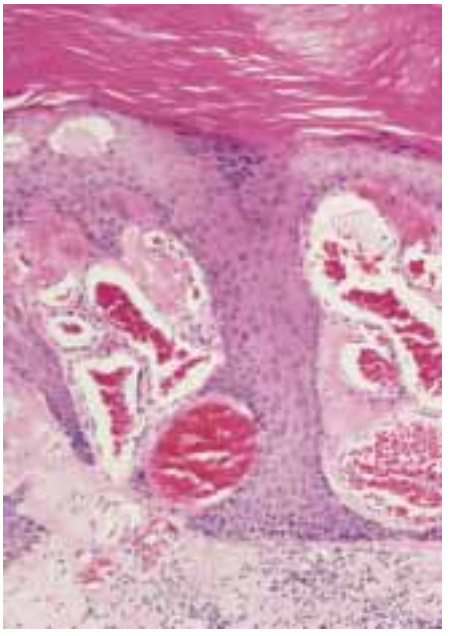

Fig. 5.27 Angiokeratoma of the penis.

Epidemiology

Factors predisposing individuals to the development of soft tissue tumours are, for the most part, poorly understood. Genetic factors, immunodeficiency states, and human herpesvirus 8 {101,412} have been implicated in the development of Kaposi sarcoma. Irradiation has been implicated in the pathogenesis of several sarcoma types, especially malignant fibrous histiocytoma, but also, angiosarcoma, malignant peripheral nerve sheath tumour, and others.

Most soft tissue tumours of the penis occur over a wide age range. Juvenile xanthogranuloma, giant cell fibroblastoma, and rhabdomyosarcoma are primarily paediatric tumours. Among nerve sheath tumours of the penis, neurofibromas have a peak incidence in the first and second decades, granular cell tumours primarily affect individuals in the

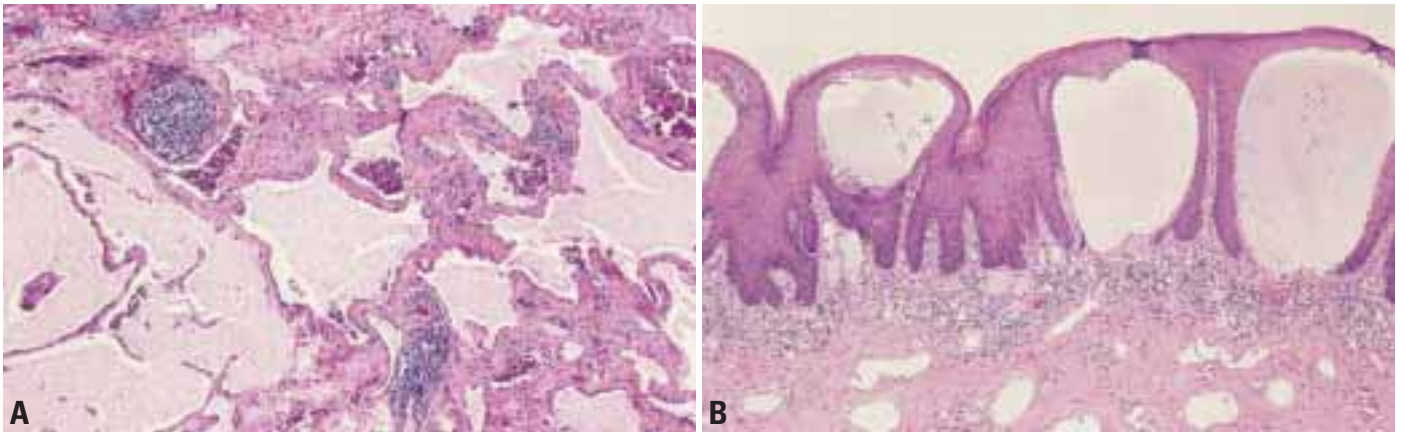

Fig. 5.28 A Lymphangioma of the penis. The presence of scattered lymphoid follicles is a helpful clue to the diagnosis. **B** Lymphangioma circumscriptum of the penis.

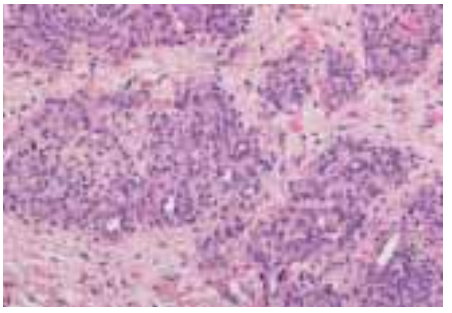

Fig. 5.29 Lobular capillary haemangioma (pyogenic granuloma) of the penis.

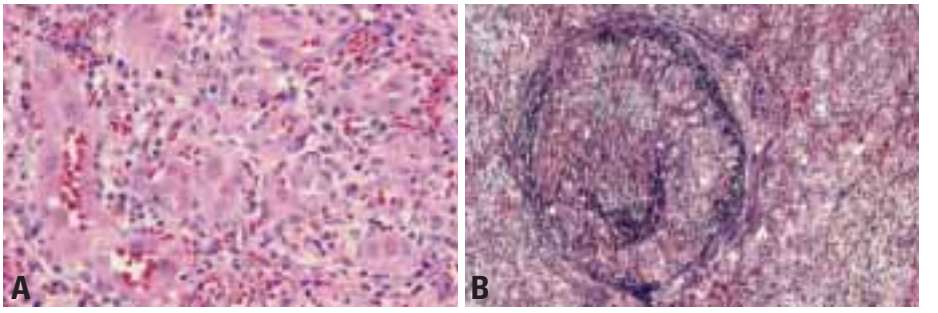

Fig. 5.30 Epithelioid haemangioma of the penis. **A** The process has immature but well formed vascular channels lined by plump epithelioid endothelial cells. A lymphocytic and eosinophilic inflammatory infiltrate is present. **B** This vascular was well demarcated and centered on a small muscular artery (note elastic lamina).

third and fourth decades, and schwannomas affect a higher percentage of patients in the fifth decade and above. Leiomyomas generally occur in mid adult life. Leiomyosarcoma, malignant fibrous histiocytoma, and angiosarcoma are usually tumours of mid and late adult life. Kaposi sarcoma of the penis diagnosed by a definitive method before the age of 60, and in the absence of other disqualifying causes for immunodeficiency (e.g. immunosuppressive/cytotoxic therapy, certain lymphoproliferative disorders, and genetic immunodeficiency syndromes), is considered an indicator of AIDS {2}.

Localization

Most benign soft tissue tumours of the penis do not exhibit a clear predilection for a specific site except myointimomas, which affect the corpus spongiosum of the glans and coronal regions, and neurofibromas and schwannomas, which more commonly affect the shaft and base. Among malignant tumours, Kaposi sarcoma has a strong predilection for the glans and prepuce, and leiomyosarcoma is somewhat more common on the shaft and base of the penis. Rhabdomyosarcomas of the penis are almost always located at the penopubic junction.

Table 5.02
Soft tissue tumours of the penis: AFIP data for 116 cases (1970-1999).

Tumour type	Number of cases	Age range (mean)
Glomus tumour	1	49
Leiomyoma	1	68
Fibrous histiocytoma	1	51
Giant cell fibroblastoma	1	1
Epithelioid haemangioendothelioma	1	51
Angiokeratoma	2	23 – 47
Lymphangioma circumscriptum (LC)	2	1 – 55
Epithelioid sarcoma	2	27
Fibromyxoma, NOS	2	25 – 41
Haemangioma variants (excluding EH)	3	28 – 60
Lymphangioma (other than LC)	3	26 – 47 (35)
Angiosarcoma	3	38 – 81 (63)
Malignant fibrous histiocytoma	3	51 – 86 (74)
Epithelioid vascular tumours of UMP	4	35 – 51 (44)
Unclassified sarcoma	5	39 – 81 (59)
Neurofibroma	6	9 – 58 (26)
Schwannoma	6	20 – 73 (47)
Granular cell tumour	7	20 – 60 (41)
Epithelioid haemangioma (EH)	9	39 – 75 (50)
Myointimoma	10	2 – 61 (29)
Leiomyosarcoma	14	43 – 70 (53)
Kaposi sarcoma	30	42 – 91 (65)

Clinical features

Most benign mesenchymal tumours of the penis present as a small, slowly enlarging, and often, painless mass. Malignant tumours generally occur at a later age, are more often tender or painful, and frequently grow more rapidly.
Superficial vascular tumours may exhibit erythematous or bluish colouration. Lymphangioma circumscriptum often presents as patches of translucent vesicles. Kaposi sarcoma presents as a patch, plaque, or nodule, often with a bluish or erythematous appearance.

Macroscopy

Haemangiomas and lymphangiomas have grossly apparent blood or lymph filled spaces, respectively. Neurofibromas have a well marginated, poorly marginated, or plexiform ("bag of worms") appearance and a solid off-white or myxoid cut surface. Schwannomas are typically well demarcated masses with white, pink or yellow colouration; they usually form a solitary nodule, but infrequently, they may have a multinodular appearance. Granular cell tumours tend to be poorly circumscribed and often have yellowish colouration and a scirrhous consistency. Malignant tumours tend to be poorly demarcated, infiltrative, and destructive masses, and often, are otherwise nonspecific from a gross standpoint.

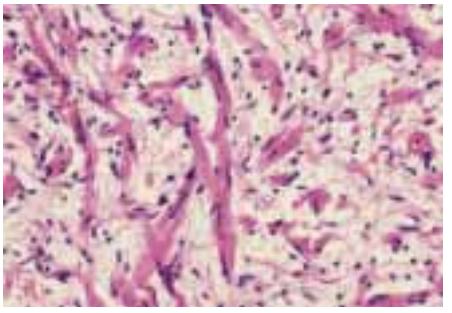

Fig. 5.31 Neurofibroma of the penis.

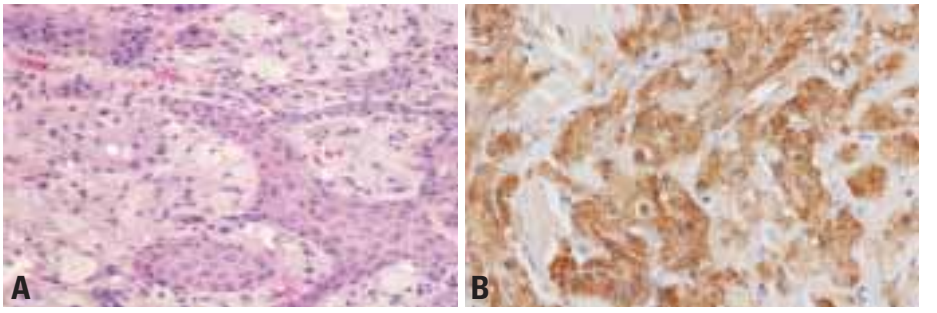

Fig. 5.32 Granular cell tumour of the penis. **A** This example was associated with prominent pseudoepitheliomatous hyperplasia of the epidermis. **B** The neoplastic cells are strongly immunoreactive for S100 protein.

Histopathology

Benign vascular lesions are classified on the basis of vessel type, growth pattern, and location. *Angiokeratoma* and *lymphangioma circumscriptum* feature superficial, dilated, blood or lymph-filled vessels, respectively. *Epithelioid haemangioma (angiolymphoid hyperplasia with eosinophilia)* contains immature, but well formed, capillary-sized vessels lined by plump epithelioid (histiocytoid) endothelial cells. This process is usually intimately associated with a small muscular artery, and it is commonly associated with a lymphocytic and eosinophilic inflammatory infiltrate.

A variety of *neurofibroma* subtypes are recognized, include solitary cutaneous, localized intraneural, plexiform, diffuse, pigmented, and epithelioid variants. All of these tumours feature S100 protein-positive Schwann cells admixed with varying numbers of EMA-positive perineurial cells, CD34-positive fibroblasts, and residual neurofilament protein-positive axons. Wagner-Meissner-like bodies are often present in diffuse neurofibroma, and melanotic stellate-shaped and spindled cells are present in pigmented neurofibroma. Atypia should not be pronounced and mitotic figures should be rare or absent.

Schwannomas (neurilemomas) are well demarcated peripheral nerve sheath tumours that classically exhibit Antoni A (cellular) and Antoni B (loose myxoid) growth patterns. Well developed Antoni A areas may exhibit nuclear palisading and contain Verocay bodies. Additional features commonly encountered in schwannomas include thick-walled vessels and perivascular xanthoma cells. In contrast with neurofibromas, atypia (often considered degenerative) is a common finding, and occasional mitoses are acceptable.

Granular cell tumours are S100 protein-positive neural neoplasms of Schwann cell derivation. These tumours feature epithelioid or spindled cells with abundant granular eosinophilic cytoplasm. Nuclear features vary, but mitotic activity is generally minimal. A fibrous connective tissue reaction may be present, and superficial examples may be associated with prominent pseudoepitheliomatous hyperplasia (sometimes mistaken for squamous carcinoma).

Myointimoma is a highly distinctive intravascular myointimal proliferation, often with multinodular or plexiform architecture, that tends to involve the corpus spongiosum. This process commonly has extensive immunoreactivity for α-smooth muscle actin, muscle-specific actin (HHF-35), and calponin, and it tends to have minimal reactivity for D33 and DE-R-11 desmin clones.

Leiomyomas consist of a proliferation of well developed smooth muscle cells with-

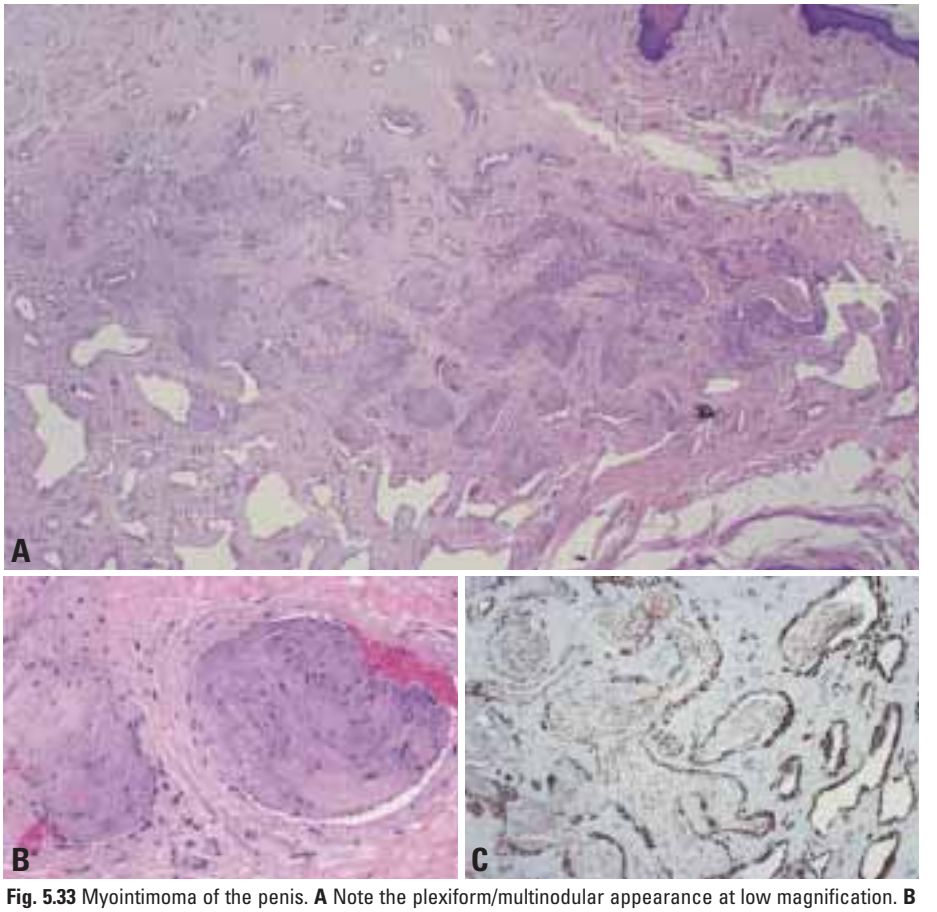

Fig. 5.33 Myointimoma of the penis. **A** Note the plexiform/multinodular appearance at low magnification. **B** This unusual process appears to originate from the vascular intima. **C** The lesional cells have immunoreactivity for calponin.

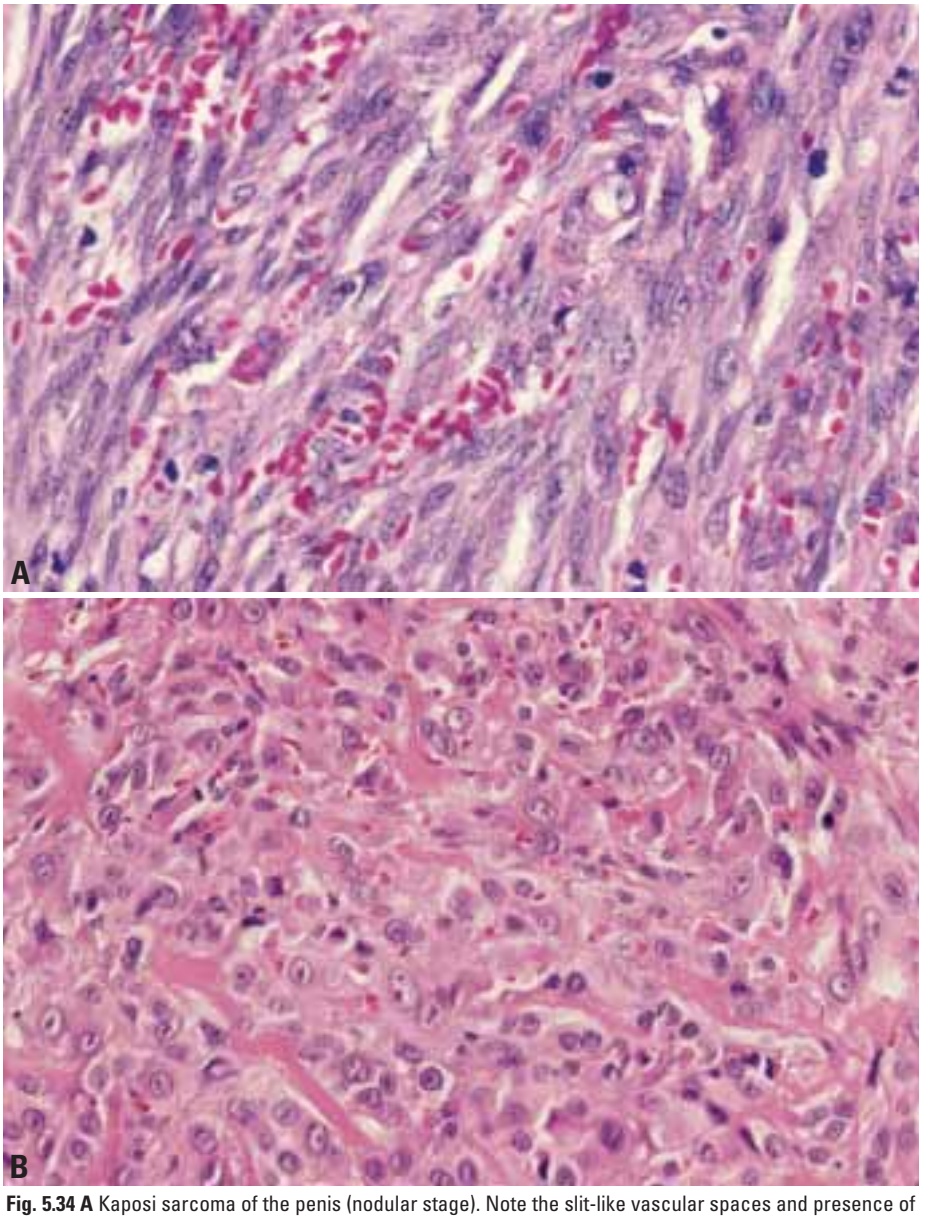

Fig. 5.34 A Kaposi sarcoma of the penis (nodular stage). Note the slit-like vascular spaces and presence of grape-like clusters of hyaline globules. **B** Epithelioid sarcoma of the penis. Note the presence of plump epithelioid tumour cells with eosinophilic cytoplasm. These cells often have an "open" chromatin pattern with a small but distinct central nucleolus. A garland growth pattern is often evident at low magnification.

out significant atypia, and generally, no mitotic activity. This diagnosis should be made only after careful examination, as leiomyomas appear to be much less common then leiomyosarcomas in this location.
Early stage (patch/plaque) lesions of *Kaposi sarcoma* consist of a proliferation of small capillary-sized vessels around pre-existing dermal vessels and adnexae. The vessels may contain apoptotic nuclei. Haemosiderin deposition, a lymphoplasmacytic inflammatory infiltrate, and grapelike clusters of intracytoplasmic hyaline globules, when present, are helpful clues. The protrusion of small proliferating vessels into the lumen of a larger pre-existing vessel (the so-called promontory sign) is also a helpful finding. Later stage (nodular) lesions of Kaposi sarcoma are dominated by spindled cells with fascicular growth and slit-like vascular spaces. Hyaline globules are typically abundant by this stage. The lesional cells of Kaposi sarcoma are usually immunoreactive for CD34, and they may also express CD31. PCR analysis for human herpesvirus 8 can be helpful in early stage or variant lesions.
Angiosarcoma has a broad morphologic spectrum. At one extreme, the process may closely resemble a benign haemangioma, and at the other, it may have a spindled appearance reminiscent of fibrosarcoma or an epithelioid appearance resembling carcinoma or melanoma. Infiltrative and interanastomosing growth; endothelial atypia with hyperchromasia; cell crowding and piling; and immunoreactivity for CD31, Factor VIIIr Ag and CD34 help establish the correct diagnosis.
Leiomyosarcomas contain spindled cells with nuclear atypia, mitotic activity, and a fascicular growth pattern. Longitudinal cytoplasmic striations and juxtanuclear vacuoles may be present. Immunoreactivity is usually detected for α-smooth muscle actin and desmin.
Malignant fibrous histiocytoma is a diagnosis of exclusion. This diagnosis is restricted to pleomorphic tumours (often with myxoid or collagenous matrix and a storiform growth pattern) that lack morphologic and immunohistochemical evidence for another specific line of differentiation (e.g. epithelial, melanocytic, myogenic or neural differentiation).

Grading

The grading of malignant soft tissue tumours is controversial. Some sarcomas are generally considered low-grade (e.g. Kaposi sarcoma) or high-grade (e.g. rhabdomyosarcoma and peripheral primitive neuroectodermal tumour). Others may be graded in one system but not in another (e.g. clear cell sarcoma, epithelioid sarcoma, and synovial sarcoma). For the majority of soft tissue sarcomas, we assign a numeric grade, based primarily on the modified French Federation of Cancer Centers Sarcoma Group system {970}.

Genetics

Specific cytogenetic or molecular genetic abnormalities have been identified for neurofibroma (allelic losses in 17q and/or mutations in the *NF1* gene), neurilemoma (allelic losses in 22q and/or mutations in the *NF2* gene), dermatofibrosarcoma protuberans [t(17;22)(q22;q13) or supernumerary ring chromosome derived from t(17;22)], clear cell sarcoma [t12;22)(q13;q12)], synovial sarcoma [t(X;18)((p11;q11)], peripheral primitive neu-

roectodermal tumour/Ewing sarcoma [primarily t(11;22)(q24;q12), t(21;22)(q22;q12), and t(7;22)(p22;q12)], and alveolar rhabdomyosarcoma [t(2;13)(q35;q14) and t(1;13)(p36;q14)] {1444}. RT-PCR tests are available for the four fully malignant tumours listed here. These tests can often be performed on fresh or formalin-fixed, paraffin-embedded tissue.

Prognosis

Superficial, benign mesenchymal lesions generally can be expected to have a low recurrence rate. Deep-seated benign lesions have a greater propensity for local recurrence. Tumours listed in the intermediate biologic potential category have a high rate of local recurrence, but only rarely give rise to metastases. The outcome for patients with Kaposi sarcoma is dependent on a variety of factors, including immune status and the extent of disease. However, the majority of patients with Kaposi sarcoma die of an unrelated event. There is insufficient data to provide site-specific prognostic information for the remainder of the sarcomas listed above.

Table 5.03
Mesenchymal tumours of the penis in the literature.

Category		Reference
Benign	Haemangioma variants	{383,761,789,811,1305,1889,1959,2361}
	Lymphangioma variants	{1356,1983}
	Neurofibroma	{1367,1599}
	Schwannoma (neurilemoma)	{1005,2300}
	Granular cell tumour	{333,2523}
	Myointimoma	{760}
	Glomus tumour	{1331,2275}
	Juvenile xanthogranuloma	{1043}
Intermediate Biological Potential	Giant cell fibroblastoma	{2398}
	Dermatofibrosarcoma protuberans	{581}
Malignant	Kaposi sarcoma	{382,1566,2232,2248}
	Epithelioid haemangioendothelioma	{1713}
	Angiosarcoma	{864,2106,2794}
	Leiomyosarcoma	{627,1173,1671,2103}
	Malignant fibrous histiocytoma (including myxofibrosarcoma)	{1714,1779}
	Rhabdomyosarcoma	{545,1998}
	Epithelioid sarcoma	{972,1136,1978,1987,2247}
	Synovial sarcoma	{49}
	Clear cell sarcoma	{2312}
	Malignant peripheral nerve sheath tumour	{581}
	Peripheral primitive neuroectodermal tumour/Ewing sarcoma	{2622}
	Extraskeletal osteosarcoma	{2271}

Lymphomas

A. Marx

Definition
Primary penile lymphomas (PL) are those that are confined to the penile skin, subcutis, and corpora cavernosa and spongiosum. Lymphomas of the urethra are counted among urinary tract lymphomas.

Synonym
Penile lymphoma.

Incidence
PL are very rare and most are considered to be primary {452}. Only 22 primary PL have been reported to date {107,123, 188,342,452,684,739,1036,1625,2508, 2787,2908}.

Clinical features and macroscopy
Painless or rarely tender swelling or ulcer of penile shaft, glans or prepuce {107}, scrotal masses {739,1503,2787}, priapism {123}, or associated Peyrone disease {2908} have been reported in PL. Systemic B symptoms appear to be an exception among primary PL {739}.

Histopathology
Several cases of diffuse large B-cell lymphomas (DLBCL) {107,1036,1625} and single cases of anaplastic large cell lymphoma (ALCL) of T-type (CD30+) {1503} and Hodgkin lymphoma have been reported as primary PL {2075}. Both nodal and cutaneous Non-Hodgkin-Lymphomas may involve the penis (secondary PL) {1416,1458}.

Precursor lesions and histogenesis (postulated cell of origin)
Precursor lesions and the histogenesis of PL are unknown. Some PL are cutaneous lymphomas {452,1458,1503}. Whether other primary PL occur due to an occult nodal lymphoma (implying systemic chemotherapy) {452} or a penile inflammatory process is unclear {107}.

Somatic genetics and genetic susceptibility
Genetic findings specific to PL have not been reported.

Prognosis and predictive factors
In the few, documented primary PL no death occurred after primary chemo- or radiochemotherapy with 42-72 months of follow-up {107,739,1514,2908}. Recurrences and dissemination were seen in a few penile lymphomas after radiotherapy {1036} or surgery as single modality treatments {684,2787}, while other cases {2508} including a probable cutaneous penile lymphoma, were apparently cured by surgery {1458,1503} or radiation {2508} alone.

Secondary tumours of the penis

C.J. Davis
F.K. Mostofi
I.A. Sesterhenn

Definition
Tumours of the penis that originate from an extra penile neoplasm.

Incidence
Metastatic carcinoma to penis is rare. By 1989 only 225 cases had been reported {2049}.

Clinical features
The presenting symptoms are frequently priapism or severe penile pain {1826}. Any patient with known cancer who develops priapism should be suspected of having metastatic disease. Other features include increased penile size, ulceration or palpable tumour nodules {2202}.

Localization
The corpus cavernosum is the most common site of metastases, but the penile skin, corpus spongiosum and mucosa of glans may be affected {2905}. A multinodular growth pattern in the CC is characteristic.

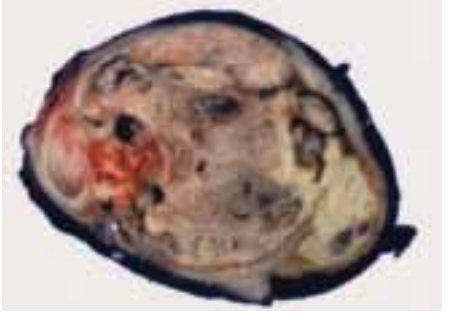

Fig. 5.36 Metastatic renal cell carcinoma. Cross section of the penis filled with RCC.

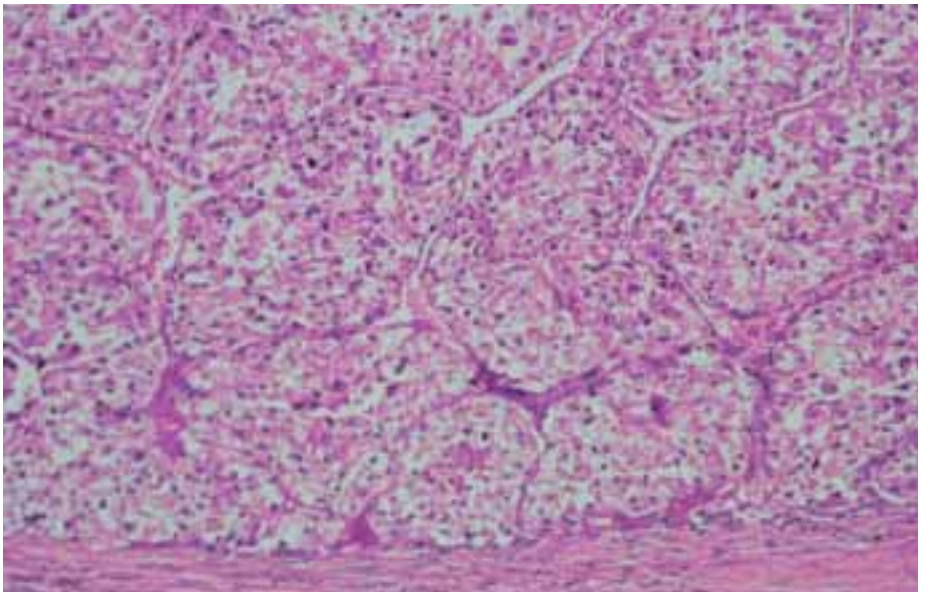

Fig. 5.35 Metastatic renal cell carcinoma. The tumour fills the corpus cavernosum. Tunica albuginea is at the top.

Origin of metastases
Reports invariably find prostate and bladder to be the most common primary sites with kidney and colon much less frequent {2905}. In a series of 60 cases, 21 were prostatic, 18 bladder, 14 undetermined primary sites, 3 colon, 2 kidney, 1 stomach and 1 pulmonary. Many other primary sites are occasionally reported.

Histopathology
Tumour deposits may be seen in any part of the penis but the common finding is filling of the vascular spaces of the erectile tissue and the tumour morphology will be typical of that seen in the primary tumour {2202}.

Prognosis
The prognosis is very poor since this usually occurs in the late stages in patients with known metastatic carcinoma. In one study 95% of patients died within weeks or months of diagnosis. In another, 71% died within 6 months {1826}.