Benign tumors and lesions

- **Non cutaneous**
  - Congenital and acquired inclusion cysts
  - Retention cysts
  - Syringomas (sweat gland tumors)
  - Neurilemoma
  - Angioma, lipoma
  - Iatrogenic pseudotumor following injections
  - Pyogenic granuloma following injections

- **Cutaneous**
  - Pearly penile papules (normal in 15% of postpubertal males)
  - Zoon balanitis (shiny, erythematous plaque on glans or prepuce)
  - Lichen planus (flat-topped violaceous papule)

Viral-related lesions

- Condyloma acuminatum
  - This is also known as genital warts
  - Related to human papillomavirus (HPV) infection.
  - There are soft, usually multiple benign lesions on the glans, prepuce and shaft; they may occur elsewhere on genitalia or perineum.
• A biopsy is worthwhile prior to topical treatment with podophyllin 5% have urethral involvement, which may require diathermy.

➢ *Bowenoid papulosis*
  ✓ Resembles carcinoma in situ, but with a benign course.
  ✓ Multiple papules appear on the penile skin, or a flat glanular lesion.
  ✓ These should be biopsied.
  ✓ HPV is the suspected cause.

➢ *Kaposi sarcoma*
  ✓ This reticuloendothelial tumor.
  ✓ Second-most common malignant penile tumor.
  ✓ In immunocompromised men, particularly in gay men with HIV/AIDS.
  ✓ Treatment is palliative, with intralesional chemotherapy, laser, cryoablation, or radiotherapy.

**Premalignant cutaneous lesions**
  ✓ Histologically benign lesions are recognized to have malignant potential.
  ✓ Occur in close association with SCC of the penis.
  ✓ A chronic red or pale lesion on the glans or prepuce is a cause for concern.
  ✓ Early follow-up after use of steroid, antibacterial, or antifungal creams is recommended.
  ✓ If persistent, biopsy is advised.

➢ *Balanitis xerotica obliterans (BXO)*
  ✓ Also known as lichen sclerosus et atrophicus.
  ✓ This is a common sclerosing condition of glans and prepuce.
  ✓ It occurs at all ages.
  ✓ Most commonly presents as non-retractile foreskin (phimosis).
  ✓ Obstructed and spraying voiding.
  ✓ Occurs in association with penile SCC.
Leukoplakia:
- Solitary or multiple whitish glanular plaques.
- Usually involve the meatus.
- Treatment is excision and histology.
- Associated with in situ SCC;
- Follow-up is required.

Erythroplasia of Queyrat:
- Known as carcinoma in situ of the glans, prepuce, or penile shaft.
- A red, velvety, circumscribed painless lesion occurs, though it may ulcerate, resulting in discharge and pain.
- Treatment is excision biopsy if possible; radiotherapy, laser ablation, or topical 5-fluorouracil may be required. Histology reveals hyperplastic mucosal cells with malignant features.

Bowen disease: this is carcinoma in situ of the remainder of the keratinizing genital or perineal skin.
- Treatment is wide local excision, laser, or cryoablation.

Buschke–Löwenstein tumor:
- Known as verrucous carcinoma or giant condyloma acuminatum,
- An aggressive locally invasive tumor of the glans.
- Metastasis is rare, but wide excision is necessary to distinguish it from SCC.
- Urethral erosion and fistulation may occur.

Squamous cell carcinoma (SCC)
- is the most common penile cancer, accounting for 95% of penile malignancies.
- Others include Kaposi sarcoma and, rarely, basal cell carcinoma, melanoma, sarcoma, and Paget disease.
- Metastases to the penis are occasionally seen from the bladder, prostate, rectum, and other primary sites.
Incidence and etiology of SCC

- 1% of male cancers.
- Age: penile cancer incidence rises during the sixth decade and peaks in the eighth decade. It is unusual <40 years of age, but has been rarely reported in children.
- Premalignant lesions: 42% of patients with penile SCC are reported to have had a pre-existing penile lesion.
- A prepuce (foreskin): penile cancer is rare in men circumcised at a young age. Smegma that forms from desquamated epithelial cells is thought to be a primary instigating factor in penile cancer; good hygiene and circumcision limit smegma accumulation.
- Geography: Highest incidence worldwide is in Brazil. It is virtually non-existent in Israel.
- Human papilloma virus (HPV) genital wart infection, especially with types 16, 18, and 21.
- Multiple sex partners.
- Smoking and tobacco.

Pathology and staging of penile SCC

- Believed to be preceded by carcinoma in situ.
- SCC starts as a slow-growing papillary, flat or ulcerative lesion on the glans (48%), prepuce (21%), glans and prepuce (9%), coronal sulcus (6%), or shaft (2%).
- The remainder is indeterminate.
- It grows locally beneath the foreskin before invading the corpora cavernosa, urethra, and, eventually, the perineum, pelvis, and prostate.
- Metastasis is initially to the superficial then deep inguinal and, subsequently, iliac and obturator lymph nodes.
- Skin necrosis, ulceration, and infection of the inguinal lymph nodes may lead to sepsis or hemorrhage from the femoral vessels.
- Blood-borne metastasis to lungs and liver is rare (1–10% of cases).
(a) Carpus cavernosum

\[ \text{T}_1 \text{ or } \text{T}_3 \]
Epithelium only

\[ \text{T}_2 \]
Corpus cavernosum or spongiosum Invaded

\[ \text{T}_1 \]
Subepithelia tissue Invaded

\[ \text{T}_3 \]
Urethra/prostate Invaded

\[ \text{T}_4 \]
Scrotum, perineum bone Invaded

(b)

\[ N_1 \]
Single superficial inguinal node

\[ N_2 \]
Multiple or bilateral superficial inguinal nodes
### Table 6.20  TNM staging of penile carcinoma

<table>
<thead>
<tr>
<th>Tx</th>
<th>Primary tumor cannot be assessed</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ</td>
</tr>
<tr>
<td>Ta</td>
<td>Noninvasive verrucous carcinoma</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor invades subepithelial connective tissue</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor invades corpus cavernosum or spongiosum</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor invades urethra or prostate</td>
</tr>
<tr>
<td>T4</td>
<td>Tumor invades other structures</td>
</tr>
<tr>
<td>Nx</td>
<td>Regional nodes cannot be assessed</td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph node metastases</td>
</tr>
<tr>
<td>N1</td>
<td>Single superficial inguinal lymph node metastasis</td>
</tr>
<tr>
<td>N2</td>
<td>Multiple or bilateral superficial inguinal lymph node metastases</td>
</tr>
<tr>
<td>N3</td>
<td>Metastases in deep inguinal or pelvic lymph nodes, unilateral or bilateral</td>
</tr>
<tr>
<td>Mx</td>
<td>Distant metastasis cannot be assessed</td>
</tr>
<tr>
<td>M0</td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastasis</td>
</tr>
</tbody>
</table>
SCCs are graded using the Broder classification system:
- **Grade I:** well differentiated, keratinization, prominent intercellular bridges, keratin pearls
- **Grade II to III:** greater nuclear atypia, increased mitotic activity, decreased keratin pearls
- **Grade IV:** cells deeply invasive, marked nuclear pleomorphism, nuclear mitoses, necrosis, lymphatic and perineural invasion, no keratin pearls

**Presentation**
- About 15–50% of patients delay presentation for >1 year because of embarrassment, personal neglect, fear, or ignorance.
- A hard, painless lump on the glans penis is the most common presentation.
- A bloody discharge may be confused with hematuria.
- Rarely, a groin mass or urinary retention are presenting symptoms.

**Investigations**
- A biopsy is indicated.
- Chest radiology, pelvic CT scan,
- serum calcium, and
- Liver function tests are usually obtained.

**Treatment**
- The management of penile cancer should take place in regional or supraregional centers that can provide multidisciplinary surgical and oncological expertise.
- The first-line treatment of penile cancer, regardless of the inguinal node status, is surgery
- Circumcision is appropriate for preputial lesions, but local recurrence is observed in 22–50%.
1/ Primary tumor:

- for smaller G1–2 T1–2 tumors
  - Penis-preserving wide excision of glanular lesions with skin graft glanular reconstruction.
  - Alternatives to surgery include laser or cryoablation, radiotherapy or brachytherapy, photodynamic therapy, or topical 5-fluorouracil.
- For G3T1 and more advanced tumors, partial or total penile amputation is required, depending on the extent of the tumor.
  - Radiotherapy remains an alternative
  - Patients with M1 disease are offered palliative surgery.

2/ Lymphadenopathy:

- Six weeks of broad-spectrum antimicrobials (e.g., Augmentin or cephalosporin) are given after the primary tumor has been removed.
- If nodes become clinically nonpalpable (50% of patients), who may then be followed up.
- For those with persistent inguinal lymphadenopathy, in the absence of demonstrable pelvic or metastatic disease, bilateral inguinal lymphadenectomy should be considered.

- Radiotherapy and chemotherapy:
  - Are alternative or adjuvant treatments for metastatic nodal disease in unfit, elderly, or inoperable patients.
- Prophylactic lymphadenectomy:
  - This is currently practiced in the United States for tumors exhibiting vascular invasion, are high grade, or stages T2–4.

- Distant metastatic disease:
  - This is treated using single-agent systemic chemotherapy: cisplatin, bleomycin, or methotrexate.
Urethral cancer

- Primary urethral cancer is rare, occurring in elderly patients.
- It is 4 times more common in women than in men.

➤ Risk factors:
- Urethral stricture and sexually transmitted disease are implicated.
- Direct spread from tumor in the bladder or prostate is more common.

➤ Pathology and staging:
- 75% are SCC, occurring in the anterior urethra;
- 15% are UC, occurring in the posterior/prostatic urethra;
- 8% are adenocarcinoma;
- And the remainder includes sarcoma and melanoma.
- Urethral cancer metastasizes to the pelvic lymph nodes from the posterior urethra
- To the inguinal nodes from the anterior urethra in 50% of patients.
Staging is by the TNM system

<table>
<thead>
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<th>T</th>
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</tr>
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<tbody>
<tr>
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</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td></td>
<td><strong>Urethra (male and female)</strong></td>
</tr>
<tr>
<td>Ta</td>
<td>Noninvasive papillary carcinoma</td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor invades subepithelial connective tissue</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor invades corpus spongiosum, prostate, or periurethral muscle</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor invades corpus cavernosum, prostatic capsule, vagina, or bladder neck</td>
</tr>
<tr>
<td>T4</td>
<td>Tumor invades adjacent organs including bladder</td>
</tr>
<tr>
<td></td>
<td><strong>Transitional cell carcinoma of the prostatic urethra</strong></td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ, prostatic urethra (pu) or prostatic ducts (pd)</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor invades subepithelial connective tissue</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor invades prostatic stroma, corpus spongiosum, or periurethral muscle</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor invades through prostatic capsule, corpus cavernosum, or bladder neck</td>
</tr>
<tr>
<td>T4</td>
<td>Tumor invades adjacent organs including bladder</td>
</tr>
<tr>
<td>Nx</td>
<td>Regional (deep inguinal and pelvic) lymph nodes cannot be assessed</td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>Metastasis in a single lymph node &lt;2 cm in greatest dimension</td>
</tr>
<tr>
<td>N2</td>
<td>Metastasis in a single lymph node &gt;2 cm in greatest dimension</td>
</tr>
<tr>
<td>Mx</td>
<td>Distant metastasis cannot be assessed</td>
</tr>
<tr>
<td>M0</td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastasis present</td>
</tr>
</tbody>
</table>
Presentation

☒ This is often late; many patients have metastatic disease at presentation
• Painless hematuria; initial, terminal, or a bloody urethral discharge
• Voiding-type LUTS (less common)
• Perineal pain (less common)
• Periurethral abscess or urethrocutaneous fistula (rare)
• Past history of sexually transmitted or stricture disease
• Examination may reveal a hard, palpable mass at the female urethral meatus or along the course of the male anterior urethra. Inguinal lymphadenopathy, chest signs, and hepatomegaly may suggest metastatic disease.

Differential diagnosis

➢ In men
  ☒ • Urethral stricture
  ☒ • Perineal abscess
  ☒ • Metastatic disease involving the corpora cavernosa
  ☒ • Urethrocutaneous fistula (secondary to benign stricture disease)

➢ In women
  ☒ • Urethral caruncle
  ☒ • Urethral cyst
  ☒ • Urethral diverticulum
  ☒ • Urethral wart (condylomata acuminata)
  ☒ • Urethral prolapse
  ☒ • Urethral vein thrombosis
  ☒ • Periurethral abscess

☒ Investigations
  ☒ Cystourethroscopy,
  ☒ Biopsy.
  ☒ Bimanual examination under anesthesia.
  ☒ Chest radiography
  ☒ abdominopelvic CT scan.
Treatment

1/ for localized anterior urethral cancer, radical surgery or radiotherapy are the options.

- Male patients would require perineal urethrostomy.
- Postoperative incontinence is minimum.
- For posterior/prostatic urethral cancer,
- Cystoprostatourethrectomy should be considered for men in good overall health,
- While anterior pelvic exenteration (excision of the pelvic lymph nodes, bladder, urethra, uterus, ovaries, and part of the vagina) should be considered for women.

2/ for locally advanced disease, a combination of preoperative radiotherapy and surgery is recommended.
3/ For metastatic disease, chemotherapy is the only option with regimens of systemic cisplatin, bleomycin, and methotrexate or 5-fluorouracil.