Malignancies of genitourinary system
Gross anatomy of Kidney

Uretur

Renal Hilum

Renal Artery and Vein
Nephrectomy Specimens

- Radical Nephrectomy (for renal tumors)

- Nephroureterectomy (resection of kidney with or without a small cuff of bladder at the end of ureter)

- Partial nephrectomy (in small renal tumors)
- Renal cell carcinoma arise from the epithelium of the renal tubules.

- The carcinomas have distinct morphologic features and arise through different constellations of genetic lesions.

- Renal cell carcinoma approximately 30,000 new cases are diagnosed each year in the United States.

- Its incidence increases with each decade of life and it is 2-3times more common in men than in women.
<table>
<thead>
<tr>
<th>Benign</th>
</tr>
</thead>
<tbody>
<tr>
<td>Papillary adenoma</td>
</tr>
<tr>
<td>Oncocytoma</td>
</tr>
<tr>
<td>Metanephric adenoma</td>
</tr>
<tr>
<td>Malignant</td>
</tr>
<tr>
<td>Clear cell renal cell carcinoma</td>
</tr>
<tr>
<td>Multilocular cystic renal cell carcinoma</td>
</tr>
<tr>
<td>Papillary renal cell carcinoma</td>
</tr>
<tr>
<td>Type 1</td>
</tr>
<tr>
<td>Type 2</td>
</tr>
<tr>
<td>Chromophobe renal cell carcinoma</td>
</tr>
<tr>
<td>Classic</td>
</tr>
<tr>
<td>Eosinophilic</td>
</tr>
<tr>
<td>Collecting duct carcinoma</td>
</tr>
</tbody>
</table>
- This large, bulging tumor shows the typical variegation of color, from yellow to tan and brown with dark areas of hemorrhage and whitish areas of stroma.
The prominent delicate vasculature surrounding alveolar clusters of cells is typical of clear cell renal cell carcinoma.
Small cells with inconspicuous pale cytoplasm cover the papillae of type 1 papillary renal cell carcinoma.
Cells with pseudo stratified nuclei and abundant cytoplasm cover the papillae of type 2 papillary renal cell carcinoma
CHROMOPHObE RENAL CELL CARCINOMA
Tubules with jagged branching lumens embedded in an abundant stroma and lined by cells with small amounts of cytoplasm are typical of collecting duct carcinoma.
GROSS ANATOMY OF URINARY BLADDER

URINARY BLADDER
HISTOLOGY OF URINARY BLADDER

(a) Micrograph of the bladder wall (17X)
(b) Epithelium lining the lumen of the bladder (360X)
Benign nuclei: oval, with nuclear groove, point towards top (normal polarity) and not hyperchromatic

- Umbrella cells
- Intermediate cells
- Basal cells

Lamina propria
UROTHELIAL CARCINOMA

- Urothelial carcinoma of the bladder is a major cause of morbidity and mortality throughout the world.

- It is typically seen in patients over 50 years of age approximately three times as common in men as in women.
- Urothelial carcinoma has been of interest epidemiologically because of its association with exposure to aniline dyes and other occupational exposure.

- Heredity is not considered to be a significant contributor.

- The majority of patients present with hematuria
Urothelial carcinoma is divided conventionally into two types, the papillary and non papillary (flat sessile) types.

<table>
<thead>
<tr>
<th>Epithelial Tumors—Benign</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urothelial papilloma</td>
</tr>
<tr>
<td>Inverted urothelial papilloma</td>
</tr>
<tr>
<td>Villous adenoma</td>
</tr>
<tr>
<td>Squamous papilloma</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Epithelial Tumors—Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urothelial carcinoma</td>
</tr>
<tr>
<td>Urothelial carcinoma in situ</td>
</tr>
<tr>
<td>Papillary urothelial neoplasm of low malignant potential</td>
</tr>
<tr>
<td>Papillary urothelial carcinoma, low grade</td>
</tr>
<tr>
<td>Papillary urothelial carcinoma, high grade</td>
</tr>
<tr>
<td>Invasive urothelial carcinoma</td>
</tr>
</tbody>
</table>
Papillary urothelial carcinoma. In this cross section of the tumor, a sharp interface is seen between the tumor and underlying tissue.
Papillary urothelial carcinoma, low grade. The urothelium is thickened, and variable nuclear enlargement and hyperchromasia are present.
HIGH GRADE UROTHELIAL CARCINOMA
Papillary urothelial carcinoma, low grade. The urothelium is thickened, and variable nuclear enlargement and hyperchromasia are present.
HIGH GRADE UROTHELIAL CARCINOMA
LOW GRADE UROTHELIAL CARCINOMA

p63
BENIGN PROSTATIC HYPERPLASIA
Prostatic intraepithelial neoplasia (PIN). The glandular structures of PIN have a complex architecture featuring epithelial proliferation and nuclear stratification.

The basal cell layer is usually retained in a lower-grade prostatic intraepithelial neoplasia; 34βE12 immunohistochemistry.
<table>
<thead>
<tr>
<th>New category</th>
<th>Histological descriptions of new grading categories</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>• Only individual, discrete well-formed glands</td>
</tr>
<tr>
<td>Grade 2</td>
<td>• Predominantly well-formed glands with lesser component of poorly formed, fused, and/or cribriform glands</td>
</tr>
<tr>
<td>Grade 3</td>
<td>• Predominantly poorly formed poorly formed, fused, and/or cribriform glands with lesser component of well-formed glands</td>
</tr>
</tbody>
</table>
| Grade 4      | • *Only* poorly formed, fused, and/or cribriform glands *or*  
|              | • Predominantly well-formed glands with lesser component lacking gland formation *or*  
|              | • Predominantly lacking gland formation and lesser component of well-formed glands (but poorly formed, fused, and/or cribriform glands can be a minor component) |
| Grade 5      | • Lacks gland formation – or has glands with necrosis -- with or without poorly formed, fused, and/or cribriform glands |
Gleason’s Pattern

1. Small, uniform glands
2. More stroma between glands
3. Distinctly infiltrative margins
4. Irregular masses of neoplastic glands
5. Only occasional gland formation

Well differentiated
Moderately differentiated
Poorly differentiated/Anaplastic
Well-differentiated adeno carcinoma. Well formed small acini are arranged in a back-to-back fashion.

The main differences between atypical small gland proliferation and adeno carcinoma of prostate are the presence of prominent nucleoli and absence of the basal cell layer in the latter.
GROSS ANATOMY OF TESTIS

- Spermatic cord
- Blood vessels and nerves
- Seminiferous tubule
- Head of epididymis
- Efferent ductule
- Ductus (vas) deferens
- Rete testis
- Tubulus rectus
- Body of epididymis
- Tail of epididymis
- Lobule
- Septum
- Tunica albuginea
- Tunica vaginalis
- Cavity of tunica vaginalis
The normal adult testis is an ovoid paired organ, each measuring 4.5 × 2.5 × 3 cm, and weighing approximately 20 grams.

They are suspended within scrotal sacs by spermatic cords.

The testis is covered by a capsule composed of an outer tunica vaginalis, the collagenous tunica albuginea, and the inner tunica vasculosa.
- The tunica vaginalis forms a sac filled with serous fluid.
- The posterior portion of the testis not covered by a capsule is called the mediastinum and contains blood vessels, nerves and lymphatics.
- Testicular neoplasms constitute approximately 1% of all cancers in men.

- Tumors of germ cell origin account for 94% to 96% of all testicular neoplasms, sex cord-stromal origin constitute 4% to 6%. The remaining testicular neoplasms of are rare for 1% of all testicular neoplasms.
Germ Cell Tumors
Intratubular germ cell neoplasia, unclassified
Other types

Tumors of One Histologic Type (Pure Forms)
- Seminoma
  - Seminoma with syncytiotrophoblastic cells
- Spermatocytic seminoma
  - Spermatocytic seminoma with sarcoma
- Embryonal carcinoma
- Yolk sac tumors
- Trophoblastic tumors
  - Choriocarcinoma
  - Trophoblastic neoplasms other than choriocarcinoma
- Monophasic choriocarcinoma
- Placental-site trophoblastic tumors
- Teratoma
  - Dermoid cyst
  - Monodermal teratoma
  - Teratoma with somatic-type malignancies
SEMINOMA
Seminoma consists of a monotonous cell population divided into lobules by thin bands of fibrovascular stroma.
The cells in seminoma are uniformly large and contain abundant clear cytoplasm. The tumor cells have a distinct cell membrane and are evenly spaced.
Placental alkaline phosphatase immunostaining of seminoma shows diffuse membranous immunoreactivity in the tumor cells.
TERATOMA

- Most commonly in the first and second decades of life.
- The tumor is well demarcated from the surrounding uninvolved testis and may be solid or multicystic.
- Cysts may be filled with clear, keratinous, gelatinous, or mucinous material. Cartilage, spicules of bone.
FEMALE REPRODUCTIVE SYSTEM

- Ovarian artery and vein
- Suspensory ligament of ovary
- Infundibulum
- Ampulla
- Isthmus
- Perimetrium
- Fundus of uterus
- Body of uterus
- Uterine tube
- Mesovarium
- Round ligament of uterus
- Broad ligament
- Ovarian ligament
- Uterine cavity
- Endometrium
- Internal os (internal orifice)
- Cervical canal
- Cervix
- Cervical os (external orifice)
- Vaginal artery
- Vaginal rugae
- Vagina

See Figure 28-19

See Figure 28-21

Posterior view
CERVIX ANATOMY

- Fallopian tube
- Uterus
- Ovary
- Glandular cells
- Squamous cells
- Cervix
- Vagina
Stratified squamous epithelium non-keratinised

Ectocervix

Transitional zone

Endocervix

Branching glands

Tall mucus secreting epithelium
- Cervical carcinoma is the most common malignancy of the female genital.

- The development of invasive squamous cell carcinoma of the cervix is causally related to HPV infection.
Approximately 25 different HPVs have been isolated from the genital tract, among which there is a spectrum of risk of developing cancer, with HPV type 16 conferring the greatest risk.

Patients with invasive squamous cell carcinoma of the cervix most commonly present with abnormal vaginal bleeding or an abnormal Papanicolaou smear.
Invasive squamous cell carcinoma, keratinizing type. Prominent keratin pearls and nests of tumor cells with central keratinization.
Invasive squamous cell carcinoma, large cell non keratinizing type. Lack of conspicuous keratin pearl formation or central keratinization of tumor nests.
OVARY ANATOMY

**Medulla** (contains neurovascular structures)

**Cuboidal epithelium**

**Cortex** (contains ovarian follicles)

**Hilum**

- Corpus luteum
- Developing corpus luteum
- Granulosa cells
- Mesovarium and blood vessels
- Vascular (Graafian) follicle
- Germ cells
- Ansae\n- Ovary
- Connective tissue
- ovarian blood vessels
- ovarian ligament
- Mesovarium and blood vessels
- Tenia albuginea
- Degenerating corpus luteum (corpus albicans)
- Nongranulosa cells
- Secondary follicle
- Fibrous (Connective) tissue
- Hilum
The three main categories of primary ovarian tumors are:-

- **Epithelial tumors**, which originate from the surface epithelium of the ovary

- **Sex cord-stromal tumors**, which arise from the ovarian stroma, sex cord derivatives, or both
Germ cell tumors, which originate from germ cells. Epithelial tumors are the most common, comprising about 60% of all ovarian tumors.

Serous and mucinous cystadenomas are the most common epithelial tumors and together account for about 30% of ovarian tumors.
### TABLE 13A-1  Common Ovarian Tumors

<table>
<thead>
<tr>
<th>Tumor</th>
<th>Percentage of Ovarian Tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign cystic teratoma</td>
<td>32</td>
</tr>
<tr>
<td>Serous cystadenoma</td>
<td>16</td>
</tr>
<tr>
<td>Mucinous cystadenoma</td>
<td>14</td>
</tr>
<tr>
<td>Serous carcinoma</td>
<td>9</td>
</tr>
<tr>
<td>Fibroma-thecoma</td>
<td>9</td>
</tr>
<tr>
<td>Borderline serous tumor</td>
<td>4</td>
</tr>
<tr>
<td>Endometrioid carcinoma</td>
<td>3</td>
</tr>
<tr>
<td>Borderline mucinous tumor</td>
<td>1</td>
</tr>
<tr>
<td>Clear cell carcinoma</td>
<td>1</td>
</tr>
<tr>
<td>Mucinous carcinoma</td>
<td>1</td>
</tr>
</tbody>
</table>

### TABLE 13A-2  Types of Epithelial Tumor of the Ovary

- Serous
- Mucinous
- Endometrioid
- Mixed mesodermal
- Clear cell
- Brenner/transitional cell
- Undifferentiated
- Rare types
- Mixed
- Unclassified
Serous cystadenoma. The cyst is lined by ciliated low columnar cells with bland, basal nuclei.
Serous carcinoma. Confluent papillary growth, characteristic of serous carcinoma.

Serous carcinoma. The tumor cells cover papillae and grow in sheets. They have large vesicular nuclei with coarse chromatin, and some have prominent nucleoli.
Mucinous Cystadenoma. His multilocular cystic neoplasm is lined by a single layer of columnar mucinous cells.

Mucinous carcinoma. Confluent pattern of growth with back-to-back glands. Some surrounded by clear spaces.
Endometrioid adenofibroma. Glands lined by a single layer of benign endometrial-type cells are surrounded by dense fibrous stroma.

Endometrioid carcinoma
TUMORS OF ENDOMETRIUM

- It is the most common invasive cancer of the female genital tract and accounts for 7% of all invasive cancers in women.
- Endometrial cancer can be identified:
  - endometrioid (type I)
  - non-endometrioid (type II)
The endometrioid subset develops on a background of prolonged estrogen stimulation and is often preceded by a premalignant stage characterized by a diagnostic lesion (endometrial intraepithelial neoplasia [EIN] or atypical endometrial hyperplasia).
- Women with ovarian estrogen-secreting tumors have a higher risk of developing endometrial cancer.

- Endometrial cancer is extremely rare in women with ovarian agenesis and in those castrated early in life.
Estrogen replacement therapy, when unopposed by progestins, is associated with increased risk in women.

In postmenopausal women, greater synthesis of estrogens in body fats from adrenal and ovarian androgen precursors occurs.
<table>
<thead>
<tr>
<th>Table 13B-1</th>
<th>Classification and Grading of Endometrial Carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endometrial adenocarcinoma, endometrioid type (Type I) (grades 1-3 based on architecture, increase in grade by one based on marked nuclear atypia)</td>
<td></td>
</tr>
<tr>
<td>• With secretory differentiation</td>
<td></td>
</tr>
<tr>
<td>• With ciliated differentiation</td>
<td></td>
</tr>
<tr>
<td>• With squamous differentiation</td>
<td></td>
</tr>
<tr>
<td>• With mucinous differentiation</td>
<td></td>
</tr>
<tr>
<td>• With squamous differentiation</td>
<td></td>
</tr>
<tr>
<td>Endometrial adenocarcinoma, non-endometrioid type (Type II) (grade not reported specifically, assumed grade 3 by definition)</td>
<td></td>
</tr>
<tr>
<td>• Serous adenocarcinoma</td>
<td></td>
</tr>
<tr>
<td>• Clear cell carcinoma</td>
<td></td>
</tr>
<tr>
<td>• Carcinosarcoma (formerly malignant mixed Müllerian tumor)</td>
<td></td>
</tr>
<tr>
<td>Endometrial carcinoma, miscellaneous types</td>
<td></td>
</tr>
<tr>
<td>• Squamous cell carcinoma</td>
<td></td>
</tr>
<tr>
<td>• Mixed carcinomas</td>
<td></td>
</tr>
<tr>
<td>• Undifferentiated carcinoma</td>
<td></td>
</tr>
<tr>
<td>Other rare types (e.g., transitional cell carcinoma)</td>
<td></td>
</tr>
</tbody>
</table>
FIGURE 13B-1  Model of endometrial tumorigenesis. Precancers are monoclonal neoplasms initiated from a polyclonal normal field by mutations that confer small increases in growth potential under the mitogenic influence of unopposed estrogen. Pre-
ENDOMETRIAL INTRAEPITHELIAL NEOPLASIA
Endometrial adenocarcinoma, presenting as a diffuse irregular nodularity on the uterine surface.
Endometrioid adenocarcinoma, showing well differentiated (left) and poorly differentiated (right) components within a single tumor.
THANK YOU