NOTES
FEMALE GENITOURINARY CANCERS

GENERALLY, WHAT ARE THEY?

PATHOLOGY & CAUSES

- Cancers arising in genitourinary organs of individuals who are biologically female

RISK FACTORS

- Genetic mutations, smoking, prolonged use of oral contraceptives, sexually transmitted infections (STIs) (e.g. human papillomavirus), immunodeficiency (e.g. HIV/AIDS)

COMPLICATIONS

- Bleeding, metastasis
- Tumors produce excess hormones → metabolic disorders
- Large tumors → compression/torsion of blood vessels → ischemia

SIGNS & SYMPTOMS

- Abnormal vaginal discharge, bleeding; pelvic pain; abdominal pain; dyspareunia

DIAGNOSIS

DIAGNOSTIC IMAGING

X-ray, CT scan, MRI, ultrasound

- Tumor visualisation, staging

LAB RESULTS

- Serum tumor markers
  - ↑ carbohydrate antigen 125 (CA-125), Papanicolaou (Pap) test
- Biopsy (definitive diagnosis)

OTHER DIAGNOSTICS

Staging

- *Tumor, nodes, metastasis (TNM) system:* 0–4
  - *T:* size, sites invaded (e.g. only uterus/extrauterine invasion)
  - *N:* degree of spread to regional lymph nodes
  - *M:* presence of distant metastasis
  - *V:* vascular invasion
- *FIGO (International Federation of Gynecology and Obstetrics):* stages
  - *Stage 0:* carcinoma *in situ* (pre-malignant lesions)
  - *Stage I:* lesions limited to primary
  - *Stage II:* nearby organs/tissues affected
  - *Stage III:* distant pelvic organs/tissues, nodes
  - *Stage IV:* distant metastases out of the pelvis

TREATMENT

SURGERY

- Tumor debulking, tumor, lymph node, organ resection

OTHER INTERVENTIONS

- Chemotherapy, radiotherapy

CERVICAL CANCER

osms.it/cervical-cancer

PATHOLOGY & CAUSES

- Cancer arising from cervix
- Mainly caused by two strands of human papillomavirus (*HPV*): 16, 18
- HPV invades two kinds of cells
  - Immature basal cells of squamous epithelium
  - Cells of squamocolumnar junction
- HPV makes viral proteins E6, E7 → interfere with cell growth regulation
- E6, E7 inhibit tumor suppressor proteins (p53) → ↓ DNA repair/↑ cell turn over → ↑ mutations → cancer
- Precancerous cervical changes
  - Cervical dysplasia, cervical intraepithelial neoplasia (CIN), adenocarcinoma in situ (AIS)

TYPES

Squamous cell carcinoma

- Most common (85–90%)

Adenocarcinoma

- Glandular (10–15%)

RISK FACTORS

- HPV 16/18 infections, smoking, prolonged use of oral contraceptives, early sexual activity (< 21 years old), multiple sexual partners, STIs, other vaginal/vulvar cancers, immunodeficiency (e.g. HIV/AIDS)

COMPLICATIONS

- Hematogenous metastases (e.g. lungs, liver, bone)

SIGNS & SYMPTOMS

- Usually asymptomatic in early stage
- Irregular/heavy vaginal bleeding, dyspareunia, postcoital bleeding, pelvic/lower back pain
- Watery, mucoid, purulent vaginal discharge
- Hematuria, hematochezia

DIAGNOSIS

DIAGNOSTIC IMAGING

Chest X-ray

- Lung metastasis

Colposcopy

- Cervical lesions

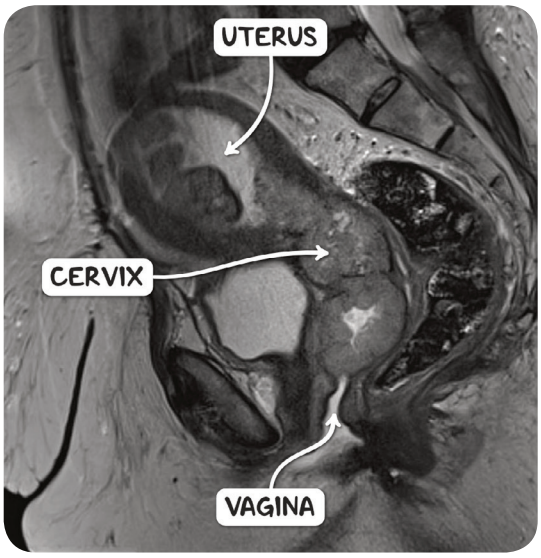

Figure 124.1 An MRI scan in the sagittal plane of the abdomen and pelvis. There is carcinoma which has entirely replaced the cervix and invaded the uterus and vagina.

LAB RESULTS

- Pap test
  - Abnormal cervical cytology
- Cervical biopsy (definitive diagnosis)

OTHER DIAGNOSTICS

- Staging
  - TNM
  - FIGO

TREATMENT

SURGERY

- CIN
  - Cryosurgery, laser ablation, loop electrosurgical excision procedure (LEEP)/large loops excision of transformation zone (LLETZ)
- Stage IA cancer
  - Conization, hysterectomy
- Stage IB, IIA cancer
  - Radical hysterectomy + bilateral pelvic lymphadenectomy
- Stage IVB, recurrent cancer
  - Pelvic exenteration

OTHER INTERVENTIONS

- Stage IB, IIA cancer
  - External beam radiation + brachytherapy
- Stage IIB, III, IVA cancer
  - Radiation therapy, brachytherapy
- Stage IVB, recurrent cancer
  - Radiation therapy, systemic chemotherapy, palliative care
- Prevention
  - Pap test, HPV vaccine

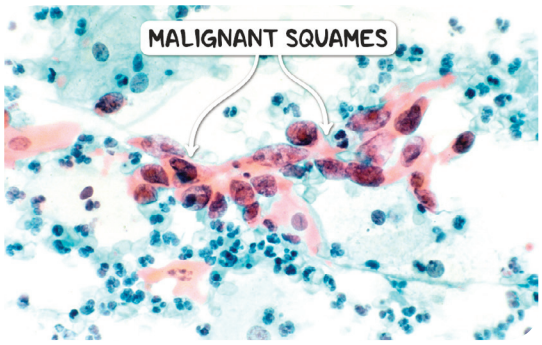

Figure 124.2 A cervical smear stained with Papanicolaou stain demonstrating cervical squamous cell carcinoma. The squamous cells have large dark, irregular nuclei and orangeophilic cytoplasm.

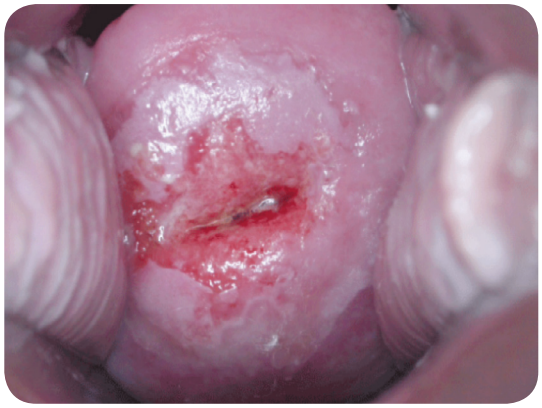

Figure 124.3 The appearance of cervical intraepithelial neoplasia at colposcopy. The area of CIN turns "acetowhite" upon application of acetic acid.

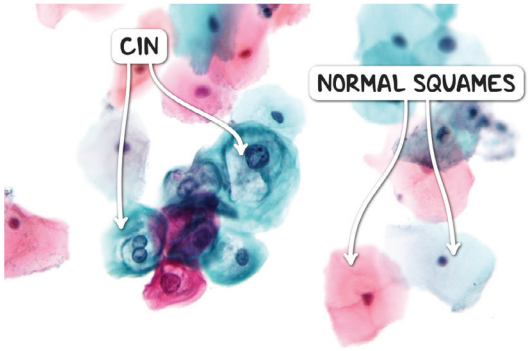

Figure 124.4 The cytological appearance of a low grade cervical intraepithelial lesion. The abnormal cells have large, folded nuclei and perinuclear halos. Normal squamous cells are seen on the right for comparison.

CHORIOCARCINOMA

osms.it/choriocarcinoma

PATHOLOGY & CAUSES

- Highly malignant epithelial tumor arising from trophoblastic tissue (e.g. molar pregnancy, abortion, ectopic, preterm/term intrauterine pregnancy)
- Germ cell tumor; may arise in ovary/testis (in individuals who are biologically male)
- Histology
  - Anaplastic cytotrophoblasts, syncytiotrophoblasts; no villi
- Altered paternal genomic imprinting → excessive expression of paternal genes → excessive proliferation of trophoblastic tissue → gestational trophoblastic disease (GTD) (e.g. choriocarcinoma)
- Excessive proliferation of syncytiotrophoblast → ↑ beta human chorionic gonadotropin (β-hCG) in plasma
- ↑ β-hCG → ovarian cysts

TYPES

Diploid

- Biparental chromosomes (e.g. after normal gestation)

Aneuploid

- Only paternal chromosomes (e.g. post-molar)

RISK FACTORS

- Complete molar pregnancy; advanced maternal age (> 40); individuals of Asian, indigenous peoples of the Americas ancestry

COMPLICATIONS

- Highly vascularized tumor → profuse bleeding
- Hematogenous metastasis to other organs (e.g. lungs, brain, liver)

SIGNS & SYMPTOMS

- Depends on metastasized organs
  - *Vagina:* profuse vaginal bleeding, vulvar dark blue papules
  - *Lungs:* chest pain, dyspnea, hemoptysis
  - *Brain, meninges:* headache, dizziness
  - *Hepatic:* jaundice, abdominal tenderness

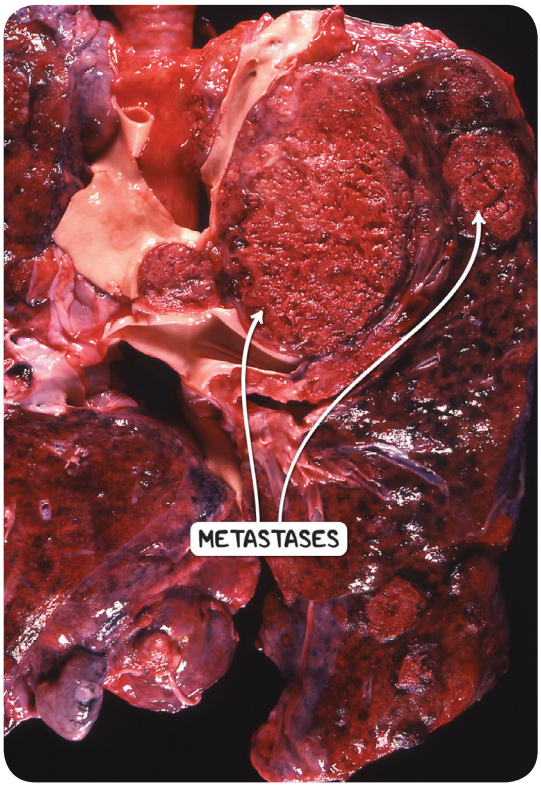

Figure 124.5 The gross pathological appearance of the lungs containing metastatic choriocarcinoma.

DIAGNOSIS

DIAGNOSTIC IMAGING

CT scan/MRI/chest X-ray

- Metastasis

Pelvic ultrasound

- Infiltrative myometrial mass

LAB RESULTS

- ↑ serum quantitative β-hCG, liver enzymes
- Complete blood count (CBC)
  - Anemia

OTHER DIAGNOSTICS

- Staging
  - FIGO

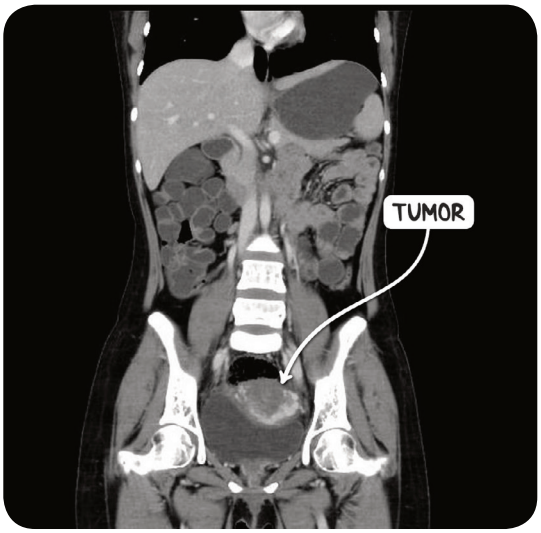

Figure 124.7 A CT scan of the abdomen and pelvis in the coronal plane demonstrating a uterine choriocarcinoma.

TREATMENT

SURGERY

- Hysterectomy, lung resection

OTHER INTERVENTIONS

- Chemotherapy, radiotherapy

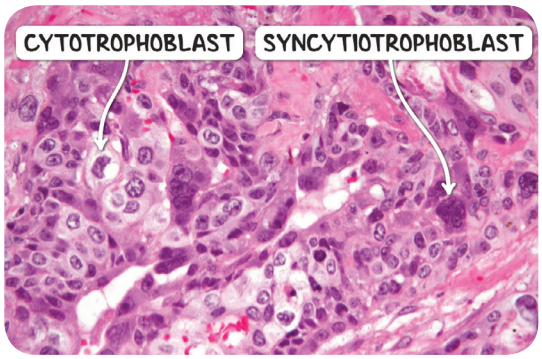

Figure 124.6 The histological appearance of a choriocarcinoma. Malignant cytotrophoblasts are stained light pink whereas the syncitiotrophoblasts are stained a darker hue.

ENDOMETRIAL CANCER

osms.it/endometrial-cancer

PATHOLOGY & CAUSES

- Cancer arising from endometrium (uterine lining)

TYPES

Endometrioid

- Result from excess estrogen
- ↑ estrogen → endometrial hyperplasia → endometrial intraepithelial neoplasia (EIN) → adenocarcinoma
- Related to gene mutations
  - *PIK3CA*, *CTNNB1*, *PTEN*, *ARID1A*, *KRAS*
- No Tp53 mutations except in Grade III

Nonendometrioid

- Estrogen-independent
- Arising from endometrial atrophy/polyp
- Usually involves Tp53 gene mutation
- *Two types:* clear cell, serous
- Clear cell
  - *Precancerous lesions:* clear cell intraepithelial neoplasia
  - Hobnail cells
  - Very aggressive (FIGO grade III)
- Serous
  - *Precancerous lesions:* endometrial intraepithelial carcinoma (EIC)
  - Presence of p53 mutations in EIC
  - May arise after radiotherapy for cervical carcinoma

SIGNS & SYMPTOMS

- Postmenopausal vaginal bleeding, abnormal menstruation (frequent, long, heavy), lower abdominal pain, unusual vaginal discharge, pelvic cramping, dyspareunia

DIAGNOSIS

DIAGNOSTIC IMAGING

CT scan

- Metastasis

Ultrasound

- Endometrium > 5mm thick in postmenopausal individuals

LAB RESULTS

- Endometrial biopsy

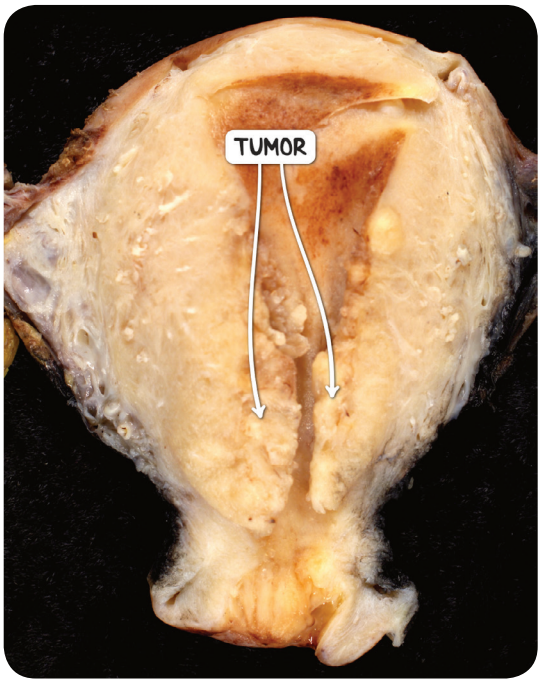

Figure 124.8 The gross pathological appearance of endometrial carcinoma of the lower uterine segment.

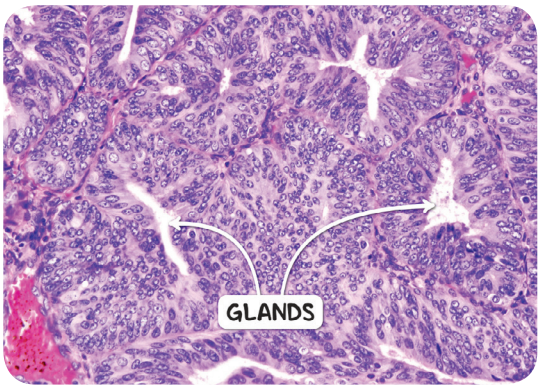

Figure 124.9 The histological appearance of endometrioid endometrial carcinoma. This low-grade variant is composed of back-to-back glandular structures with minimal underlying stroma.

TREATMENT

SURGERY

- Hysterectomy, pelvic/para-aortic lymphadenectomy

OTHER INTERVENTIONS

- Chemotherapy, radiotherapy, hormone therapy

GERM CELL OVARIAN TUMOR

osms.it/germ-cell-ovarian-tumor

PATHOLOGY & CAUSES

- Tumors that arise from primordial germ cells of ovaries, benign/malignant, produce β-hCG

TYPES

Teratomas

- Contain all types of tissues (e.g. hair, teeth, neurons)
- Immature teratomas
  - Specifically arise from neuroectoderm cells; usually malignant
- Mature cystic teratomas (AKA dermoid cysts)
  - Arise from any germ layers; common in young individuals who are biologically female

Yolk sac tumor (endodermal sinus tumor)

- Germ cells differentiate into yolk sac tissue
- Most common germ cell tumor in children
- Very aggressive
- *Schiller–Duval Bodies:* rings of cells around central blood vessels

Dysgerminoma

- Most common malignant ovarian tumor
- Germ cells turn into oocytes → grow uncontrollably → cancer
- Central nuclei surrounded by clear cytoplasm

RISK FACTORS

- Endometriosis, polycystic ovarian syndrome (PCOS)
- Genetic
  - *BRCA-1/BRCA-2* mutations
- Lynch syndrome (hereditary nonpolyposis colorectal cancer)

SIGNS & SYMPTOMS

- Sister Mary Joseph Nodule (umbilical metastasis)
- ↑ β-hCG
  - Precocious puberty, unusual vaginal bleeding, pregnancy symptoms (e.g. breast tenderness, mood swing, nausea)
- Abdominal distension, bowel obstruction, abdominal/pelvic pain, dyspareunia

DIAGNOSIS

DIAGNOSTIC IMAGING

CT scan/MRI

- Pelvic masses

Pelvic ultrasound

- Cystic/solid pelvic masses

LAB RESULTS

- Serum tumor markers
  - ↑ β-hCG, alpha fetoprotein (not always present with immature teratomas), lactate dehydrogenase (in dysgerminomas)
- Biopsy (definitive diagnosis)

TREATMENT

SURGERY

- Resection of affected ovary
- Bilateral pelvic, para-aortic lymphadenectomy
- Omentectomy

OTHER INTERVENTIONS

- Chemotherapy (if metastasized), radiotherapy

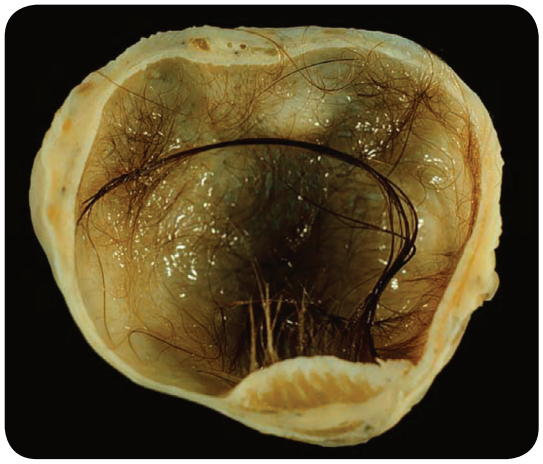

Figure 124.11 A mature cystic teratoma, the most common form of ovarian germ-cell tumor. This specimen contains mature dermal elements which give rise to the hair seen here.

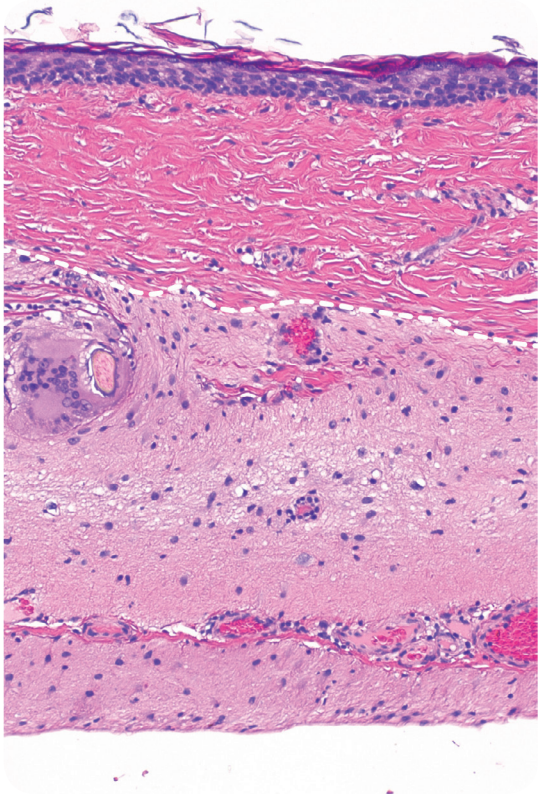

Figure 124.10 The histological appearance of a mature cystic teratoma. There is a dermal component (upper section) and a neural component (lower section).

KRUKENBERG TUMOR

osms.it/krukenberg-tumor

PATHOLOGY & CAUSES

- Ovarian cancer metastasized from another primary site
- Usually metastasizes from gastrointestinal (GI) tract/breast
- Likely spreads to ovaries by lymphatics
- Involves both ovaries
- Mucin-secreting signet ring cells

SIGNS & SYMPTOMS

- Pelvic/abdominal pain
- Bloating
- Ascites
- Dyspareunia
- Vaginal bleeding

DIAGNOSIS

DIAGNOSTIC IMAGING

CT scan/MRI

- Ovarian mass coexisting colic/gastric lesions

LAB RESULTS

- Biopsy (definitive diagnosis)
  - Ovary

OTHER DIAGNOSTICS

- Laparotomy
  - Ovarian mass + tumors in GI tract

TREATMENT

SURGERY

- Remove metastases

OTHER INTERVENTIONS

- Chemotherapy

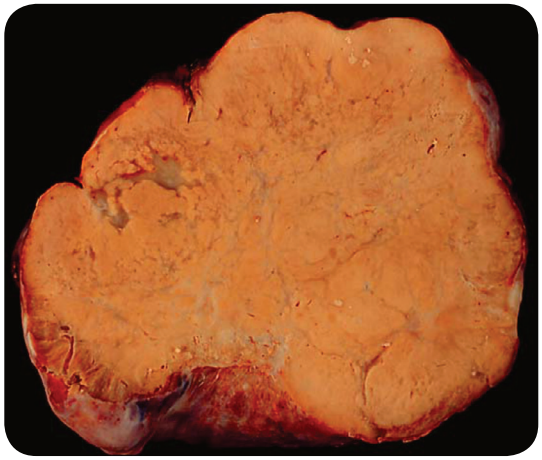

Figure 124.12 The gross pathological appearance of a Krukenberg tumor. The ovary has been entirely replaced by metastasis.

SEX CORD-GONADAL STROMAL TUMOR

osms.it/sex_cord-gonadal_stromal_tumor

PATHOLOGY & CAUSES

- Arise from ovarian follicle cells, stromal/connective tissue cells
- Benign/malignant

TYPES

Granulosa-theca cell tumor

- Most common malignant stromal tumor in middle-aged individuals who are biologically female
- Causes estradiol overproduction → early puberty, uterine bleeding, breast tenderness
- Call–Exner bodies
  - Tiny fluid pockets scattered in tissue

Sertoli-Leydig cell tumors

- Similar to testicular sertoli, Leydig cell tumors
- Made of primitive gonadal stroma → secretion of testosterone → hirsutism
- Reinke crystals (pink, rod-like)

Fibroma

- Benign
- Made of fibroblasts
- Needle-like strands (elongated nuclei) under microscope
- Associated with ascites, pleural effusion
- Compress uterine round ligament → pulling sensation in groin

RISK FACTORS

- Endometriosis, PCOS
- Genetic
  - *BRCA-1/BRCA-2* mutations
- Lynch syndrome

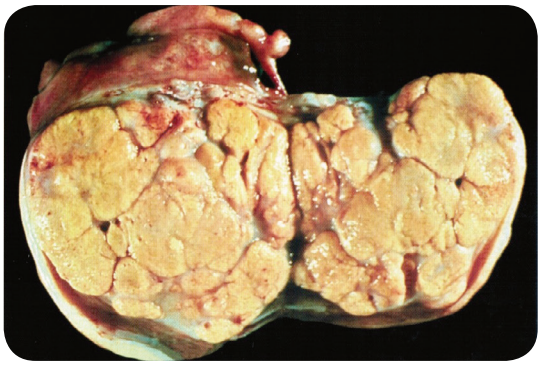

Figure 124.13 The gross pathological appearance of a Sertoli–Leydig cell tumor, a kind of sex cord stromal tumor. The cut surface is yellow and lobulated.

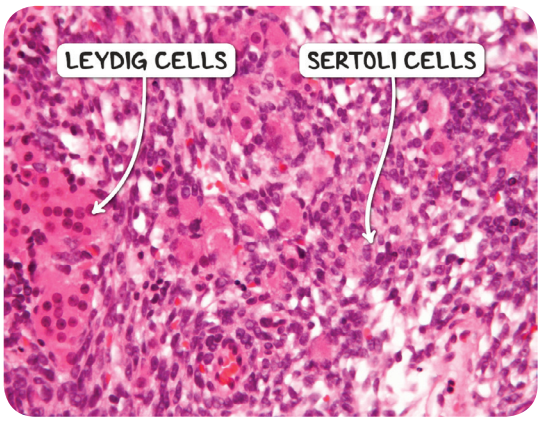

Figure 124.14 The histological appearance of a Sertoli–Leydig cell tumor. There are two popualtions of cells. The Leydig cells have large amounts of eosinophilic cytoplasm, whereas the Sertoli cells have less cytoplasm which is pale in appearance.

SIGNS & SYMPTOMS

- Uterine bleeding, breast tenderness, early puberty (in young individuals who are biologically female), Sister Mary Joseph Nodule (umbilical metastasis), ascites, abdominal masses, bowel obstruction, abdominal distension, abdominal/pelvic pain, bloating, dyspareunia

DIAGNOSIS

DIAGNOSTIC IMAGING

Pelvic ultrasound/CT scan/MRI

- Solid/cystic masses

LAB RESULTS

- Serum tumor markers
  - ↑ β-hCG, neural cell adhesion molecule (NCAM)
- Biopsy (definitive diagnosis)

TREATMENT

SURGERY

- If postmenopausal/childbearing completed
  - Abdominal hysterectomy, bilateral salpingo-oophorectomy
- Fertility-sparing with one affected ovary
  - Unilateral salpingo-oophorectomy for early-stage disease

OTHER INTERVENTIONS

- Chemotherapy (if metastasized)
- Radiotherapy

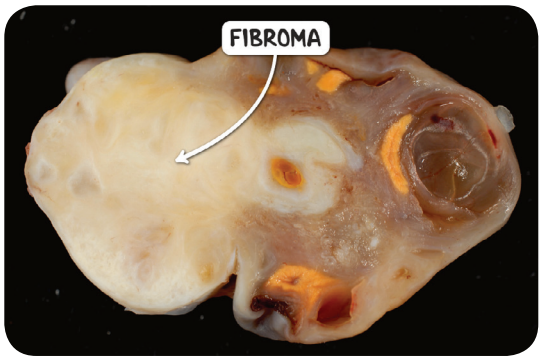

Figure 124.15 The gross pathology of an ovarian fibroma. The tumor has a homogenous, firm, cream-colored surface.

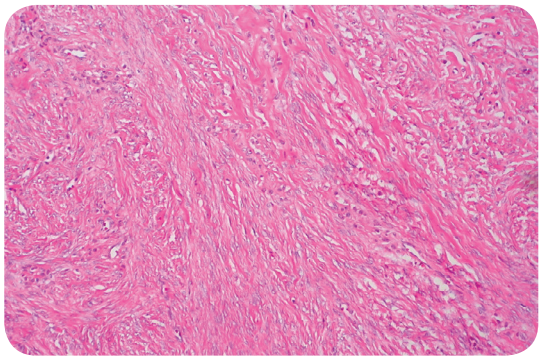

Figure 124.16 The histological appearance of an ovarian fibroma. The tumor is composed of spindles with interesecting bundles of collagen.

SURFACE EPITHELIAL-STROMAL TUMOR

osms.it/surface_epithelial-stromal_tumor

PATHOLOGY & CAUSES

- AKA ovarian adenocarcinoma
- Most common type of ovarian tumor
- Benign/malignant/borderline
- Originates from ovarian surface epithelium, fallopian tubes
- Mutation in epithelial cells → uncontrollable division → tumors

TYPES

Serous

- Benign/malignant/borderline
- Usually bilateral
- Serous cystadenoma if benign
- Serous cystadenocarcinoma if malignant
- Psammoma bodies → cystadenocarcinomas

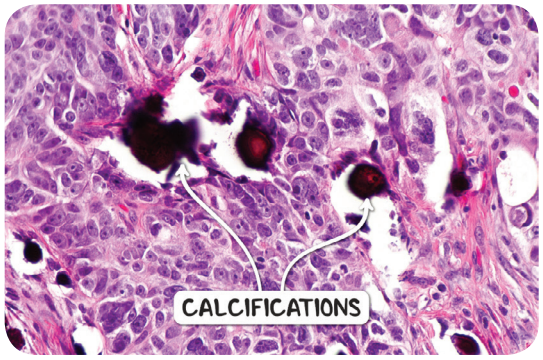

Figure 124.17 The histological appearance of an ovarian, high-grade serous carcinoma. There is wild cellular and nuclear pleomorphism, marked atypia and psammomatous calcification.

Endometrioid

- Cyst filled with dark blood (chocolate color)
- AKA chocolate cysts
- Develop from ectopic endometrial cells

Mucinous

- Usually unilateral
- Characterized by lining of tall columnar epithelial cells
- Mucinous cystadenoma if benign
- Mucinous cystadenocarcinoma if malignant
- Can cause pseudomyxoma peritonei
- Huge cystic masses (> 25kg/55lbs)

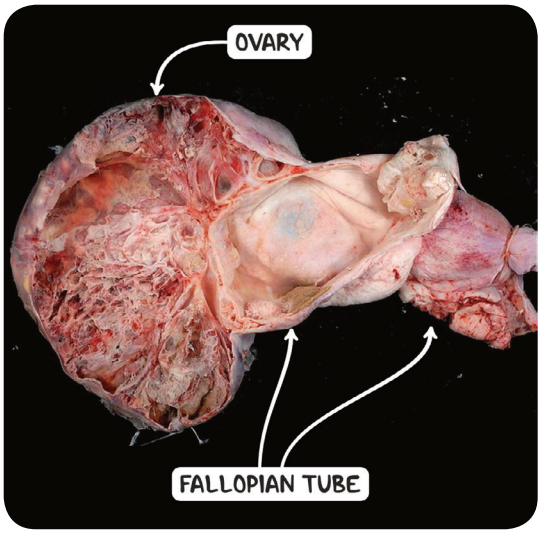

Figure 124.18 The gross pathological appearance of an ovarian mucinos neoplasm. The tumor is composed of innumerable mucin-filled cysts lined by mucin-producing epithelium.

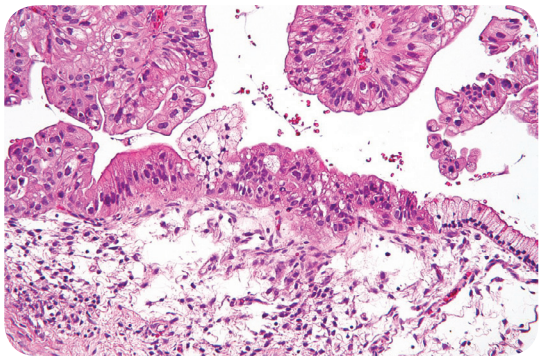

Figure 124.19 The histological appearance of a mucinous neoplasm of the ovary. There are multiple cystic spaces all of which are lined by columnar epithelium.

Clear cell

- Large epithelial cells with clear cytoplasm
- Associated with endometrioid carcinoma of ovaries

Transitional/Brenner

- Resembles bladder epithelium (transitional cells)
- Can be associated with endometriosis
- Similar to cell carcinoma of endometrium

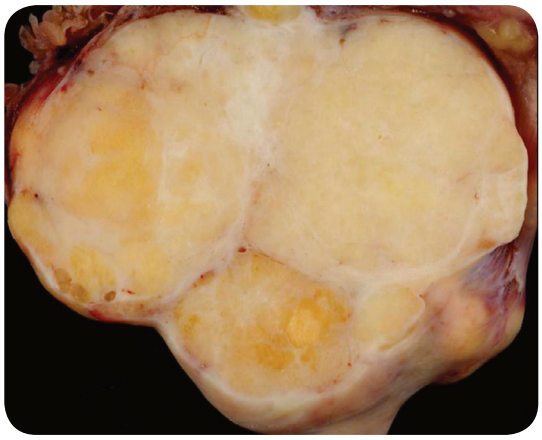

Figure 124.20 The gross pathological appearance of a Brenner tumor. The tumor is sharply circumscribed, firm and has a pale tan to yellow cut surface.

RISK FACTORS

- Endometriosis, PCOS
- Genetic
  - *BRCA-1/BRCA-2 mutations*
- Lynch syndrome

SIGNS & SYMPTOMS

- Uterine bleeding, breast tenderness, early puberty, Sister Mary Joseph Nodule (umbilical metastasis), ascites, abdominal masses, bowel obstruction, abdominal distension, abdominal/pelvic pain, bloating, dyspareunia

DIAGNOSIS

DIAGNOSTIC IMAGING

Pelvic ultrasound, CT scan/MRI

- Cystic ovarian masses

LAB RESULTS

- Serum tumor markers
  - ↑ β-hCG
- Biopsy (definitive diagnosis)

TREATMENT

SURGERY

- If postmenopausal/childbearing completed
  - Abdominal hysterectomy, bilateral salpingo-oophorectomy
- Fertility-sparing with one affected ovary
  - Unilateral salpingo-oophorectomy for early-stage disease

OTHER INTERVENTIONS

- Chemotherapy (if metastasized)
- Radiotherapy
- Serum CA-125 levels (monitor response to therapy)