

Female reproductive system pathology

Female reproductive system

Structure [Fig. 15-1, 15-2]

- vulva (labia majora, labia minora, clitoris, urethral orifice)
- vagina
- cervix
- uterus
- fallopian tubes
- ovaries

Function [Fig. 15-1]

- reproduction

Histology

- stratified squamous mucosa (vulva, vagina, ectocervix)
- glandular epithelium (endocervix, endometrium, fallopian tube)
- germ cells (ovary)

Menstrual Cycle

Female reproductive system pathology

Developmental abnormalities

Hermaphroditism

- discordance between genotypic and phenotypic sex

True hermaphroditism

- have both male and female gonads

Male pseudohermaphroditism

- genotypically male, phenotypically female

Female pseudohermaphroditism

- genotypically female, phenotypically male

Infectious diseases [Fig. 15-5]

Sexually transmitted diseases

- common (HSV, Chlamydia, HPV)
- present with vaginal discharge, lesions, pelvic pain, dyspareunia

Genital herpes (Herpes Simplex virus 2)

- vesicles on genitalia that coalesce and ulcerate
- appear 3-7 days after exposure (only 30% develop lesions)
- remains dormant in nerves, reactivation
- important to be aware because don't want vaginal delivery if active

Human papilloma virus (HPV)

- labial, vaginal and cervical warts (condyloma)
- certain types associated with carcinoma (see below)
- condyloma acuminatum is large vulvar wart (HPV 6,11)

Sexually transmitted diseases

Chlamydia (Chlamydia trachomatis)

- present with urethritis or cervicitis with discharge, PID

Gonorrhea (Neisseria gonorrhoeae)

- urethritis or cervicitis with discharge, PID

Syphilis (Treponema pallidum)

- vulvar ulcers

Bacterial vaginosis

- Candida
- Trichomonas
- Gardnerella

Female reproductive system pathology

Infections

Pelvic inflammatory disease

- chronic, extensive infection of upper reproductive tract
- usually secondary to STD (Neisseria, Chlamydia)
- salpingitis, tubo-ovarian abscess, peritonitis
- complications
 - chronic non-specific infection [fever, malaise, fatigue]
 - infertility secondary to scarring of fallopian tubes
 - pelvic mass with pain
 - spread of infection

Endometrial hyperplasia

- normal menstrual cycle requires normal functioning of the hypothalamic-pituitary-ovarian axis (figure 15-5)
- endometrial hyperplasia is thickening of the endometrial mucosa due to continued estrogen stimulation with inadequate progesterone
- anovulatory cycles (no ovulation therefore no progesterone secretion)
 - functional causes
 - puberty, anxiety, athlete
 - organic
 - excess estrogen (OCP, tumors)

Complex vs. simple hyperplasia

- atypical hyperplasia
 - increased risk of endometrial adenocarcinoma

Neoplasms of lower reproductive tract

Carcinoma of vulva

- squamous cell carcinoma
- raised or ulcerated lesion
- pre-neoplastic change may present as white or red patch
- biopsy to assess
- surgical excision +/- adjuvant therapy

Carcinoma of vagina

- squamous cell carcinoma
- clear cell carcinoma
 - women born to mothers on DES during pregnancy

Carcinoma of cervix

- reduced mortality due to Pap test (early diagnosis)
- risk factors
 - sexual intercourse at early age, multiple partners, HPV infection (certain types), other venereal diseases
 - environmental component and other factors
- squamous cell carcinoma
 - precursor lesion = dysplasia (Cervical intra-epithelial neoplasia) [Fig. 15-6]
 - lack of normal maturation of squamous epithelium
 - occurs at transition zone
 - graded mild, moderate, severe
 - cells shed into vagina (Pap smear)
 - HPV types 16, 18, 31, 33, 34, 35 associated
 - koilocytic change refers to characteristic changes due to HPV

Female reproductive system pathology

Neoplasia of the uterus

Leiomyoma (fibroid)

- benign neoplasm derived from smooth muscle in wall of uterus
- most common uterine neoplasm
- responsive to estrogen, arise during reproductive age
- usually asymptomatic
- may produce symptoms due to mass effects, bleeding

Leiomyosarcoma

- malignant neoplasm derived from smooth muscle in wall of uterus
- very rare

Endometrial adenocarcinoma

- malignant neoplasm derived from epithelial cells in endometrium
- most common malignant tumor of female reproductive tract
- elderly females, vaginal bleed
- risk factors (related to increased estrogen (hyperestrinism))
 - estrogen secreting tumor, exogenous estrogen
 - obesity
 - nulliparous or early menarche, late menopause
- stage most important prognostic feature [Fig. 15- 9]
- grade is also important (low, intermediate, high)
- diagnosis: endometrial biopsy, dilation and curettage
- therapy: hysterectomy +/- adjuvant therapy

Ovarian cysts

- fluid filled cavities lined by epithelium
- usually arise from unruptured follicles (follicular cysts)
 - may also represent cystic corpora lutea or inclusions of surface cells
- usually small, solitary, asymptomatic
- if large, then further investigation to rule out neoplasm

Polycystic ovary syndrome

- multiple cysts in both ovaries due to complex hormonal disturbances of the hypothalamic-pituitary-ovarian-adrenal axis
- presents with menstrual irregularities
- cause of infertility

Ovarian neoplasms

Introduction [Fig. 15-12]

- second most common group of tumors of female reproductive tract
- highest mortality of female reproductive tract tumors
- three major groups of neoplasms based on histogenetics
 - surface epithelial tumors
 - germ cell tumors
 - sex cord stromal tumors
- malignant ovarian tumors are uncommon in young females
- risk factors not well defined
 - ovarian dysgenesis
 - BRCA1 and BRCA2 gene mutations
- oral contraceptives not linked to ovarian neoplasms

Female reproductive system pathology

Ovarian neoplasms

Surface epithelial tumors

- 70 % of ovarian neoplasms
- spectrum of histologic types
 - serous, mucinous, endometrioid, clear cell and transitional cell types

Serous epithelial tumors

- most common
- typically cystic, filled with clear fluid
- benign, borderline malignant, and malignant tumors
- 25 % of benign tumors and 50 % of malignant tumors are bilateral
- distinction of benign versus malignant requires histologic examination

Mucinous epithelial tumors

- also typically cystic, filled with viscous fluid
- benign, borderline malignant, and malignant tumors
- 25 % of benign tumors and 50 % of malignant tumors are bilateral
- distinction of benign versus malignant requires histologic examination

Endometrioid epithelial tumors

- typically solid
- malignant

Germ cell tumors

- 20 % of ovarian tumors, occur in young females

Teratoma

- most common ovarian neoplasm in young females
- cystic, contain hair, sebaceous material (dermoid cysts)
- may contain teeth, bone cartilage
- benign
 - may undergo malignant transformation (malignant teratoma)

Immature teratoma

- teratoma that contains immature neural tissue
- may behave malignantly

Fibroma

- benign neoplasm of fibroblasts

Thecoma

- benign, solid and firm neoplasm of spindle cells (theca cells)
- produce estrogens

Granulosa cell tumor

- neoplasm of granulosa cells
- benign or malignant, may produce estrogen

Metastases

Female reproductive system pathology

Infertility

- ovum related
- sperm related
- genital organ factors
 - PID
 - Asherman's syndrome
- systemic factors

Diseases of pregnancy

Ectopic pregnancy

- implantation of fertilized ovum outside the uterine cavity
- usually occurs in fallopian tube
- trophoblast cells of placenta invade wall of tube, begins enlarging
- may rupture
 - surgical emergency

Placenta accreta

- abnormally deep penetration of placental villi into wall of uterus

Placenta previa

- abnormal placental implantation site in lower uterine segment

Toxemia of pregnancy

- disease of pregnancy of unknown pathogenesis resulting in characteristic symptom complex in the mother

Preeclampsia

- presents with hypertension, edema, and proteinuria
- occurs in third trimester
- may progress to eclampsia

Eclampsia

- hypertension, edema, proteinuria and seizures
- life threatening, must treat seizures, deliver baby

Gestational trophoblastic disease

- abnormalities of placentation resulting in tumor-like changes or malignant transformation

Hydatidiform mole

- developmental abnormality of placenta
- trophoblastic proliferation, hydropic degeneration of chorionic villi
- enlarged uterus with no fetal movement, high HCG

Complete mole

- no identifiable fetus, abnormal fertilization (46XX, all paternal)

Incomplete mole

- usually some fetal parts, abnormal fertilization (69 chromosomes)

Choriocarcinoma

- rare highly malignant tumor of placental origin, treat with methotrexate

Female reproductive system pathology

Abortion

- interruption of pregnancy prior to fetal viability (< 500 g, 20 wks)

Spontaneous abortions

- no identifiable cause (1/3 of all pregnancies)

Complete abortion

- fetus and placenta expelled, normal function returns

Incomplete abortion

- retention of some fetal or placental material

Missed abortion

- death of fetus in utero, passed several weeks later

Threatened abortion

- cervical os closed, spotting of blood

Endometriosis

- endometrial tissue (uterine glands + stroma) located outside the uterus
- various locations, typically ovary, peritoneum
- cycle in response to hormonal influences
- pathogenesis
 - retrograde flow
 - traumatic implantation
- common, may cause pain
- may cause infertility
- benign condition
- chocolate cyst of ovary

Breast pathology

Normal Breast

Function

- function is to produce milk (nourish newborn)

Structure [Figs. 16-1, 16-3]

- modified apocrine sweat gland
- lobules (ducts + terminal buds) drain into larger duct system

hormonally influenced changes

- males, pre-pubertal females have nipple + ducts
- post-pubertal female
 - proliferation of ducts and early acini
- pregnant female
 - terminal buds develop into acini
 - prolactin released in response to infant's suck
 - milk produced

Breast pathology

Inflammation

Acute mastitis

- acute inflammation of the breast
- lactating female
- bacterial infection
- abscess may develop

Chronic mastitis

- rare disease of unknown etiology
- may mimic breast cancer

Fibrocystic change

- benign changes in breast tissue due to various factors including hormonal influences and age
- females of reproductive age
- fibrosis of intralobular stroma
- cystic dilation of epithelial ducts
- epithelial hyperplasia
- various symptoms

Gynecomastia

- increased proliferation of male breast due to various factors

Breast pathology

Breast neoplasms

Fibroadenoma

- benign neoplasm of breast epithelial and stromal elements
- well circumscribed, firm, mobile mass
- young females

Breast cancer

- most common cancer in females
- second most common cause of cancer related deaths in females
- hormonal, environmental and genetic influences
 - familial breast cancers
 - BRCA-1, BRCA-2 tumor suppressor genes
 - increased incidence of other cancers
- risk factors
 - female sex (100x males)
 - genetic predisposition
 - hormonal factors
 - prolonged estrogen exposure
 - » early menarche, late menopause
 - » nulliparous
 - other malignancies
 - contralateral breast carcinoma
 - endometrial carcinoma
 - premalignant changes
 - carcinoma in situ, atypical hyperplasia
 - Age
 - Race
- there are different forms of breast cancer
- most common breast cancer is infiltrating ductal carcinoma
 - adenocarcinoma
 - desmoplastic response of stroma
 - lymphatic spread (axillary nodes drain most of the breast)
 - presents as mass
 - early detection
 - breast self-examination
 - mammography [Fig. 16-10]
 - fine needle aspiration
 - incisional biopsy
- therapy
 - Surgical resection
 - lumpectomy
 - mastectomy
 - axillary dissection
 - radiation
 - chemotherapy
 - tamoxifen
 - herceptin
- Prognosis
 - staging most important [Fig. 16-8]
 - histologic subtypes
 - histological grading
 - estrogen receptor status