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)
    - genital ulcers

Bacterial vaginoses
- 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 viscus 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
- abnorma plental 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