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Arabian Gulf University
College of Medicine and Medical Sciences

Kaplan Videos (Notes)

Year 5 (Gynecology)

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Chapter (1): Basic Principles of Gynecology

Prepared by: Ali Jassim Alhashli

Female Reproductive Anatomy

- Uterus:
  - Embryology: fusion of $\frac{2}{3}$ Mullerian Ducts
  - Major structures:
    - Body (corpus): mostly composed of smooth muscle
    - Cornu (origin of fallopian tubes)
    - Isthmus (joining body with cervix)
    - Cervix: mostly composed of collagen
  - Internal layers:
    - Serosa (outer-layer)
    - Myometrium (smooth muscle)
    - Endometrium (good vasculature for implantation of early embryo)
  - Ligaments:
    - Broad ligament → both sides of uterus to lateral pelvic walls
    - Round "
    - Cardinal "
    - Uterosacral "
  - Positions:
    - Anteverted
    - Retroverted (adhesions, chronic endometriosis, PID)
    - Mid-position
- Oviducts:
  - Extending from uterus to ovaries
  - 4 segments:
    - Interstitium
    - Isthmus
    - Ampulla
    - Infundibulum
  - Functions:
    - Facilitate sperm migration (in one direction) from uterus to ampulla
    - Transporting zygote from tube to uterine cavity
  - Attachments:
    - Medially: uterine body
    - Laterally: pelvic side wall
    - Inferiorly: broad ligament
  - Blood supply:
    - Uterine artery
    - Ovarian "

- Ovaries:
  - Containing oocytes within follicles
  - Producing reproductive & sexual hormones
  - Attachments:
    - Ovarian ligament to uterine fundus
    - Suspensory ligament to pelvic side wall
    - Mesovarium to broad ligament
  - Lymphatic drainage: para-aortic lymph nodes
  - Ovulation from Graafian follicle

- Vagina:
  - Tubular structure, 8-9 cm long, extending from introitus to cervix
  - Traverses the urogenital diaphragm through the genital hiatus of levator ani
  - Functions:
    - Female reproductive organ
    - Outflow tract for menstrual flow
    - Birth canal in delivery

Tanner Stages of Development

- Anatomical findings seen on physical examination of a developing adolescent
- Tanner stages: pubic hair
  - I: no (prepubertal)
  - II: long downy hair
  - III: coarse curly hair
  - IV: adult-like hair but sparing medial thighs
  - V: hair extends to medial surface of thighs
- Tanner stages: breasts
  - I: no (prepubertal)
  - II: Breast buds form
  - III: Breast elevates
  - IV: areola forms a secondary mound
  - V: adult breast, areola retains to contour

Gynecologic Procedures

- Gynecologic ultrasound:
  - low-energy, high-frequency sound waves
  - Transvaginal: ↑ resolution; only detecting lower pelvic masses
  - Transabdominal: ↓ resolution; imaging whole pelvis and abdomen

- Pap smear:
  - Outpatient screening procedure for pre-malignant cervical changes allowing early intervention to prevent cervical cancer
  - Cytologic specimens from transformation zone (T-zone) and endocervical canal using endocervical brush
  - 2 types:
    - Traditional: specimen smeared on glass slide and fixed
    - Liquid-based: specimens obtained by spatula and brush, then shaken in "formalin".
  - T-zone: stratified squamous epithelium meeting columnar epithelium
  - Advantages of liquid-based pap smear:
    - Monolayer cells
    - Air-drying eliminated
    - HPV-DNA test on residual specimen (especially for 16 & 18)

- Colposcopy:
  - Outpatient procedure using binocular short-focal length instrument with a built-in light source to look in the vagina through a speculum
  - Exocervix is visually examined to localise areas of abnormal epithelium
  - Abnormal areas include:
    - Punctuation
    - Mosaicism
    - White epithelium
    - Abnormal vessels
  - A biopsy is taken and sent to histo-pathology

- Cone biopsy:
  - Outpatient surgical procedure performed in OT under LA or GIA
  - Cone-shaped tissue specimen is obtained with a scalpel
  - Types:
    - Wide-shallow cone: pap smear is worse than colposcopically-directed biopsy.
    - Narrow-deep cone: lesion extends from exocervix into endocervical canal
  - Tissue sent to pathology
  - Risks:
    - Incompetent cervix
    - Cervical stenosis

- Loop Electrosurgical Exicion Procedure (LEEP):
  - Outpatient procedure performed without anesthesia
  - A thin, low-voltage electrified wire loop cuts out abnormal cervical tissue identified with colposcopy.
  - Advantages:
    - Visual conformation that abnormal tissue has been removed
    - Tissue specimen can be sent for histological diagnosis
  - LEEP follow up:
    - Pap smear every 3-6 months for $\geq$ years

- Cryotherapy:
  - Outpatient procedure performed without anesthesia
  - Liquid nitrogen or CO_2 circulates through a probe placed against cervix. This freezes the tissue for 2-3 minutes → destroying cervical tissue
  - Cryotherapy follow-up:
    - Repeat pap-smears every 3-6 months for $\geq$ years

- Hysterectomy:
  - Major inpatient surgical procedure performed in OT under regional or general anesthesia for both diagnosis as well as therapy.
  - Purpose → to remove the uterus
  - Procedure can be performed:
    - Vaginally (example: prolapse)
    - Abdominally (example: radical hysterectomy)
  - Types of hysterectomy:
    - Subtotal: removing body of uterus & leaving cervix in place
    - Total: most common; removing both body & cervix of uterus
    - Radical: removing whole uterus and broad ligament performed with early stage of cervical carcinoma

- Hysteroscopy:
  - Outpatient procedure performed in OT under LA or GIA for both diagnosis and possibly therapy.
  - A fiberoptic scope is placed through a previously dilated cervix to directly visualize endometrial cavity
  - Saline infused to distend uterine cavity allowing visualization

- Laparoscopy:
  - Minor outpatient surgical procedure performed in OT under GIA for both diagnosis as well as possibly therapy
  - Abdomino-pelvic cavity is distended with CO_2 to distend the abdomen and lift abdominal wall away from the viscera
  - Fiberoptic scope passed through umbilicus
  - For: endometriosis, adhesions, advanced ectopic pregnancy

- Hysterosalpingogram:
  - Outpatient diagnostic radiologic imaging procedure performed without anesthesia.
  - Cannula placed in endocervical canal and radio-opaque fluid is injected allowing assessment of uterine malformations; tubal pathology can also be assessed

- D&C:
  - Outpatient surgical procedure performed under anesthesia under LA or GA in OT
  - Cervix is dilated → curette used to scrape endometrium obtaining larger amounts of endometrial tissue than with an endometrial biopsy.
  - Tissue sent to pathology

- Endometrial biopsy:
  - Outpatient procedure performed with topical anesthesia
  - Done for post-menopausal bleeding
  - Hollow suction cannula is placed into uterine cavity and suction is applied. As cannula is rotated, limited amounts of endometrial tissue are aspired into it.
  - Retrieved tissue is placed into formalin and sent to pathology

- Mammography:
  - Outpatient office procedure performed by radiology
  - Performed as:
    - Screening test: for breast cancer is asymptomatic women
    - Diagnostic test: for a specific breast complaint.
  - Risks:
    Ionizing radiation exposure < 0.1 Rad
  - Screening mammography:
    - Two views are taken of each breast
    - Craniocaudal & lateral views
  - Recommendations for screening:
    - > 35 if risk factors present (e.g. breast cancer in 1st-degree relatives, family history of BRCA gene).
    - > 40 routine screening annually

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Chapter (2): Pelvic Relaxation

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Uterine and Vaginal Prolapse

- Uterine prolapse:
  - Etiology:
    - Multiparity → resulting in pelvic floor injury
  - As uterine prolapse progresses, anteverted uterus will have the same plane with vagina.
  - Classification:
    - Early
    - 1st degree
    - 2nd " → cervix reaching vaginal opening
    - 3rd "
    - Procidentia: uterus is outside the body
- Vaginal prolapse:
  - Anterior wall involved → cystocele
  - Posterior " " → rectocele → stool collecting in the cele
  - Pouch of Douglas inv. → enterocele
- Diagnosis:
  - Pelvic exam
  - Patient ↑ intraabdominal pressure (then look for prolapse)
- Management:
  - Medical:
    - Kegel exercises
    - Estrogen replacement (if post-menopausal)
    - Vaginal pessaries
  - Surgical:
    - Vaginal hysterectomy
    - Vaginal repair (anterior/posterior vaginal walls)

Urinary Incontinence

- Physiology:
  - Micturation:
    - Contracting detrusor muscle → by parasym. system on cholinergic receptors
    - Relaxing external urethral sphincter
  - Continence:
    - Relaxing detrusor muscle → by sym. system on β-receptors
    - Contracting external urethral sphincter → by sym. system on α-receptors
- Cystometric studies:
  - Patient empties bladder; catheter inserted; RV is measured (normally ≤50 ml)
    ; filling bladder with saline → then noticing if there are any bladder cont.
    - Ask patient when she feels fullness (200-225 ml)
    - Ask patient when she can't hold it anymore (400-500 ml)

↳ Urethral pressure maintains urine in bladder as long as it is ↑ than bladder pressure.

- Classification:

[1] sensory irritative:
- ↳ Etiology: infection, stone in bladder, tumor or foreign body
- ↳ History: urgency, frequency, dysuria (nocturia present)
- ↳ Exam:
  - ↳ suprapubic tenderness (infection present)
  - ↳ Pelvic and neuro exam → normal
- ↳ Inv.
  - ↳ WBCs and bacteria → infection (urine culture ⊕)
  - ↳ RBCs → tumor, stone or foreign body
- ↳ Management:
  - ↳ Antibiotic for infection
  - ↳ Cystoscopy: to know what is in bladder (with microscopic hematuria)

[2] Stress incontinence:
- ↳ Etiology: loss of support of bladder neck & proximal urethra
- ↳ History: small amounts of urine lost in spurts with coughing, sneezing (no nocturia)
- ↳ Exam:
  - ↳ Neuro exam: normal
  - ↳ ⊕ Q-tip test
- ↳ Inv. all normal
- ↳ Management:
  - ↳ Medical: Kegels exercises; hormonal replacement therapy
  - ↳ Surgical: urethropexy (elevating and supporting urethra)

[3] Urge / hypertonic:
- ↳ History: large amount of urine lost without warning! There is urgency and nocturia
- ↳ Inv.
  - ↳ Involuntary detrusor contractions
- ↳ Management:
  - ↳ Anticholinergics: (oxybutynin)
  - ↳ NSAIDs
  - ↳ Tricyclic antidepressants

[4] Overflow / hypotonic:
- ↳ History: small amount of urine lost intermittently day & night
- ↳ Exam: neuro exam abnormal (no innervation of $S_2 - S_4$)
- ↳ Inv: ↑ residual volume; detrusor contractions are absent
- ↳ Management:
  - ↳ Cholinergics (bethanecol)
  - ↳ Intermittent self-catheter

[5] Fistula:

- History: continual urine loss day & night associated with pelvic surgery
- Inv. intravenous pyelogram shows dye leakage
- Management: surgical repair

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Chapter (4): Disorders of The Cervix and Uterus

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Cervical lesions

- Polyps:
  - Finger-like growths start on surface of cervix and protrude through external os
  - Associated with:
    - Chronic inflammation
    - Abnormal response to ↑ levels of estrogen
    - Thrombosed cervical blood vessels
  - Prevalance: older multiparous womnen
  - Findings: smooth, red/purple, finger-like projections from endocervical canal with no impact on pregnancy
  - Management: removal be gently twisting it with a ring forcep or use of electrocautery or laser. Antibiotics are given after removal. Tissue sent to histopathology

- Nabothian cyst:
  - Asymptomatic mucus-filled cyst on surface of cervix
  - Mucus producing glandular cells become covered by squamous epithelium through metaplasia
  - Findings: small, white, pimple-like elevations
  - Prevalance: multiparous women.
  - Management: ignored because it is asymptomatic

- Cervicitis:
  - Inflammation of cervix
  - Causes:
    - STDs (gonorrhea and chlamydia)
  - Signs:
    - Friable, bleeding mucosa
    - or mucopurulent vaginal discharge
  - Diagnosis: DNA probe
  - Management: antibiotics

Cervical Neoplasia

- Cervical dysplasia:
  - Presentation: asymptomatic; most regress; few progress to cervical cancer within 10 years

- Response to HPV:
  - 65%. regress spontaneously
  - 20%. remain the same
  - 15%. progress to become worse

HPV: 6 & 11 → benign (condyloma)
HPV: 16 & 18 → ↑ risk of cervical cancer

- Risk factors of cervical dysplasia:
  - Early age of intercourse (< 16 years → due to immature T-zone)
  - Multiple sexual partners
  - Cigarette smoking
  - Immunosuppression
- Screening cervical dysplasia:
  - Pap smear:
    - Reduced death rates 70-80% from cervical cancer
    - Definition: cytological screening of transformation zone
    - 2 specimens:
      - Exocervical: using spatula
      - Endocervical: using brush

      } specimen is smeared on glass slide & fixed or directly inersed in formalin (liquid-based)
    - Bathesda III (2001) classification:
      - Negative
      - AISC-US: Atypical Squamous cells - Unknown Significance
      - ASC-H: " " " - High grade
      - LSIL: Low-grade Squamous Intraepithelial Lesion
      - HSIL: high-grade squamous Intraepithelial Lesion
      - Cancer
    - Histological classification:
      - CIN-I: mild dysplasia → 1/3 thickness basal cells (LSIL)
      - CIN-II: moderate dysplasia → 1/2 thickness basal cells (HSIL)
      - CIN-III: severe dysplasia & CIS → full thickness basal cells (HSIL)

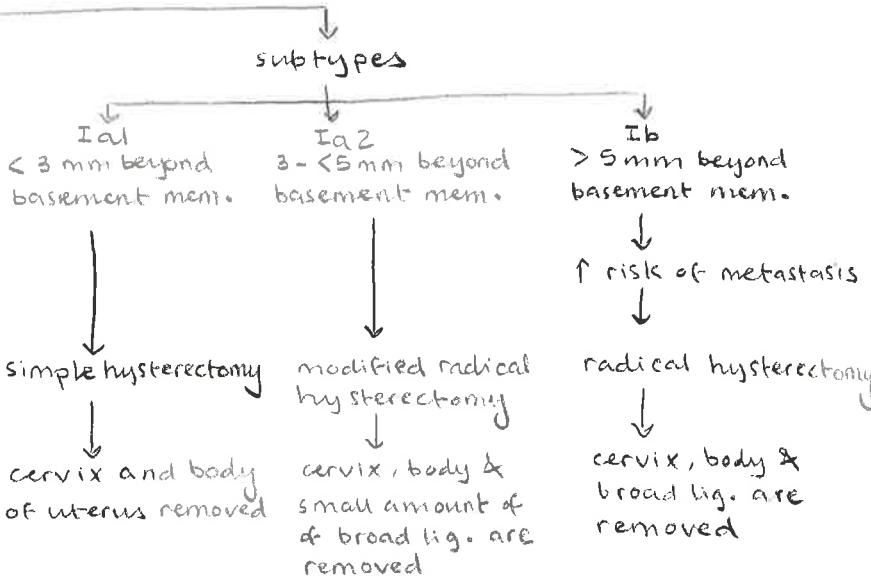
        ↓ basement membrane remains intact
- Management of ASC-US:
  - HPV DNA test
    - 16 & 18 → colposcopy and biopsy
    - 6 & 11 → repeat pap smear within 1 year
- Diagnostic approaches:
  - Accelerated pap smear (6 months)
  - HPV DNA typing
  - Colposcopy → done with
    - ASC-H
    - LSIL
    - HSIL
    - CA
- Management:

CIN-I:
- OBSERVATION: repeat pap, colp, HPV-DNA
- ABLATION: cryo, laser
- EXCISION: LEEP, cold-knife cone

} CIN-II or CIN-III

- HYSTERECTOMY: only recurrent CIN 2 or 3

- Invasive cervical cancer:
  - Definition: basement membrane is penetrated
  - Presentation: post-coital bleeding (due to trauma from penis against cervix)
  - Epidemiology: mean-age diagnosis is 45 year
  - Diagnostic test: cervical biopsy
  - Staging (how far does it goes): cervical cancer is clinically staged
    - I: limited to cervix
    - II: adjacent to cervix
    - III: further from cervix
    - IV: furthest from cervix



- Cervical neoplasia in pregnancy:
  - Effect of preg. on disease: none
  - Colposcopy & biopsy: yes
  - Perform Endocervical curettage: no due to ↑ vascularity
  - Management:
    - CIN: intraepithelial (basement membrane is intact)
      - pap smear & colposcopy: every 3 months
      - 2 months post-partum: re-evaluate & treat (most will regress)
    - Microinvasion (3-5 mm):
      - Cone biopsy: to check if there is frank invasion
      - Vaginal delivery is allowed
      - 2 months post-partum: treat residual lesions
    - Frank invasion (>5mm):
      - < 24 wks: ignore pregnancy & treat cancer
      - > 24 wks: wait to 32 wks → CS → treat cancer by staging

- Prevention of cervical cancer:
  - Quadrivalent (6, 11, 16 & 18) HPV recombinant vaccine
    - target age: 11-12 years

Mullerian Anomalies

- Uterine anomalies (7 types):
  - Causes:
    - Failure of one of the two mullerian ducts to form
    - Failure of fusion
    - Failure of fused mullerian ducts to dissolve the septum
  - Types:
    1. Hypoplasia/agenesis:
       - lacking vagina, a cervix, fallopian tubes or entire vagina and body of uterus (except for fundus)
       - Associated with urinary tract anomalies
    2. Unicornuate uterus:
       - One of mullerian ducts fails to form
    3. Didelphus uterus:
       - Double uterus due to failure of ducts to fuse
       - Each uterus has a cervix or both may share the cervix
       - 2/3 cases → 2 cervix, 2 vagina separated by a thin wall
    4. Bicornuate uterus (most common):
       - Failure of fusion between mullerian ducts at the top
       - 2 separate single horn uterine bodies sharing one cervix
    5. Septate uterus:
       - two ducts fuse but there is a failure in degeneration of median septum
    6. Arcuate uterus:
       - Uterus is essentially normal in shape with a small, midline indentation in the uterine fundus which results from failure to completely dissolve the median septum.
    7. DES uterus:
       - T-shaped uterine cavity
       - Short cervix or incompletely formed cervix

Enlarged Uterus

- Causes:
  - Pregnancy → confirmed by β-hCG
  - Leiomyoma
  - Adenomyosis
  - Leiomyosarcoma (rare)

- Leiomyoma:
  - Locations within uterus:
    - Subserosal: under serosa (bumpy: bumpy feel of uterus; can be pedunculated)
    - Intramural: within wall of uterus (no felt on phys. examination)
    - Submucosal: under mucosa (deforming uterine cavity; associated with menorrhagia)

- Leiomyomas (cont.):
  - Grow slowly: most common; left without intervention
  - Rapid growth: especially with ↑ estrogen during pregnancy
  - Degeneration: producing pain (outgrows blood supply)
  - Shrinkage with:
    - ↓ estrogen (menopause)
    - GnRH agonists: minimizing bleeding but ↑ difficulty with myomectomy
  - Diagnosis:
    - Pelvic exam: enlarged, asymmetric, non-tender, non-pregnant uterus
    - US:
      - Abdominal or vaginal (intramural or subserosal)
      - Saline infusion (submucosal)
    - Hysteroscopy:
      - Direct visualization of submucosal and removal.
    - Definitive diagnosis:
      - Histological diagnosis of surgically excised tissue
  - Management:
    - Observation: most of the time
    - Pre-surgical shrinkage: GnRH-agonists reducing up to 70% of the size
    - Myomectomy: preserving fertility
    - Embolization: preserving uterus
    - Hysterectomy: fertility completed
- Adenomyomas:
  - Endometrial glands and stroma within the wall of uterus
  - Criteria:
    - enlarged non-pregnant uterus
    - Dysmenorrhea
    - Menorrhagia
  - Management:
    - Medical: IUD
    - Surgical: hysterectomy

Endometrial Neoplasia

- Endometrial cancer:
  - Age: 60's
  - Pathophysiology: unopposed estrogen
    - Excessive hyperstimulation of endometrium without the stabilizing effect of progesterone.
  - Risk factors:
    - Obesity
    - HTN
    - DM
    - Nulliparity
    - Late menopause
  - Diagnostic tests:
    - * Endometrial biopsy
    - Hysteroscopy
    - Saline sonogram
  - Staging (surgical):
    - I: limitend to uterus
    - II: extension to cervix
    - III: adjacent to uterus
    - IV: distant metastasis

    I → subtypes:
    - Ia: only endometrium
    - Ib: < 50% myometrial invasion
    - IC: > 50% myometrial invasion
  - Management:
    - Total abdominal hysterectomy and bilateral salpingo-oopherectomy
    - Radiation and chemotherapy with advanced stages in addition TAH - BSO
  - Prevention:
    - Posmenopausal women with uterus: estrogen + progestin
    - Rproductive age women: only progestin (medroxyprogesterone acetate)
  - Patient presenting with post-menopausal bleeding:
    - Sample from uterus:
      - Endometrial biopsy
      - Hysteroscope
    - Causes:
      - Atrophy: estrogen + progestin
      - Benign polyp: hysteroscopic resection
      - Hyperplasia:
        - Without atypia → progestin only
        - With atypia → Total Vaginal or Total Abdominal Hysterectomy
      - Endometrial cancer → surgical stagin & grading → TAH - BSO + chemo & radiotherapy with advanced stages

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Chapter (5): Disorders of The Ovaries and Oviducts

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Physiologic Enlargement of Ovaries

- Functional ovarian cysts:
  - Etiology: ovarian cyst arising from normal physiologic event but size is exaggerated due to inappropriate maturation
  - Appearance: thin-walled, fluid-filled, no septations or calcifications
  - Examples:
    - Follicular cyst: 1st half of cycle (preovulatory)
    - Corpus luteum cysts (postovulatory)
  - Management: conservative (they will involute with time) (??)
- Polycystic Ovarian Syndrome (PCOS):
  - Appearance: bilateral enlarged ovaries with multiple peripheral cysts (20-100 in each ovary)
  - Etiology: ↑ androgens & ↑ insulin levels induce arrest of follicles in ovaries at various stages of development.
  - There is an association of PCOS with valproic acid.
  - Management: conservative (??)
- Ovarian hyperthecosis:
  - Refers to nests of luteinized theca cells throughout the ovarian stroma which produce androgens
  - Clinical features: similar to PCOS
  - Most women are obese and have a long history of severe hirsutism & virilization
  - May occur in postmenopausal women.
  - Mechanism: ↑ ovarian androgens → ↑ peripheral estrogen production → ↑ risk of endometrial hyperplasia and cancer
  - Management: oral contraceptives:
    - Suppressing androgen production (by reducing LH stimulation of theca cells)
    - Decreasing free androgens (by stimulating sex hormone binding globulin)
- Luteomas of pregnancy:
  - Rare, non-neoplastic tumor-like mass of the ovary that emerges during pregnancy & regresses spontaneously after delivery
  - Asymptomatic; found incidentally during a CS or postpartum tubal ligation
  - Can be hormonally active producing androgens resulting in maternal and fetal hirsutism and virilization
- Theca lutein cysts:
  - Benign but stimulated by ↑ FSH & hCG
  - Associations: twins and molar preg. (due to ↑ hCG)
  - Natural course: postpartum spontaneous regression
  - Management: conservative.

Prepubertal Pelvic Mass

- Differential of prepubertal pelvic mass:
  - → Ovarian cancer : could be
  - → Functional ovarian cyst: no chance!
- Surgical diagnosis:
  - → Simple mass → laparoscopy
  - → Complex mass → laparotomy (vertical midline incision)
    - → Benign → cystectomy
    - → Malignant → unilateral salpingo-oophorectomy (preserving reproductive function)
  - → Prognosis : 95% survival with chemotherapy

Premenopausal Pelvic Mass

- Ultrasound appearance of ovarian masses:
  - → Cystic : smooth, fluid-filled, round, no septations, no calcifications
  - → Complex : cystic areas and septations
  - → Solid appearance
- Simple cyst:
  - → Functional ovarian cyst:
    - → Follicular cyst
    - → Or corpus luteum cyst

    } observe, if it persists → laparoscopy
  - → Non-neoplastic, non-functional ovarian cysts:
    - → They can be simple, complex or solid
    - → Examples:
      - → paraovarian cyst
      - → Endometrioma

      } laparoscopy if benign, laparotomy if malignant
  - → Neoplastic (benign or malignant):
    - → They can be complex or solid
    - → Examples:
      - → Dermoid cyst
      - → Dysgerminoma

      } laparoscopy if benign, laparotomy if malignant

Painful Adnexal Mass

- Assessment of ovarian torsion with ultrasound : ↓ color Flow Doppler
- Ovarian artery and vein run through → ovarian ligament
- Thin-walled ovarian vein will get occluded first
- Patient presents with sudden severe lower abdominal pain
- Management (surgical):
  - → Cystectomy (if ovary is still viable)
  - → Oophorectomy (if ovary is necrotic)

Post-menopausal Pelvic Mass

- Most common gynecological cancers:
  1. Endometrium → in 60's
  2. Ovary → in 60's
  3. Cervix → in 40's
  4. Vulva → in 60's

- Ovarian cancer:
  - → Def: pelvic mass after menopause (when ovaries supposed to be shrinked)
  - → Diagnostic tests:
    - → CT-scan or MRI of abdomen & pelvis
  - → Screening test:
    - → Bimanual pelvic examination, but NOT ultrasound due to ↑ false-positive results!
  - → Risk factors:
    - → BRCA1 gene (+ family history)
    - → ↑ of lifetime ovulations
  - → Protective factors:
    - → ↓ lifetime ovulations: OCPs, PCOS, tubal ligation, breast-feeding and short reproductive life.
  - → Symptoms prior to diagnosis:
    - → 3 months before → 75% of pt have GI symptoms! Bloating, fullness, pressure & lack of energy
    - → 6 months before → 50% of pt have pain
  - → Spread: intraperitoneal spread to the whole abdomen + para-aortic lymph nodes
  - → Classification of ovarian cancer:
    - → Epithelial (80%): in older women; most common serous; CA-125 & CEA
    - → Germ cell (15%): in younger women
      - → Dysgerminoma → LDH
      - → Endodermal sinus → α-FP
      - → Choriocarcinoma → HCG
    - → Stromal (5%): in all age groups
      - → Granulosa cell → producing estrogen
      - → Sertoli-Leydig cell → producing testosterone
    - → Metastatic tumors to ovaries (bilateral): from endometrium, GI tract & breast; Krukenberg from stomach
  - → Ovarian cancer tumor markers:
    - → Benign causes of ↑ CA-125 (↓ specificity thus not used for screening of OC)
      - → Leiomyomas
      - → Adenomyosis
      - → Endometriosis
  - → Surgical staging:
    - → Stage-I: limited to ovaries
      - → Ia: one ovary; capsule intact and cytology is ⊖
      - → Ib: both ovaries; capsule intact and cytology is ⊖
      - → IC: one or both ovaries; capsule ruptured; cytology ⊕
    - → Stage-II: extension to pelvis
    - → Stage-III: peritoneal metastasis or ⊕ lymph nodes (most common)
    - → Stage-IV: distant metastasis

- Management:
  - Basic: surgical exploration
  - Specific:
    - Surgical staging
    - TAH - BSO
    - Omentectomy
    - Debulking → take as much tumors as it is possible → ↑ mean survival
    - Chemotherapy → taxol ; carboplatinum

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Chapter (6): Gestational Trophoblastic Neoplasia

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Gestational Trophoblastic Neoplasia

** Placental tumor of syncytiotrophoblast **

- History:
  - Vaginal bleeding (with passage of vesicles)
  - ↑ nausea and vomiting (due to ↑ β-hCG); pre-eclampsia < 20 wks
- Physical examination:
  - Uterus larger than dates
  - No FHT
- Diagnosis:
  - Ultrasound:
    - Complete mole: fetus absent; snow-storm appearance
    - Partial mole: fetus present; honeycomb thickened placenta
  - Pre-op workup:
    - β-hCG (in serum)
    - Chest x-ray (common site of metastasis: lungs)
    - Blood cross-match
- Management:
  - Suction D&C → tissue sent to histopathology
    - Benign:
      - Complete or incomplete mole
      - Serial β-hCG titers + oral contraceptives for 1 year
    - Malignant:
      - Good prog. (metastasis to pelvis or lungs) - >95% cure
        - Single-agent chemotherapy; oral cont. for 1 year
      - Poor prognosis (metastasis to brain or liver) - 65% cure
        - multiple-agent chemotherapy; oral cont. for 5 years

- Benign GTN:
  - Complete mole:
    - Empty egg + 2n sperm
    - 46, XX
    - Fetus absent
    - 15-20% malignancy
  - Incomplete mole:
    - Normal egg + 2 sperms
    - 69, XXY (triploidy)
    - Fetus present but non-viable.
    - < 5% malignancy
- Risk factors of GTN:
  - Geography: Taiwan & philippines
  - Age: < 20; > 35
  - Nutrition: folate deficiency

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Chapter (7): Sexually Transmitted Diseases

Prepared by: Ali Jassim Alhashli

STDs with Ulcers

- STD organisms:
  - Bacteria:
    - Chancroid, Donovanosis, Lymphogranuloma venereum
    - Gonorrhea, chlamydia and syphilis
  - Viruses:
    - HPV
    - HSV
    - HBV
    - HIV
  - Protozoan:
    - Trichomoniasis

- STDs with and without ulcers:

with ulcers		without ulcers
painful	← chancroid	Chlamydia
painless	← Gran inguinale	HPV
painful	← Genital herpes	Gonorrhea
painless	← LGV	HBV
painless	← Syphilis	HIV

- HSV (painful ulcers):
  - Vesicles breaking down and becoming ulcers
- Syphilis:
  - Caused by the bacteria: Treponema pallidum
  - Primary syphilis is characterized by → chancer (painless ulcer)
- Chancroid (painful ulcers):
  - ↑ in Sub-Saharan Africa
  - It is an HIV-cofactor
  - Exam: ragged edge
  - Diagnosis: ⊕ culture of H. ducreyi
  - Treatment: azithromycin.
- Lymphogranuloma venereum:
  - Symptoms: painless ulcer
  - Exam: groove sign (lymph nodes enlargement on either sides of inguinal ligament)
  - Diagnosis: aspiration of lymph node → ⊕ culture
  - Treatment: doxycycline or erythromycin
  - Associated with squamous carcinoma of vulva
- Donovanosis:
  - Found in South Africa, South America & Northern Australia
  - Symptoms: painless ulcer
  - Exam: beefy-red ulcer
  - Diagnosis: Donovan bodies (inclusions within lymphocytes)
  - Treatment: doxycycline

STDs Without Ulcers

- Condyloma Acuminatum:
  - Caused by: HPV (6 & 11: ↓ risk of cancer)
  - Transmission can occur with subclinical lesions
  - ↑ with HIV, DM & pregnancy
  - 70% of pt are sub-clinical, but syptoms (if present) are:
    - Pain
    - Odor
    - Bleeding

    } with large or infected lesions
  - Exam: cauliflower condyloma (most likely on cervix)
  - Diagnosis: visual (biopsy rarely needed)
  - Treatment (only for clinical lesions):
    - Small (topical): podophyllin & imiquimod (ALDARA)
    - Large (ablation): cryo, laser or excision
- Chlamydia:
  - Group affected: teenagers (< 20 yrs)
  - It is a common bacterial STD (intracellular gram ⊖ bacteria)
  - It causes adhesions → resulting in PID → and eventually infertility
    - acute salpingo-oophoritis
  - Neonatal ophthalmic chlamydia → conjunctivitis
    - Chronic ophthalmic chlamydia scarring causes → blindness
  - Exam: mucopurulent cervicitis
  - Investigations: PCR amplification or DNA probes
  - Management: azithromycin or doxycycline (old)
    - You should treat the sexual partner
- Gonorrhea:
  - Prior to antibiotics → it was the most common disease of adult men
  - Neisseria gonorrhea → gram ⊖ intracellular diplococci
  - Can involve:
    - Lower reproductive tract:
      - Bartholin abscess or cyst
    - Upper reproductive tract:
      - PID
    - Disseminated disease
      - Septic arthritis
  - It can causes ophthalmic gonorrhea in adults / neonates
  - Diagnosis: cervical & rectal swab cultures
  - Treatment: whenever you have gonorrhea you should also treat for chlamydia
    - cefixime (single oral dose) + azithromycin (single oral dose)
- HIV:
  - Everybody must be screened between ages 13 – 64 yrs

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Chapter (8): Pelvic Pain

Prepared by: Ali Jassim Alhashli

Pelvic Inflammatory Disease

- Pelvic infection - mechanisms:
  - Endometritis → carried by lymphatics
  - Pelvic TB → carried hematogenously from lung to pelvis
  - * Acute PID → ascending infection from vagina
    - Left untreated → chronic PID
    - Get worse → tubo-ovarian abscess

- Acute PID:
  - 5 clinical criteria:
    - Bilateral pelvic tenderness
    - Purulent cervix
    - Tender cervix
    - ↑ ESR
    - ↑ WBCs
  - Treatment:
    - In-patient: IV cephalosporin & doxycyclin
    - Out-patient: ofloxacin PO for 14 days

- Chronic PID:
  - Criteria:
    - Bilateral pelvic tenderness
    - NO purulent cervix
    - Tender cervix
    - Normal ESR
    - Normal WBCs
  - Diagnosis: laparoscopy.
  - Treatment (challenging): mild analgesic

- Risk Factors:
  - Age < 20 yrs!
  - STDs
  - Multiple sexual partners

- Cervicitis:
  - Mucopurulent cervical discharge (pus on examination)
  - Symptoms: none
  - Investigations: ⊕ gonorrhea and/or chlamydia
  - Management:
    - Chlamydia → azithromycin (1 oral dose)
    - Gonorrhea → cefixime (1 oral dose).

- Acute salpingo-oophoritis:
  - Ascending infection from lower tract to upper tract
  - Symptoms: bilateral pelvic pain
  - Physical examination:
    - Mucopurulent cervical discharge
    - Cervical motion tenderness
    - Bilateral abdomeno-pelvic tenderness
  - Investigative findings:
    - ↑ WBC & ESR
    - ⊕ cultures
    - laparoscopy
  - Management:
    - Out-patient:
      - Criteria:
        - Certain diagnosis
        - No systemic infection
        - No pelvic abscess
      - Ofloxacin, PO, 14 days
    - In-patient:
      - Criteria:
        - Uncertain diagnosis
        - Out-patient treatment failure.
        - IUD
        - Systemic infection (high fever)
        - Pelvic abscess
      - Gonorrhea: IV cephalosporin
        Chlamydia: IV doxycycline

- Chronic PID:
  - Symptoms: chronic bilateral pelvic pain
  - Physical examination:
    - NO mucopurulent cervical discharge; NO tachycardia; NO fever
    - Cervical motion tenderness
    - Bilateral abdomeno-pelvic tenderness
  - Investigative findings:
    - Normal WBC & ESR
    - ⊖ cultures
    - US: may show hydrosalpinges
  - Management:
    - Mild analgesics
    - Adhesion lysis
    - Ongoing chronic pain: TAH-BSO (+ estrogen replacement therapy)

Primary Dysmenorrhea

- Recurrent, crampy lower abdominal pain along with nausea, vomiting and diarrhea (GI symptoms) that occurs during menstruation in absence of pelvic pathology
- Among adolescent females
- Symptoms:
  - Starting: several hrs prior to menses & continue for 1-3 days
  - Epidemiology: onset with occurrance of ovulatory cycles
- Pathogenesis:
  - ↑ production of endometrial PGF2α → dysrhythmic uterine contractions hypercontractility & ↑ uterine muscle tone → uterine ischemia!
  - ↑ production of PGI → nausea, vomiting & diarrhea (via stimulation of GI smooth muscle).
- Management:
  - NSAIDs (DOC) → inhibiting PG synthesis
  - Continuous oral contraceptives (2nd choice)

Secondary Dysmenorrhea

- Occurring after age of 20 or 30; there is pelvic pathology; pain is dull & aching; no nausea, vomiting or diarrhea
- Endometriosis:
  - Definition: endometrial glands & stroma located outside uterus
  - Pathophysiology:
    - Retrograde menses (backward through fallopian tubes) & autoimmune
    - Most common site: ovaries; others:
      - Cul desac
      - Uterosacral ligament (nodularity).
      - Rectosigmoid

      } Uterus may become retroverted adherent & non-mobile
  - Clinical findings:
    - Dyspareunia (pain with sex)
    - Uterosacral ligament nodularity → Felt by rectovaginal exam
    - Infertility
  - Diagnosis: laparoscopy visualization, US (chocolate cyst)
  - Aim of treatment is to create:
    - Pseudopregnancy → continuous MPA + combination OCPs
    - Pseudomenopause → Danocrine
      ✱Leuprolide (GnRH agonist)
  - Surgical treatment:
    - Conservative (preserving fertility): laser vaporization + adhesion lysis
    - Aggressive: TAH-BSO (provide estrogen replacement)
      - NOT WORKING!

- Adenomyosis:
  - Enlarged non-pregnant uterus + 2nd dysmenorrhea + menorrhagia
  - Uterus on physical exam:
    - Symmetric
    - Soft
    - Tender

    } remember that leiomyoma is → Asymmetric, Firm, non-tender
  - Management:
    - Medical: Mirena
    - Surgical: hysterectomy

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Chapter (9): Fertility Control

Prepared by: Ali Jassim Alhashli

Overview of Fertility Control

- Extremely effective
  - IUDs
  - DMPA
  - Implants
  - Sterilization
- Very effective
  - OCs
  - Patch
  - Ring
- less effective
  - Male & female condoms
  - Cervical cap & diaphragm
  - Withdrawal

HOW ARE THESE SUPPRESSED?

- Fertility requirements:
  - Ovulation → All steroid contraception
  - Functional & patent fallopian tubes → tubal ligation
  - Sperm are present and functional → vasectomy, barrier or spermicides
  - Intercourse → at time of ovulation → Natural family planning
  - Cervical mucus must be favorable → progestin steroids thicken cervical mucus
  - Endometrium is receptive → progestic steroids & IUD
- Ideal contraceptive characteristics:
  - Inexpensive
  - Easy and simple to use
  - Use unrelated to time of intercourse
  - Freely reversible effects
  - Readily available
  - Free of side effects

Barrier / Spermicidal Methods

- Advantages:
  - ↓ transmission of gonorrhea, chlamydia & syphilis
  - No systemic side effects
- Disadvantages:
  - ↑ HIV transmission
  - 20% Failure!
- Condoms:
  - Sheath placed on the erect penis
  - Most common barrier method
- Diaphragm:
  - Holds spermicide against cervix ↔ place 2 hrs before sex / Leave it for 6 hrs after sex
  - Individual fitting (different sizes) → might cause urinary retention if so tight
- Spermicide:
  - Jellies or foams
  - Nonoxynol-9 (is the active ingredient)
    - Disrupting membranes on the head of the sperm
    - Might cause genital irritation

Steroid Contraception

- Progestin-only modality:
  - Oral daily pill (mini pill) → used every day at exactly the same time
    - Working primarily by affecting cervical mucus
  - IM injection (DMPA): given once every 3 months → side effects:
    - Irregular unpredictable bleeding
    - Prolonged return of fertility
    - ↓ bone density
    - Weight gain
  - Subcutaneous implants (implanon) → etonorgestrel for 3 years
  - Morning-after pill (preven) → levenorgestrel
  - IUD: Mirena
- Estrogen-progestin modality:
  - Oral pill: 21 days on / 7 days off
  - IM injection (Lunelle): no longer in the market
  - Trans-dermal patch (Ortho-Evra)
  - Vaginal ring (Nuva ring) → etonogestrel + ethinyl estradiol
- MOA of steroid contraception:
  - Pituitary: suppressing LH-surge
  - Ovary: suppressing ovulation
  - Endometrium: producing atrophy
  - Cervix: thicker cervical mucus
- Oral contraceptives use → ethinyl estradiol (synthetic estrogen)
- Metabolic effects of steroid contraception:
  - Estrogen-mediated → thrombosis & endometrial cancer
    - stimulating a healthy lipid-profile: ↑ HDL; ↓ LDL
      While progestins do the opposite
- Contraindications for steroid contraception:
  - ABSOLUTE:
    - Pregnancy!
    - Acute liver disease
    - History of vascular diseases
    - Hormonally-dependent cancers (breast & endometrial)
- Oral pills (estrogen + progesterone: 21 days on; 7 days off)

Intrauterine Contraception

- MOA:
  - Sperm transport inhibited → primarily with copper-IUDs
  - ↑ tubal motality → resulting in failure of implantation of immature zygote
  - Inhibiting implantation → through endometrial inflammation
  - Phagocytosis of sperms & blastocysts
  - Cervical mucus altered → with levenorgestrel-IUDs
- Contraindication of use:
  - Pregnancy!
  - Pelvic malignancy
  - Vaginal bleeding
  - Salpingitis
- Complications of IUDs:
  - Expulsion from uterus → ↑ in young, low parity women
  - Ectopic pregnancy
  - Septic abortion
  - Uterine perforation → at time of insertion
  - PID → ↑ in first 2 months (if an STD is present)
- There are mainly 2 types of IUDs (used nowadays):
  - Nova-T: containing copper (for 10 years)
  - Mirena: containing levenorgestrel (for 5 years)
- Case: IUD in uterus; pregnancy test ⊕ → What should you do?
  - Remove IUD (to ↓ risk of spontaneous abortion from 55% to 20%)

Natural Family Planning

- Avoiding having intercourse at the time of ovulation (period of fertility)
- Ovulation is predicted by:
  - Basal body temperature
    - Measured in morning from vagina
    - It rises at time of ovulation due to thermogenic effect of progesterone secreted by corpus luteum
  - Change in cervical mucus:
    - Before ovulation: Stretchy cervical mucus (spinbarkeit)
    - After ovulation: thick and sticky
- "Folk" methods to inhibit pregnancy:
  - Coitus interruptus:
    - Advantages: inexpensive; readily available
    - Disadvantages: requires discipline; semen in vagina can get into cervical mucus even before ejaculation.
  - Post-coital douche:
    - Theory: flush semen out of vagina
    - Limitation: sperm can get into cervical mucus within 90 seconds!

Sterilization

	Tubal ligation	Vasectomy
Destroy / remove	oviducts	vas deferens
cosidered	permanent	permanent
where performed	OT	office
Anesthesia	GA	LA
Failure rate	1:200	1:500
sucess criteria	-	azoospermia after 12 ejaculations
complications	-	anti-sperm antibodies

- Basic principles of contraception:
  - Estrogen + progestin steroids: healthy women (especially young)
  - Progestin only steroids:
    - Those who are lactating
    - Contraindication of estrogen use: history of thrombosis or vascular diseases
    - Smokers > 35 yrs
  - IUDs:
    - Monogomous
    - Multiparous women
    - No salpingitis
  - Barriers:
    - Motivated
    - ↓ fertility
    - multiple sexual partners (to prevent STDs)
  - Natural:
    - Religious reasons!
  - Sterilization:
    - For those who completed childbearing

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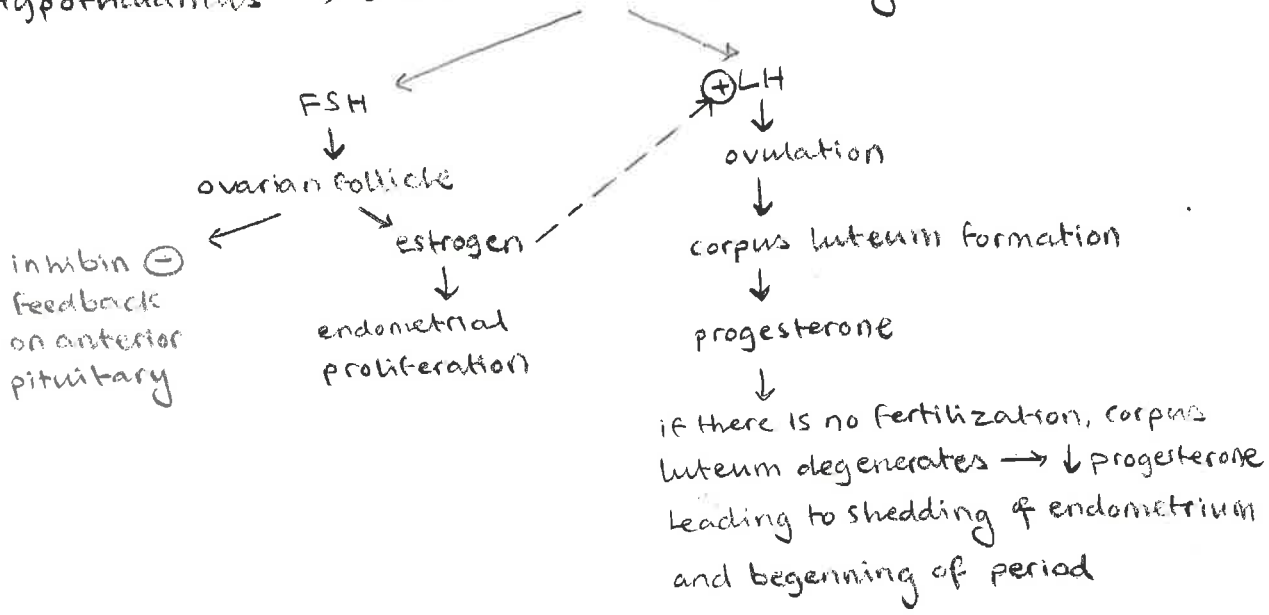
Chapter (11): Menstrual Abnormalities

Prepared by: Ali Jassim Alhashli

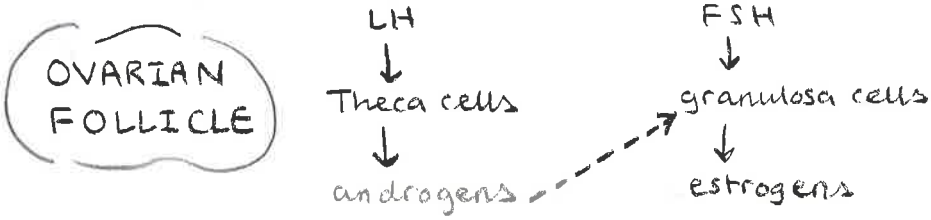
Overview of Menstrual Physiology

- Menarche:
  - When 1st menstrual flow begins
  - Mean age: 12-13 yrs
  - Notice initial menstrual periods are anovulatory (2-3 years)
- Reproductive years:
  - Monthly menstrual flow
  - lasting 360 cycles
  - There is a reproductive potential
- Menopause:
  - Last menstrual flow
  - mean age: 51 yrs
  - Signifies the end of reproductive potential
- Normal menstrual cycle:
  - Layers of endometrium:
    - Functionalis zone: superficial layer which sheds-of with each menstrual cycle (when progesterone levels fall)
    - Basalis zone: the zone from which regeneration takes place
  - Phases of endometrium:
    - Menstrual phase: 2-7 days
    - Proliferative phase: ↑ estrogen stimulating proliferation of endometrium
    - Ovulation: midcycle (at day 14 in a 28-day-cycle)
    - Secretory phase (fixed 14 days): ↑ progesterone
  - Regulation:
    - Hypothalamus → GnRH → anterior pituitary



  - Phases of ovarian follicle:
    - Follicular phase: there is recruitment of many follicles but growth of dominant one
    - Ovulation
    - Luteal phase

- Normal menstrual cycle (continued):



Pre-menarchal Vaginal Bleeding

- The most common reason for a little girl to have vaginal bleeding is a foreign body!
- Definition: bleeding before puberty.
- Differential diagnosis:
  - Vaginal foreign body (most common)
  - Neoplasm
  - Sexual abuse
  - Rare causes: ovarian, pituitary and adrenal tumors
- Diagnosis:
  - Pelvic examination under sedation
  - CT or MRI: of head, abdomen and pelvis (done if nothing is find with pelvic ex.)

Abnormal Vaginal Bleeding

- Terminologies:
  - Menorrhagia: predictable heavy bleeding
  - Hypomenorrhea: predictable cycle with minimal blood flow
  - Polymenorrhea: predictable & regular cycles but less than 3 weeks apart!
  - Oligomenorrhea: predictable cycles occurring more than 5 weeks apart!
  - Metrorrhagia: predictable cycle every 4 weeks but in between there is un-predictable irregular bleeding
  - Menometrorrhagia: no predictability of any kind in terms of frequency, duration and amount
- Abnormal vaginal bleeding:
  - Lower genital tract lesions → pelvic examination
  - Pregnancy complications → check β-hCG & do ultrasound
  - Anovulation → due to unopposed estrogen; Rx → MPA or combined oral contraceptives
  - Uterine lesion (fibroid or polyp) → saline sonography, hysteroscopy, endometrial biopsy
- Menstrual cycle:
  - Mean = 28 days
  - But there is variation = 21-35 days (abnormal bleeding → outside this range)

Primary Amenorrhea

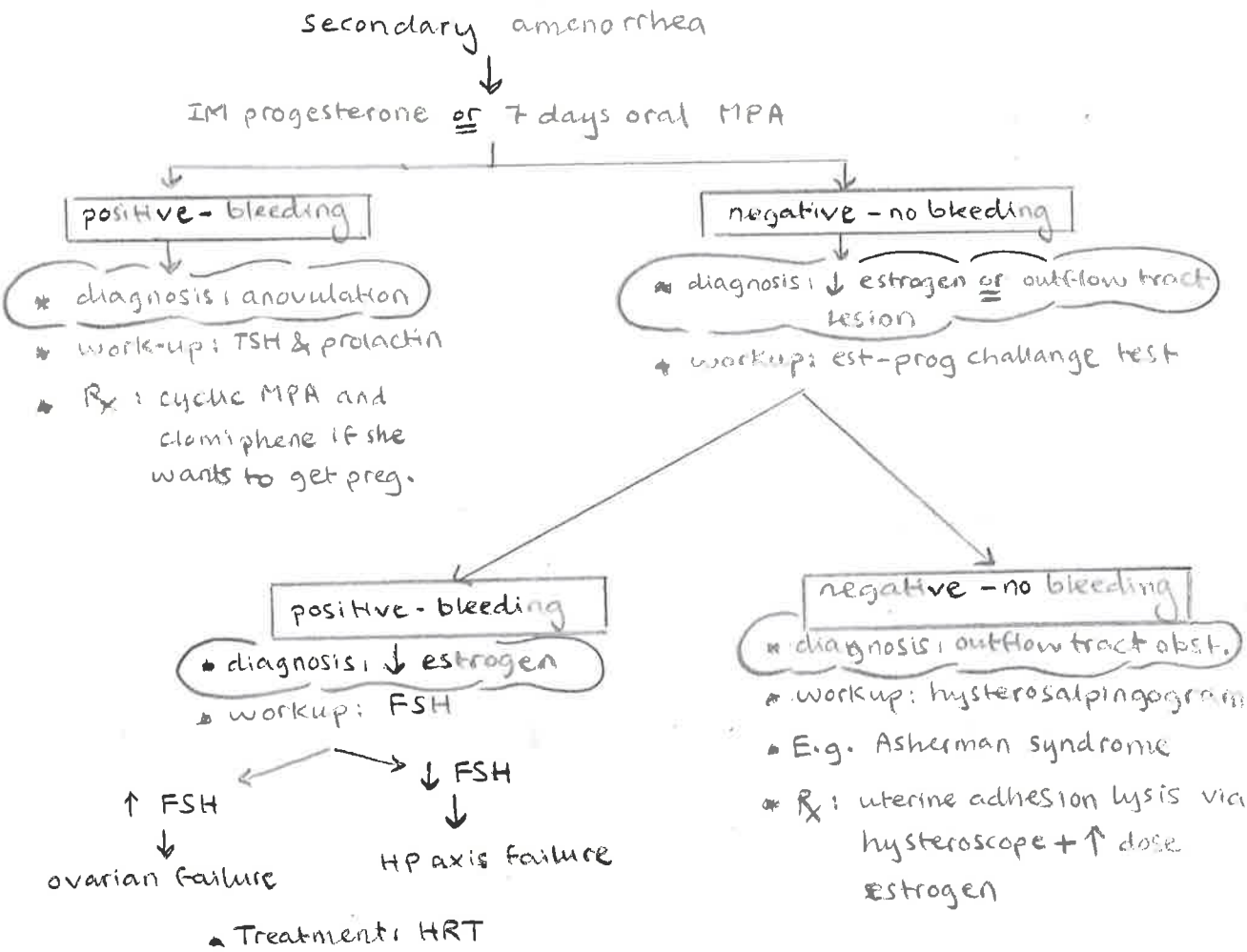
- Definition:
  - Absence of menses at age 14 without secondary sexual characteristics
  - " " " " " 16 with " " "
- Primary amenorrhea classification:
  - Breast ⊕ ; uterus ⊕
    - Vaginal agenesis / septum
    - Imperforate hymen → menstrual flow accumulating reaching up to uterine cavity
  - Breast ⊕ ; uterus ⊖
    - Mullerian agenesis
    - Androgen insensitivity
  - Breast ⊖ ; uterus ⊕
    - Gonadal dysgenesis (turner syndrome)
    - Hypothalamic-Pituitary-Ovarian failure (Kallman syndrome)

Breast ⊕ ; uterus ⊖	Mullerian agenesis 46,XX	Androgen insensitivity 46,XY
Uterus absent?	idiopathic	MIF (from testes)
Estrogen from?	ovaries	testes !
pubic hair?	present	absent (no androgen receptors)
testosterone level?	female level	male level
Treatment	no hormones create vagina IVF - surrogate	estrogen create vagina remove testes

Breast ⊖ ; uterus ⊕	turner syn. 45, X	HPO axis failure 46, XX
FSH?	↑	↓
No estrogen?	no ovarian follicles	follicles not stimulated
Ovaries?	"streak" gonads	normal
treatment?	estrogen + progestin	estrogen + progetin
Diagnostic test?	-	CNS imaging

Secondary Amenorrhea

- Secondary amenorrhea:
  - Pregnancy → check β-hCG
  - Anovulation → progesterone is not present → thus thin, watery cervical mucus
  - Estrogen deficiency
  - Outflow tract lesion
- Secondary amenorrhea:
  - Diagnosis (no menses for):
    - 3 months if previous regular menses
    - 6 months if previous irregular menses
  - Pathophysiology (based on FSH levels):
    - HYPO gonadotropic → hypothalamic-pituitary dysfunction
    - HYPER gonadotropic → ovarian follicular failure
    - EU gonadotropic → preg., anovulation, uterine anomalies, outflow tract lesion



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Chapter (12): Hormonal Disorders

Prepared by: Ali Jassim Alhashli

Polycystic Ovarian Syndrome (PCOS)

- HA - IR - AN syndrome:
  - HA → Hyper Androgenism
  - IR → Insulin Resistance
  - AN → Acanthosis Nigracans
- PCOS (ovaries are enlarged due to multiple peripheral cystic follicles)
  - Definition: condition of chronic anovulation resulting in
    - Infertility → due to chronic anovulation
    - Irregular bleeding
    - Obesity
    - Hirsutism → due to ↑ testosterone
  - Management:
    - Chronic anovulation → infertility → clomiphene (old) / metformin (New)
    - Irregular bleeding → progestins (old) / oral contraceptives (New)
    - So the newer combination is → metformin + oral contraceptives
  - Enlarged ovaries:
    - Described as necklace of cysts (on ultrasound)
    - Management: drilling (6-8) → not done anymore!

Infertility (15%)

- Infertility:
  1. Anovulation
  2. Semen problem (male-factor infertility)
  3. Tubal disease
  4. Unexplained
- Definitions:
  - Infertility: no pregnancy after 12 months of regular sex without use of contracep.
  - Fecundity: percentage of contraception in one month of timed intercourse
- Semen analysis:
  - Normal values: concentration > 15 million/ml
    > 50% motile
    > 50% normal
    } if results are abnormal, repeat after 4-6 weeks
  - Timing: obtain after 3-4 days abstinence
    examine within 1 hour

- How to assess tubal diseases?
  - Hystersalpingogram (HSG): contrast is injected through an intrauterine catheter
    contrast should spill into peritoneal cavity
    If normal HSG → no further testing
    If abnormal HSG → consider laparoscopy
      - Tuboplasty
      - Salpingectomy & IVF

- In-Vitro-Fertilization (IVF):
  - Oligozoospermia
  - Irreparable tubes
  - Unexplained infertility
  } indications
  - Procedure:
    - Transvaginal sono egg retrieval
    - IVF or ICSI
    - Hormonally prepare uterus to receive embryos
    - Embryo(s) transfer on day 3-4
      - Single embryo transfer in young women to avoid multiple pregnancy

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Menopause

- Mean age = 51 yrs (no functional follicles remain)
- Genetically determined; unaffected by pregnancy or oral contraceptives; in smokers it occurs 2 yrs earlier
- premature menopause → occurring before age of 40 (mostly idiopathic!)
- Perimenopause: 3-5 yrs before actual menopause
  - Menses become anovulatory & decrease in frequency
- Diagnosis:
  - Serial elevated FSH for ≥ 3 months
- Symptoms:
  - Amenorrhea (100%)
  - Hot flushes: less in obese women (due to ↑ estrogen amount in them)
- Effects of estrogen deficiency:

Early	Intermediate	Late
* Hot flushes * Sweating * Insomnia * Menstral irregularity * Psychological symptoms	* Vaginal atrophy * Pain with intercourse * Stress incontinence * Skin atrophy	* Osteoporosis fractures * CVD (common cause of death) * Alzheimer's disease

- Hormone Replacement Therapy (HRT):

	Estrogen + Progestin	Estrogen only
Vaginal dryness	↓	↓
Hot flushes	↓	↓
Vasomotor symptoms	↓	↓
Osteoporosis	↓	↓
Breast cancer	↑	NO CHANGE
Heart disease	↑	NO CHANGE
Stroke	↑	↑

- Recommendations for HRT:
  - ↳ No uterus: estrogen only (no need to prevent endometrial hyperplasia)
  - ↳ With uterus: estrogen + progestin (progestin prevents endometrial hyperplasia)