THE FEMALE REPRODUCTIVE SYSTEM

CHAPTERS 46 & 47
I'll impress the boss and order some of that feng shui he's always talking about!
THE HYPOTHALAMIC-PITUITARY-OVARIAN AXIS

- A QUICK REVIEW.
- GnRh, FSH, LH, ESTROGEN, PROGESTERONE.
- OVULATION, FOLLICULAR PHASE, LUTEAL PHASE.
- THE FOLLICLE AND CORPUS LUTEUM.
- EFFECTS ON THE ENDOMETRIUM.
- POSITIVE AND NEGATIVE FEEDBACK.
- EFFECTS OF ESTROGEN- see text.
FIBROCYSTIC BREAST DISEASE

- Common.
- Estrogen-dependent. Worse in the luteal phase.
- 1) Cystic dilation of terminal ducts.
- 2) Increase in fibrous tissue.
- 3) Proliferation of terminal duct epithelium.
- Causes painful, “granular” breast masses.
- Some forms increase the risk for breast cancer.
- Need to rule out cancer, not assume a mass is fibrocytic in origin.
BREAST CANCER

- Most common malignancy in the female.

- 2nd most common cause of cancer death behind lung.

- 400 deaths per year in males.
BREAST CANCER

RISK FACTORS

- 1) Age.
- 2) Family Hx- 1st degree relatives.
- 3) Hx benign breast disease- atypical hyperplasia.

However → most have no risk factors.
BREAST CANCER

GENETIC FACTORS

- 10% are hereditary.
- BrCa1 and BrCa2 genes.
- Genetic mutations cause up to 80% of cancers in women less than 50 years of age.
VAGINITIS

- Covered in the Ob / Gyn module.
- Will not address it here.
CERVICITIS

- Acute or chronic.
- Often secondary to uterine or vaginal infections.

**ORGANISMS:**
- C. albicans, T. vaginalis, Gardnerella vaginalis.
- N. gonorrhea, Chlamydia, Ureaplasma, Herpes.
- Chlamydia- most common.

- Signs / Sx’s: cervix is red, edematous; mucopurulent discharge; low back pain, dysmenorrhea, dyspareunia.
CERVICAL CANCER AND DYSPLASIA

- Cervical cancer begins as a precursor lesion called dysplasia = cervical intraepithelial neoplasia. Detected by the Pap smear.

**CLASSIFICATION SYSTEMS**

- **The dysplasia system**: mild, moderate, severe, CIS, invasive disease.
- **The CIN system**: Benign, CIN 1, 2, 3, invasive.
- **The Bethesda System**: negative, ASCUS, Low-grade SIL, High-grade SIL, invasive.
CERVICAL CANCER AND DYSPLASIA

- Evaluation and treatment varies, depending on findings on Pap smear and presence of risk factors, HPV type.
- Colposcopy w/ biopsy.
- HPV typing.
- LEEP, LETZ, cone biopsy.
- Low-grade lesions can regress spontaneously.
- High-grade lesions more likely to progress to invasive disease.
CERVICAL CANCER AND DYSPLASIA

**RISK FACTORS**

- Rare in celibate women.
- Multiple sexual partners; partners w/ multiple partners.
- Age at 1st intercourse.
- Smoking.
- Hx of STD’s- Herpes, HPV, chlamydia, HIV.
- HIV- cervical cancer is one of the 26 conditions listed by the CDC on their “AIDS surveillance case definition.”
CERVICAL CANCER AND DYSPLASIA

RISK FACTORS - HPV

- “High-risk” sub-types / strains of HPV have been identified as more likely to progress to invasive disease. “Oncogenic” sub-types.
- Types 16 & 18; also 31, 33, 35, 39, 45, 52, 58, and 59 to a lesser extent.
- Particularly aggressive in patients who smoke or have immunosuppression- HIV, steroids, etc.
- These can be identified in women with CIN and can aid in planning evaluation, follow-up, and treatment.
ENDOMETRIAL CANCER

- 2 TYPES:
  - 1) TYPE I- endometrioid- related to prolonged, unopposed estrogen.
  - 2) TYPE II- serous- unrelated to estrogen; some are genetic; worse prognosis.
ENDOMETRIAL CANCER

**UNOPPOSED ESTROGEN**

- Leads to endometrial hyperplasia and malignancy.
- Obesity w/ peripheral conversion of androstenedione to estrone.
- Anovulatory cycles, infertility.
- Unopposed ERT.
- Altered estrogen metabolism- diabetes, PCO, hypertension.
ENDOMETRIAL CANCER

- High index of suspicion in a patient with abnormal bleeding after age 40-45, liberal use of endometrial biopsy will catch most cases.
- ALL women with postmenopausal bleeding even / especially those on ERT, require endometrial biopsy.
- Prognosis excellent with early Dx.
PELVIC INFLAMMATORY DISEASE

- Ascending infection of the uterus (endometritis), tubes (salpingitis), and ovaries (oophoritis).
- Most commonly w/ gonorrhea and chlamydia.
- Also polymicrobial w/ : Mycoplasma, ureaplasma, bacteroides, peptostreptococcus, E coli, haemophilus, Strep agalactiae.
- Risk actors: multiple parters, IUD, ages 16-24, unmarried, nulliparous.
PELVIC INFLAMMATORY DISEASE

**MANIFESTATIONS**

- Pelvic, abdominal pain.
- Purulent discharge, bleeding.
- Fever, leukocytosis.
- Adnexal tenderness, tenderness on lateral cervical motion of pelvic exam.
- Scarring of the tubes can result in infertility, increase the risk of tubal pregnancy, and evolve into chronic pelvic pain.
ENDOMETRIOSIS

- The presence of endometrial tissue outside of the uterus. “Implants.”
- LOCATIONS: Most commonly the pelvis: ovaries, broad ligament, uterosacral ligaments, cul-de-sac. Also the vagina, vulva, perineum, bowel serosa. Rarely the lung, nostrils, umbilicus.
ENDOMETRIOSIS

THEORIES RE ITS GENESIS

- Multiple theories. I heard 9 presented at a seminar. The attractive ones are:
  - 1) Retrograde menstruation.
  - 2) Coelomic metaplasia.
  - 3) Venous / lymphatic dissemination.

Why does it develop in some and not others? Not clear. Immunologic factors have been looked at.
ENDOMETRIOSIS

- Implants respond to hormonal changes as if they were in the uterus → proliferative → secretory → “sloughing” (bleeding).
- Bleeding elicits fibrosis → scarring → adhesions.

MANIFESTATIONS

- Classic triad: dysmenorrhea, dyspareunia, infertility.
- Chronic pelvic pain, painful BM’s.
- Adhesions → bowel obstruction.
ENDOMETRIOSIS

**DIAGNOSIS**
- Laparoscopy w/ biopsy.

**TREATMENT**
- Depends on desire for preservation of fertility and extent of disease.
- 2 Flavors:
ENDOMETRIOSIS

TREATMENT

- **Conservative:**
  - 1) Surgical- laser, cauterization of lesions, lysis of adhesions.
  - 2) Medical- NSAIDS; hormonal: non-cycling OCP’s, GnRh analogs.
  - 3) Combined medical and surgical.

- Goal is pain relief, fertility.
- Disease inevitably recurs, though pregnancy can have an ameliorating effect on recurrence.
ENDOMETRIOSIS

TREATMENT

- **Definitive / Curative:**
- Removal of the “source” of the problem—estrogen.
- TAH / BSO.
- ERT after TAH / BSO for endometriosis- can stimulate recurrence, as the implants are still there.
FIBROIDS

- Uterine leiomyomata.
- Benign tumors of uterine smooth muscle.
- Common, esp in blacks.
- Estrogen responsive, regress at menopause.
- 3 types:
  - 1) Intramural.
  - 2) Submucous.
  - 3) Subserosal.
- Also pedunculated.
FIBROIDS

MANIFESTATIONS

1) Asymptomatic in many.
2) Bleeding, menorrhagia, metrorrhagia, anemia.
3) Pelvic pain, heaviness, dyspareunia, dysmenorrhea.
4) Pressure on bladder, rectum.
5) Outgrow their blood supply → infarction.
6) Occasionally infertility, premature delivery, pregnancy loss.
ECTOPIC PREGNANCY

- Implantation outside the uterus. Most commonly the tube, but also ovarian, cervical, and abdominal
- Leading cause of maternal mortality in the 1st trimester

RISK FACTORS

- Tubal disease (PID), prior tubal ligation or reversal, infertility, progestin only contraceptives, prior therapeutic abortion, previous ectopic.
ECTOPIC PREGNANCY

MANIFESTATIONS

- Think ectopic w/ amenorrhea, pain, bleeding.
- As the trophoblasts invade the tubal wall and the gestation expands, rupture of the tube can result w/ intra-abdominal hemorrhage, which can be fatal.
- Pain referred to the shoulder.
ECTOPIC PREGNANCY

**DIAGNOSIS**

- HCG and ultrasound.
- HCG- does not rise normally, may fall.
- Ultrasound- empty uterus, adnexal mass.
OVARIAN CYSTS

- 2 TYPES:
  - 1) NEOPLASMS.
  - 2) FUNCTIONAL (FOLLICULAR) CYSTS.

- ALSO PCO SYNDROME AKA STEIN-LEVENTHAL SYNDROME. A gynecologic as well as an endocrine disorder. See text.
FUNCTIONAL OVARIAN CYSTS

- Result from a follicle that fails to rupture and continues to grow.
- **Distinguished from a neoplasm by:**
  - **SIZE**- above 6-7cm, think neoplasm.
  - **APPEARANCE**- cystic, thin wall, unilocular. When solid, thick-walled, or multilocular, think neoplasm.
- Treatment is hormonal- suppression of FSH, LH. Surgical treatment for rupture, torsion, hemorrhage into the cysts, etc.
BENIGN OVARIAN NEOPLASMS

- See text.
- Note some are functioning- hormone-producing.
- Various tissue types: dermoids / teratomas, etc.
OVARIAN CANCER

- 75% have metastases at time of Dx.
- Results in low survival rate.

**RISK FACTORS:**
- Age. 65-85.
- Length of time of uninterrupted ovulation.
- Genetic / familial.
- Link to BrCa1 and BrCa2.
- High-fat “Western” diet.
- Talc.
Un fortunately, symptoms are not usually manifest until late.

Even then, symptoms are vague: abdominal discomfort, bloating, flatulence, indigestion.

As a result, diagnosis is delayed.

Need to maintain a high index of suspicion and evaluate / image accordingly.

No reliable screening tests.
DISORDERS OF PELVIC SUPPORT

- CYSTOCOEL.
- RECTOCOEL.
- ENTEROCOEL.
- UTERINE PROLAPSE.
- SEE TEXT.
- SUI CAN BE A SIGNIFICANT COMPONENT OF PELVIC RELAXATION.
VARIATIONS IN UTERINE POSITION

- ANTEFLEXION.
- RETROFLEXION.
- RETROVERSION.

Having a retroverted uterus is like being left handed. It’s not the statistical norm, but typically not a problem. A normal variant.

Occasionally can be associated with dyspareunia.

Can be caused by endometriosis, adhesions, etc.
DYSFUNCTIONAL MENSTRUAL CYCLES

- Due to alterations in the hormonal control of ovulation / menstruation.
- Oligo / anovulation.
- The bleeding is called dysfunctional uterine bleeding or D.U.B.
- MENORRHAGIA- excessive bleeding at menses
- METRORRHAGIA- bleeding between periods.
- MENOMETRORRHAGIA- excessive bleeding during and between menses.
DYSFUNCTIONAL MENSTRUAL CYCLES

- Usually due to a disturbance in the hypothalamic-pituitary-ovarian axis.
- Stress, rapid weight loss, obesity.
- Other endocrine disorders - hyperprolactinemia, etc.
- Anovulatory cycles - associated with sustained elevation of estrogen, no progesterone, and irregular sloughing, usually painless. Associated with increased risk of uterine cancer if prolonged
DYSMENORRHEA

2 EXCITING FLAVORS:

1) PRIMARY: attributed to the effects of prostaglandins on uterine contractions. Treatment is with prostaglandin synthetase inhibitors (NSAID’s), OCP’s. Diagnosis of exclusion.

2) SECONDARY: caused by underlying pelvic pathology- endometriosis, fibroids, PID, etc. Treatment is to address the underlying pathology.
PMS

- A syndrome characterized by a cluster of symptoms occurring during the luteal phase.
- Increases with age. Most who seek treatment are in their 30’s and beyond.

**SYMPTOMS**

- Breast tenderness and swelling. Edema
- Abdominal pain, headache, backache.
- Psychological, emotional, behavioral. More later.
- See table 47-2, Pg 1088.
PMS

**DIAGNOSIS**

- 1 symptom is sufficient for the diagnosis of PMS, as long as it occurs / worsens in the luteal phase.

- Charting can be helpful- for 3 months, focusing on symptoms, their timing in the cycle, and comparison to baseline in the follicular phase.
PMS

ETIOLOGY

- Not known specifically, no single cause ID’d.
- Likely is multifactorial.
- Hormonal etiologies abound, and are tempting, but definitive proof is flimsy.
- Suspected culprits: progesterone, imbalance in estrogen / progesterone ratios, prolactin, aldosterone, prostaglandins, B6 / dopamine / serotonin
PMDD

**DIAGNOSTIC FEATURES:**
Need 5 of these for the Dx

- 1) Markedly depressed mood.
- 2) Marked anxiety or tension.
- 3) Labile mood.
- 4) Persistent anger / irritability, interpersonal conflicts.
- 5) Decreased interest in usual activities.
- 6) Difficulty concentrating.
- 7) Lack of energy fatigue, lethargy.
PMDD

**DIAGNOSTIC FEATURES (CONT.)**

- 8) Change in appetite, sleep.
- 9) Feeling out of control, overwhelmed.
- 10) Feeling hopeless or self-deprecating
- 11) Physical symptoms as above.

- Symptoms significant enough to affect work, social or personal interactions; must improve after the onset of menses.
- Need to R/O other psychiatric disorders, as well as metabolic disturbances.
INFERTILITY
ASK DOCTOR ERNIE

"Deer Dr. Ernie, are there any inherited traits that never skip a generation?"

FERTILITY.

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INFERTILITY

- Inability to conceive after 1 year of unprotected intercourse.
- Affects 15% of couples.
- Male factors- 30-40%.
- Female factors- 30-40%.
- Both- 30-40%.
- Cause unknown- 10-25%.
MALE INFERTILITY

Due to:

1) Azoospermia- no sperm.
2) Oligospermia- not enough sperm.
3) Asthenospermia- poor motility.
MALE INFERTILITY

CAUSES

- Varicocele - common.
- Hypogonadism - various causes, pituitary, etc.
- Infection - mumps orchitis.
- Anti-sperm antibodies.
- Cryptorchidism.
- Gonadotoxins.
MALE INFERTILITY

SEMEN ANALYSIS

- EVALUATES:
- VOLUME.
- DENSITY- the “sperm count.” Expressed as # of sperm per ml.
- MOTILITY, VIABILITY.
- MORPHOLOGY.
- VISCOSITY.
MALE INFERTILITY

OTHER TESTS:

- Cervical mucous penetration assay- post-coital test, Penetrak.
- Sperm penetration test- Zona Free Hamster Ovum assay.
MALE INFERTILITY

- Evaluation includes a history, physical exam, and semen analysis.
- Focus on evidence of normal male secondary sex characteristics (Kleinfelter’s Syndrome) and anatomy of the genitalia (varicocele).
- Hormonal studies rarely needed in the male unless there is evidence of hypogonadism.
FEMALE INFERTILITY

CAUSES

1) OVULATORY DEFECTS- oligo-anovulation; hyperprolactinemia, hypothyroidism.
2) LUTEAL PHASE DEFECT.
3) ABNORMALITIES OF CERVICAL MUCOUS
4) ANTI-SPERM ANTIBODIES.
5) UTERINE ABNORMALITIES.
6) TUBAL OCCLUSION, DAMAGE.
7) ENDOMETRIOSIS.
FEMALE INFERTILITY

EVALUATION

- 1) Physical exam.
- 2) Cultures for STD’s.
- 3) Confirmation of ovulation- BBT, home dipstick thingies.
- 4) R/O luteal phase defect- serum progesterone day 21-22, endometrial biopsy day 18-19.
- 5) Cervical Mucous Eval- Post-coital test.
- 6) Hysterosalpingogram.
- 7) Laparoscopy w/ tubal dye study.
STD’S

CHAPTER 48
WHAT GROOMS USUALLY ASK.

ALEX TREBEK POPS THE QUESTION.
HUMAN PAPILLOMA VIRUS

- HPV. COMMON. COMMON. COMMON.
- **CAUSES:**
  - 1) CONDYLOMA ACUMINATA- genital warts.
  - 2) CERVICAL INTRAEPITHELIAL NEOPLASIA-CIN; high-risk sub-types, esp 16 and 18.
- Subclinical infection is common.
- Resolution of lesions may occur spontaneously, but current thinking is the infection is life long.
- Condoms not completely protective.
GENITAL HERPES

- Herpes Simplex Virus – HSV – Types I & II.
- Transmitted via:
  - 1) Sexual contact.
  - 2) Orogenital contact.
  - 3) Autoinoculation- need to be careful not to also infect the eye- keratitis.
- After initial outbreak, virus remains dormant in the dorsal root ganglia, and reactivate.
GENITAL HERPES

THE OUTBREAK

- Incubation period 2-10 days.
- The prodrome- itching, tingling, burning.
- The vesicle- fluid-filled lesions, rupture after 5 days.
- The ulcer- very painful.
- Ulcer crusts over, heals.
GENITAL HERPES

THE OUTBREAK

- Primary outbreak lasts 2-4 weeks.
- Primary outbreak can be associated w/ systemic manifestations- fever, malaise, lymphadenopathy, etc., due to lack of antibodies
GENITAL HERPES

THE OUTBREAK

- HSV II more likely to be associated with recurrent outbreaks.
- Recurrences not quite as severe and not associated with systemic manifestations due to the presence of antibodies.
- Treatment with anti-viral drugs Zovirax (acyclovir) and Valtrex lessen the intensity of and shorten the duration of primary outbreaks, and reduce the incidence of recurrences.
GENITAL HERPES

THE OUTBREAK

- Diagnosis is by viral culture.
- Serology- presence of antibodies to HSV II confirms prior genital herpes, but antibodies to HSV I do not differentiate between oral and genital infection.
GENITAL HERPES

- NEONATAL INFECTION

- Rule of 50’s- 50% of babies born and exposed to HSV will get infected; of those 50% will die; of the survivors, 50% will have residual neurologic damage from herpes encephalitis.

- Prevention- delivery by C-section if active lesions are present.

- Other protocols exist to do cervical cultures on asymptomatic pregnant women prior to labor, but no universal agreement on this.
CHLAMYDIA

- Most common STD in the U.S.
- Causes:
  1) Urethritis ("non-gonococcal urethritis"), prostatitis, epididymitis in the male.
  2) PID and cervicitis in the female.
- When symptomatic, symptoms are those of PID, but milder.
- Up to 75% of women and 50% of males are asymptomatic.
CHLAMYDIA

- The asymptomatic nature leads to a lack of detection and increased transmission.
- Routine testing recommended at the time of the annual Pap / pelvic.
- 40% of women w/ untreated chlamydia will develop PID, and 20% of these will become infertile as a result of tubal damage.