

Problem-Based Clinical Cases

Obstetrics and Gynecology Rotation

Gyn Cases Updated March 2015

OB Cases Updated March 2015

By Medical Student and Resident Education Committee

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Section I: General Gynecology

4. Breast Disorders: 49 year-old Jean, G3 P2 Ab1, presents at your office complaining of a left breast lump. Your examination confirms a right breast upper outer quadrant 3 cm discrete, nontender, cystic mass.

DDX:

1. Fibrocystic DZ
 - Most Common Breast Disease in
 - Tender with hyperplastic changes
 - due to decreased progesterone or increased estrogen
 - Get a mammogram to rule out cancer
 - FNA to help in diagnosis
 - Provera, Tamoxifen, Parlodel to treat, diuretic to decrease edema
2. Fibroadenoma
 - Most Common Benign Tumor
 - Well circumscribed and freely moveable
 - increased with pregnancy; regress with menopause
 - Treatment involves surgical excision
 - Usually found in females < 30
3. Intraductal papilloma
 - papillary growth within a duct
 - usually solitary and located under the areola
 - usually develops just before or during menopause
 - presents with bloody discharge
 - excisional biopsy of involved duct
4. Mammary duct ectasia (Comedomastitis, Plasma Cell Mastitis)
 - Common in 40's
 - presents with nipple discharge
 - presents with pain and tenderness (due to dilation of the ducts)
 - chronic intraductal and periductal inflammation
5. Galactocele
 - Ductal obstruction
 - milky thick discharge
6. Carcinoma
 - 90% ductal; 10% lobular (often bilateral)
 - Paget's 3% arises in secretory ducts and skin of the areola
 - PM women have a greater chance of being hormone receptor + which is associated with a better prognosis
 - most important prognosticator is axillary node involvement
 - Rx with sx, chemo, and hormonal rx if HR+

HX:

- Nipple discharge
- family history
- age at menarche
- age at menopause
- dietary fat intake
- history of irradiation

Risk Factors for Breast Cancer

Table 4. Factors That Increase the Relative Risk of Breast Cancer in Women	
Relative Risk	Factor
>4.0	Female Age (65+ vs <65 years, although risk increases across all ages until age 80) Certain inherited genetic mutations for breast cancer (BRCA1 and/or BRCA2) Two or more first-degree relatives with breast cancer diagnosed at an early age Personal history of breast cancer High breast tissue density Biopsy-confirmed atypical hyperplasia
2.1–4.0	One first-degree relative with breast cancer High-dose radiation to chest High bone density (postmenopausal)
1.1–2.0 Factors that affect circulating hormones	Late age at first full-term pregnancy (>30 years) Early menarche (<12 years) Late menopause (>55 years) No full-term pregnancies Never breastfed a child Recent oral contraceptive use Recent and long-term use of estrogen and progestin Obesity (postmenopausal)
Other factors	Personal history of endometrial or ovarian cancer Alcohol consumption Height (tall) High socioeconomic status Ashkenazi Jewish heritage

PE:

- Nipple retraction
- skin dimpling
- lymph node exam
- look for erythema and edema
- is it fixed or movable
- is it solid or cystic

LABS:

- Hormone receptor assay
- mammogram

Prevention and Screening:

- Teach patient’s breast “self awareness”
- Assess “high risk group” – Women with a 20% or greater lifetime risk of developing breast cancer (BRCA1 and BRCA 2 mutation, first degree relative with BRCA1 or 2, history of radiation to the chest between ages 10-30 yo, other genetic syndromes)
- For “average” risk - recommend screening with mammography annually starting at age 40
- For “high risk” – recommend “enhanced screening” - twice-yearly clinical breast examinations, annual mammography, annual breast MRI, and instruction in breast self-examination.

5. Contraception: 16-year-old Lisa, G1 P0 Ab1, presents at your office requesting an intra-uterine contraceptive device.

Types of Contraceptives: (percentage failure rates)

- 1.) Intrauterine(0.2-0.8%)
- 2.) Barrier(15-30%)
- 4.) Hormonal (1-10%)
- 5.) Physiologic

6.) Sterilization(0.5%)

Mechanism of Action:

1. Hormonal contraception Includes combination OCPs, progestin only pills, implants, depo, vaginal ring, patch. About 1/3 of all sexually active women in the US use OCPs. Almost all OCPs use a combination of estrogen and progesterone to prevent fertilization. These hormones suppress the hypothalamic gonadotropin-releasing factors with subsequent suppression of FSH and LH. Estrogen suppresses FSH, this preventing selection and emergence of the dominant follicle. Estrogen also stabilized the endometrium. Progesterone suppresses LH secretion and the LH surge, thus preventing ovulation. Progesterone also alters cervical mucous to prevent penetration by spermatozoa, causes the endometrium to be atrophic, and impairs tubal motility/peristalsis. Although progestin and estrogen components work synergistically, progestin provides more of the contraceptive effect, whereas estrogen regularizes the menstrual cycles.
 - A. Complications: venous thrombosis, pulmonary embolism, CVA, MI, HTN, amenorrhea, cholelithiasis, hepatocellular adenoma, breast mass. Risks increase with smoking.
 - B. Contraindications: DVT, PE, CVD, CVA, pregnancy, estrogen positive cancer, abnormal LFTs, known or suspected breast cancer, undiagnosed abnormal vaginal bleeding
 - C. Types:
 - Monophasic (fixed combination): take E & P on days 1-21 and placebo on days 22-28. Increased estrogen increases the side effects of headache, weight gain, nausea, and edema. Decreased estrogen and progesterone increases the risk of breakthrough bleeding and increases the failure rate.
 - Multiphasic: Low dose estrogen with varying doses of progesterone on days 1-21.
 - Progestin only pills: Not as effective and can cause breakthrough bleeding. Normal ovulation continues to occur in 40% of these patients using progestin only pills. This method is more dependent on the endometrium and cervical mucus effects of progesterone – gonadotropins are not consistently suppressed. Good option for women in which estrogen is contraindicated.
 - Nexplanon: Releases a daily dose of progestin. Works by thickening cervical mucus and inhibiting ovulation. Most common side effect is irregular, unpredictable bleeding.
 - Depo-provera: Lasts three months. Can cause irregular bleeding patterns secondary to unstable endometrium since there is no estrogen. Side effects include breast tenderness, weight gain, and depression.
 - D. Benefits: Decreases the risk of ovarian and endometrial cancer and decreased risk of ectopic pregnancy, less benign breast disease, more regular menses with less flow, anemia, and dysmenorrhea, possibly fewer fibroids, possibly fewer ovarian cysts
2. Intrauterine contraception involves the insertion of a small device into uterus with the hopes of inhibiting implantation, altering tubal motility, or inflaming the endometrium. Copper IUDs work primarily as a spermicide, inhibiting sperm motility and the acrosomal reaction necessary for fertilization. Progesterone IUDs work primarily by preventing the sperm and the egg from meeting, thickening cervical mucus and creating an unfavorable uterine environment. There is the added benefit of atrophy of the endometrium, altering the cervical mucus, and the partial inhibition of ovarian follicular development. Intrauterine contraceptive devices are associated with a relatively low failure rate (<1% pregnancy rate) but do suffer from a higher rate of extrauterine pregnancy compared to women not using contraception. Slight increased risk of infection for 20 days after IUD insertion.
 - A. Types:
 - Mirena (levonorgestrel) releases progesterone and must be replaced every 5 years
 - Paraguard contains copper and needs to be replaced every 10 years
 - B. Side effects: Increased vaginal bleeding and menstrual pain experienced by 5-10% of women and often result in their request to discontinue IUD use.
 - C. Complications: Expulsion of IUD, pregnancy, perforation of uterine wall when inserted, increased risk of tubo-ovarian abscess(esp. among younger nulliparous females with >1 sex partner). PID is not as common with the newer IUDs but still a significant risk factor. In low risk women there is no higher incidence of PID with IUD use.

3. Barrier methods involve the use of an artificial device to insert into the vagina or fitted to the penis with the intent to retain the products of intercourse. High risk of failure given that each of these methods depends on the proper use before or at the time of intercourse.
 - A. Types:
 - Condoms have a 2% failure rate in consistent couples and a 15-20% failure rate in occasional users. They are best indicated for STD prevention.
 - Vaginal diaphragms have a 15-20% failure rate, but when combined with a spermicidal jelly and left in for 6-8 hours post-coitus failure rate declines to 2%. Diaphragms are associated with side effects of bladder irritation and cystitis, also colonization with *S. aureus* if left in too long. Must be fitted to the individual patient.
 - Cervical caps must be properly fitted and should be left in place for up to 48 hours after intercourse to be effective
4. Spermicide has a 18-30% failure rate. Spermicides contain surfactants to disrupt cervical membranes. Should be placed in the vagina up to 30 minutes before intercourse.
5. Fertility awareness methods: Includes calendar method in which women calculate fertile periods and avoid intercourse at this time; basal body temperature method based on the biphasic rise in basal body temperature of 0.5F – 1F that is indicative of ovulation, cervical mucus methods where the woman notes changes in the mucus around ovulation and abstains from intercourse during the 4 day fertile period
6. Sterilization involves manipulation of parts of male and female anatomy such that conception is prevented by failure of gametes to combine.
 - Vasectomy: <1% failure and can be successfully reversed in some cases.
 - Tubal ligation: <1% failure rate. Increase risk of ectopic. Various forms including coagulation, spring clips, postpartum ligation, interval LSC ligation, Essure via hysteroscopy

Management:

Concerns about pelvic infections and subsequent fertility often limit the use of IUDs to women who are at low risk for sexually transmitted disease and to those less likely to desire further children, i.e., monogamous multigravid patients. Since this patient is a young female with no living children, *an IUD is probably not a good choice for her*. She should be counseled about other birth control options such as hormonal methods with condom usage for STD protection as well as possible consequences of risky sexual behavior.

7. **Dysmenorrhea: 28 year-old Martha, G2 P1 Ab 1, comes to your office complaining of severe pain with her menstrual periods for past 7 months. She had not had pain such as this previous.**

Definition: Painful menstruation, can be severe enough to prevent women from performing normal activities. May also be accompanied by diarrhea, nausea, vomiting, headache, and dizziness.

Pathophysiology: Dysmenorrhea can be primary or secondary

1. Primary usually appears within 6-12 months of menarche (duration is usually 48-72 hours) and is thought to be physiologic in origin. Females with dysmenorrhea have increased PGF₂ α and PGE₂ which increases under influence of progesterone. Dysmenorrhea is thought to be caused by increased prostaglandin release during ovulatory cycles. The prostaglandin is released as a consequence of endometrial lysis/shedding. Additionally, necrosis of endometrial cells provides increased substrate arachidonic acid from cell walls for prostaglandin synthesis. Females with this condition have increased uterine activity manifested by increase resting tone, increase contractility, and increased frequency of contractions.
2. Secondary is painful menstruation that is caused by structural abnormalities or disease processes that occur outside the uterus, within the uterine wall, or within the uterine cavity. Typically that starts well after menarche. The pain is not limited to menses. The underlying pathologic mechanism is not well understood, but may involve PGs. Common causes include endometriosis, tumors, adhesions, leiomyoma, polyps, infection. Usually associated with secondary dysmenorrhea are dyspareunia, infertility, and abnormal bleeding.

Differential Diagnosis:**Extrauterine Causes**

Endometriosis- pain extends premenstrual or postmenstrual and may be continuous; ovary #1 location then cul-de-sac, then posterior broad ligament, uterosacral ligament, fallopian tube, sigmoid colon and appendix, round ligament

Tumors

Adhesions

Inflammation

Psychogenic

Non-gyn causes – inflammatory bowel disease, irritable bowel syndrome, TB

PID-initially pain is menstrual, but with each cycle extends to premenstrual; pelvic tenderness, and dyspareunia

Pelvic congestion syndrome

Ectopic pregnancy

Ovarian Cyst

Intramural Causes

Adenomyosis- typically bulky, bulbous uterus; dx of exclusion

Fibroids-uterus is generally enlarged, can see leiomyoma on US

Intrauterine Causes

Polyps

IUD questionable association with PID

Cervical stenosis

Endometrial CA

Congenital Obstructive Mullerian malformations

History:

Describe the pain: It is usually cramp-like, strongest over the lower abdomen and radiating to the lower back and inner thigh. The timing is an onset usually within 2 years of menarche for primary amenorrhea (when the hypothalamic-pituitary axis has developed and ovulation is occurring) and later in life for secondary amenorrhea. The duration of the pain lasts for a few hours before or just after the onset of menstruation and lasts 8-72 hours. The pain can occur with sexual intercourse.

Severity of Symptoms: impact of daily activities, school, etc.

Associated symptoms: Nausea, vomiting, headache, bloating, fatigue, diarrhea, and dysuria

Menstrual history: Age at menarche, the regularity of the cycles, the amount and duration of flow

Meds tried

Sexual history with contraceptive history

Family history

In the above history the woman describes secondary amenorrhea based on her age, and the recent onset of this pain only seven months ago. A sexual history, family history, and contraceptive history would be important as well as PE to ascertain which of the underlying disease processes may be present.

Physical Exam:

After a complete physical exam, the most important focus is the pelvic exam. Be sure to check for uterine tenderness, adnexal tenderness/fullness, fixation of the uterus, tender uterosacral nodularity (sign of endometriosis) cervical stenosis, and perform a bimanual and rectal exam noting any masses. Note the PE in primary amenorrhea is usually normal. In secondary amenorrhea, the underlying disease process can manifest on PE.

Work-Up:

Pregnancy test (all women of child bearing years)

Pap smear

Urine and cervical cultures to r/o infection
 Consider endometrial biopsy
 US
 Laparoscopy

Management:Primary dysmenorrhea:

Reassurance and explanation

NSAIDs: Prostaglandin synthetase inhibitors. Typical first line therapy. Should be started at onset of menses (or 1-2 days before start of menses if severe) and continued for the first 1-2 days of menstrual cycle or for usual duration of cramps.

OCPs: Usually second line therapy. Combination OCPs can suppress ovulation thus decreasing the amount of endometrium which will decrease the amount of uterine prostaglandin levels and reduction of menstrual flow

Surgical Measures (last line of management)

D&C/HSC/LSC

Hysterectomy

Presacral neurectomy – rare, causes disruption of the presacral nerves, the superior hypogastric plexus, which is found in the retroperitoneal tissue from the 4th lumbar vertebra

Psychotherapy

Hypnotherapy

Transcutaneous nerve stimulation

Secondary Dysmenorrhea:

Treat the underlying disease process:

1. Endometriosis: Expectant management, medication management: OCPs, progesterone therapy in the form of depot medroxyprogesterone acetate or implants (suppresses GnRH release and in turn, ovarian steroidogenesis), Danazol suppresses LH and FSH surges, preventing ovarian. Laser or electrocauterization of the endometrial implants via laparoscopy is palliative. Extirpative surgery reserved as a final effort including TAH/BSO/LOA/removal of endometriotic implants.
2. Adenomyosis: ultimate treatment is total abdominal or vaginal hysterectomy with preservation of the ovaries if the patient is <45 years of age. Any menorrhagia should be investigated by endometrial biopsy or D&C to r/o endometrial CA. Otherwise treatment is palliative and if the dysmenorrhea is disabling, a GnRH agonist may provide relief.
3. Leiomyoma: prudent observation, myomectomy, or GnRH agonists. If no fertility is desired, hysterectomy.
4. Ovarian Cysts: If patient is of reproductive years and adnexal cyst is <6cm in diameter wait and examine patient again after next menses. OCPs may be beneficial to suppress gonadotropin levels and help prevent the formation of additional cyst. If the cyst is 6-8 cm or it is fixed or feels solid, pelvic US to ensure it is unilocular. If mass is >8 cm painful, multilocular, or partially solid, surgical exploration is needed given concern for malignancy.

8. Dyspareunia: 26 yo Judy, G2P1Ab1, presents to your office complaining of painful intercourse
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Definition: Pain during sexual intercourse, may be deep pain or pain at the introitus with penetration

Primary dyspareunia: pain present at first intercourse

Secondary dyspareunia: pain developed after previously pain free intercourse

Complete dyspareunia: pain with each sexual experience

Situational dyspareunia: pain with some experiences or partners but not others

Differential Diagnosis:

1. Vulvovaginitis
2. Endometriosis
3. Vaginismus
4. Incompletely stretched hymen

5. Insufficient vaginal lubrication
6. Vaginal atrophy
7. Infections
8. Neoplastic conditions
9. Idiopathic
10. Adenexal mass
11. Adhesions
12. Uterine Retroversion
13. Seminal Plasma Hypersensitivity
14. Cystitis/Interstitial Cystitis

History:

1. Onset, duration and nature of pain.
 - a. chronic problems may point to vaginismus or hymenal problems
 - b. pain with deep penetration may be due to endometriosis or adenexal mass
2. Vaginal discharge, itching, burning, spotting may suggest vaginitis, cervicitis, neoplasm
3. Previous similar episode that resolved with or without treatment (ex. Recurrenrt HSV/UTI)
4. History of dysmenorrhea as with endometriosis
5. Any additional discomfort associated with the pain as with pelvic congestion or adenexal mass
6. Prior History of PID or pelvic surgery - possibly causing adhesions, scarring leading to narrowing of vagina/introitus
7. History of sexual assault or abuse – possible psychological cause of vaginismus
8. Past medical history or psychological history: skin disorder, IBS, etc. can be related to vaginismus
9. Contraception method: local contracption (condoms, gels, diaphragms) may be irritating and switching to another method may eliminate pain

Physical: A careful pelvic exam should follow inspection of the external genitalia.

1. Should begin with inspection: confirm normal architecture, note absence or presence of lesions, inspect vulvar skin
2. Perform speculum exam: note condition/architecture of vagina, vaginal or cervical lesions along with performing necessary cultures, wet prep, etc.
3. Palpation: palpate abdomen, vulvar and perineum, uterus, posterior cul-de-sac, uterosacral ligaments, ovaries and note areas of tenderness

Lab Workup:

Cervical Cx or Bx
 Endometrial Bx
 Wet prep
 KOH prep
 Cx or Bx of superficial skin lesions (ex. HSV)
 Vulvar/vaginal Bx of lesions
 Urine C&S
 Gonorrhoea/Chlamydia cultures

DDX and Management:

1. Vulvovaginitis – typically present w/ pruritis and discharge
 - A) Trichomonas (trichomonads)
 - B) Candidiasis (hyphae)
 - C) Bacterial Vaginosis (clue cells)
 Treat with appropriate abx or antifungal
2. Endometriosis
 Etiology- Endometrial glands and stroma outside the endometrial cavity
 Common sites:

Ovary (60% of cases will have ovarian involvement)
 Broad ligament
 Cul-de-sac or peritoneal surfaces
 Uterosacral ligaments
 Posterior cervix
 Rectovaginal septum
 Appendix
 Rectosigmoid colon
 Vesicouterine fold
 Laparotomy or c-section scar (rare)

Epidemiology: Occurs in 15% of women. Begins in the 20's, becomes apparent in the 30's and regresses after menopause. If seen in children or adolescents, look for obstructive genital anomalies.

Theories of Pathogenesis:

Halban theory- vascular and lymphatic spread; 20% of pts will have lymphatic involvement

Meyer theory- Mullerian metaplasia theory: Peritoneal mesothelium undergoes metaplasia to transform into endometrial tissue under influence of unknown stimuli.

Sampson Theory- Retrograde menstrual flow with endometrial fragments implanting on the ovaries or peritoneal surfaces where they adhere and grow. [Recall that Sampson's artery runs through the round ligament]

Symptoms: The classic triad -**Dysmenorrhea**, **Dyapareunia**, **Dyschezia**

On pelvic exam the posterior fornix, uterosacral ligaments and cul-de-sac are very tender.

Classic physical findings are - Tender nodule of the cul-de-sac or tender adnexal mass

Pre and post menstrual spotting is characteristic.

Menorrhagia is not seen - menstrual bleeding will usually diminish with endometriosis.

Infertility ~30-40% of couples will be infertile if the female has endometriosis.

Dx - Laparoscopy definitive

Treatment:

Large lesions - (6 -20 cm) Surgical resection.

Excision, fulguration, laser of endometriotic implants and removal of adhesions usually via laparoscopy – conservative treatment

TAH/BSO—definitive treatment

Small lesions:

If asymptomatic observe every 6 mos.

If symptomatic:

1) Depo provera, OCPs

2) Danazol for 6-9 mos, suppresses LH and FSH release, can cause pseudomenopause with androgenic SE

3) GnRH agonist (Depot Lupron) for 6 months: Shuts down cycle w/o androgenic SE

3. Vaginismus - Voluntary or involuntary contraction of muscles around introitus w/ penetration. Typically results from pain, fear, sexual trauma, negative social attitudes toward sex as a child. Dx by careful sexual history and interview
 Treatment - sexual counseling and education, desensitization techniques: use of self-dilation with dilators of increasing diameter, patient must be in control of progressive steps.

4. Incompletely stretched hymen

Rare instances may require manual dilation, general anesthesia

Pt will complain of painful intercourse from initial event to present

5. Insufficient Vaginal Lubrication: most common cause of dyspareunia in menopausal women
 Possibly due to:

Inadequate time for sexual arousal

Low estrogen effect during lactation

Post-menopausal change

Physical examination of introitus and vagina will demonstrate estrogen effect. If estrogen is present the vaginal mucosa appears moist, healthy with rugal folds; If estrogen is low or

absent the vaginal mucosa is dry, there are few rugal folds, and a thinned reddened epithelium is present.

Treatment: Allow sufficient time for sexual arousal if estrogen is present, otherwise estrogen cream may be helpful.

Nonhormonal therapy: can use moisturizers, lubricants

6. Vaginal Atrophy (due to estrogen)
See above
7. Infectious process other than Vulvovaginitis
Acute or chronic cervicitis
Acute or chronic endometriosis
Adnexal abscess, tubal abscess (salpingitis)
Chronic PID resulting in pelvic adhesions or uterine incarceration within the pelvis
HPV - Initial burning followed by 24-48 hours of a burning sensation. Look for lesions
Tx: Treat of infectious process and temporary abstinence from coitus will usually resolve pain.
Surgical extirpation may be necessary if due to adhesions.
8. Neoplastic conditions
Ovarian cancer will often give a sense of fullness with dyspareunia
Vaginal and vulvar cancers can be painful
Fibroids can cause dyspareunia if resulted in the incarceration of the uterus within the pelvis.
9. Idiopathic - No other observable causes (Psychosexual conflicts? History of Child abuse?)
Dx: Colposcopy of painful region with bx taken of any suspicious lesion (R/O HPV) Dx by exclusion is often the case
Tx: Supportive discussions and counseling - resolution of conflicts

9. Ectopic Pregnancy: 17 year-old Raquel, G2 P0 Ab2, is seen in the ER for unilateral pelvic and left lower abdominal pain. She admits to recent vaginal bleeding. She is afebrile. Qualitative serum beta-HCG is positive.

Definition: any pregnancy that implants anywhere other than the endometrial lining of the uterus; this condition significantly jeopardizes the mother and is incompatible with continuing the pregnancy. It is the second leading cause of maternal mortality in the US. #1 cause of 1st trimester maternal mortality. Account for 1.5% of reported pregnancies in the US.

Pathophysiology:

- (i) caused by either altered tubal transport w/in damaged endosalpinx or an abnormal fertilized ovum.
- (ii) 98% implant inside the tubes (**80% in the ampulla**, 12% in the isthmus, 6% in fimbria, 2% in cornua, <1% in ovary, 1-2% abdomen).
- (iii) catastrophic bleeding may occur when the implanting pregnancy erodes into blood vessels or ruptures through structures. Pregnancy expelled from tube can implant in the abdominal cavity.
- (iv) Without intervention, natural course of tubal pregnancy will result in (1) tubal abortion-expulsion of products of conception through the fimbriated end-tissue can regress or reimplant in abdominal cavity (2) tubal rupture- a/w significant intra-abdominal hemorrhage often necessitating surgical intervention, or (3) spontaneous resolution

Differential Dx:

GYN associated--

- (i) threatened/incomplete/missed abortion
- (ii) ruptured ovarian cyst
- (iii) acute PID
- (iv) adnexal torsion
- (v) degenerating leiomyoma
- (vi) normal intrauterine pregnancy
- (vii) hemorrhagic corpus luteal cyst
- (viii) placental polyp

Other causes--appendicitis, pyelonephritis, pancreatitis, gastroenteritis, nephrolithiasis

History/Risk factors: The classic triad for presentation is amenorrhea followed by vaginal bleeding and abd pain. Other presenting sx include syncope, dizziness, nausea, shoulder pain worse w/ inspiration, and pregnancy symptoms.

Risk factors:

- (i) salpingitis/PID (6-fold increase) → more common w/ chlamydial infection than gonorrhea
- (ii) previous ectopic pregnancy (10-fold increase)
- (iii) age greater than 35 (3-fold increase)
- (iv) greater than 50% occur in women who have had 3 or more pregnancies
- (v) Black and Hispanic women have a higher incidence
- (vi) h/o tubal sterilization, tubal reconstruction, DES exposure, smoking

-If pt is s/p sterilization procedure, the pregnancy is more likely to be an ectopic.

-IUD use and elective pregnancy termination are NOT predisposing risk factors for ectopic preg.

Work up/Therapy:

Abdominal and pelvic findings are usually minimal in pts before tubal rupture. Prior to rupture, dx of ectopic primarily based on lab and US finding.

If there is a high clinical suspicion of ectopic pregnancy with rupture and pt is hemodynamically unstable, they should be taken to surgery for an **immediate laparotomy vs. laparoscopy** → 75% of pts with rupture will have marked abd tenderness and cervical motion tenderness. 20% with have palpable mass/fullness posterolateral to uterus

Stable patient: **urine and serum qualitative and quantitative HCG** levels drawn, with negative results ruling out the dx.

If the quants come back **<1500-2000** (below the level known as the “discriminatory zone”), they should be repeated in 48 hours to ensure appropriate trend. In a normal IUP, hCG levels should increase by at least 53% in 48 hours. Once quant is >1500-2000, TVUS should be repeated. If there is not an approximate rise in 48 hours, an ectopic pregnancy or an abnormal IUP should be suspected. Of note, 15% of normal pregnancies will have an abnormal doubling time, and 17% of ectopic pregnancies have normal hCG doubling times.

Quants **above 1500-2000** call for a transvaginal u/s to visualize an IUP. (TVUS should be able to identify an IUP by the time hCG level reaches 1000-2000.

*In patients with quants between 1500-2000, no visualization of IU sac by u/s carries a 90% likelihood of an ectopic pregnancy.

*Rhogam should be administered to Rh negative patients

Once you have diagnosed an ectopic, there are two management options:

1. Medical management (Methotrexate)
 - a. Absolute contraindication: unstable patient, ruptured ectopic
 - b. Relative contraindications (decrease chance of success)
 - i. B-hcg >5,000
 - ii. Ectopic size >3.5 cm
 - iii. Presence of fetal cardiac activity
 - iv. Unreliable patient (unlikely to follow up appropriately)
2. Surgical management
 - a. Most can be managed laparoscopically.
 - b. Can do salpingostomy (incision along the tube to remove ectopic) vs salpingectomy (remove tube)

10. Enlarged uterus: 31 year old Judy, G3 P3, comes to your office for a routine annual exam. On pelvic examination you find her uterus is enlarged.

Differential Diagnosis:

Most likely causes--

1. pregnancy --don't miss this one, it will make you look bad
 2. fibroids (uterine leiomyomas)--benign smooth muscle tumor of uterus
 - seen in 20% of women by 40y.o.a.
 - most common indication for major surgery/hysterectomy in women
 - blacks > whites
 - hormonally responsive- estrogen may induce rapid growth in high-E states like pregnancy, OCP use and HRT use. Often shrink after menopause.
 - in pregnancy, inc risk of PTL, fetal growth abnl, malpresentation, pelvic pain, C/S & PPH
 - most are asymptomatic, but pts. may experience pain, menorrhagia, urgency, constipation, anemia, and CHF (blood loss)
 - usually in midline
 3. uterine leiomyosarcoma- rare but aggressive sarcoma. Common misconception that these cancers arise from fibroids; however, they are actually most likely an entirely separate process.
 4. endometrial hyperplasia- MC precursor to endometrial adenocarcinoma
 - usually secondary to increased estrogen or obesity
 - can be cystic glandular or adenomatous
 - often accompanied by abnormal uterine bleeding (AUB), heavy enough to include clots
 5. endometrial CA--the most common GYN malignancy. 1* process in development of endo hyperplasia/CA is overgrowth of endometrium in response to excess unopposed estrogen
 - typically disease of post-menopausal women. **15-25% of postmenopausal women with bleeding have endometrial cancer.**
 - Most common presenting symptom = AUB, esp. postmenopausal bleeding
 - Most are adenocarcinomas
 - risk factors: obesity, nulliparity, late menopause, early menarche, h/o infertility, HTN, DM, breast/colon/ovarian CA, chronic unopposed estrogen
 6. adenomyosis- the presence of ectopic endometrial tissue within the myometrium
 7. hematocolpos/hematometria- obstruction of menstrual outflow due to imperforate hymen, cervical/vaginal stenosis
- Other things that could be mistaken for uterine enlargement--
8. tuboovarian abscess
 9. ovarian neoplasm
 10. colorectal CA or other colorectal pathology

History:

Menstrual history, contraceptive history, focusing on dysmenorrhea, menorrhagia, metrorrhagia.
 Does patient pass clots?
 Abdominal or pelvic pain?
 Feeling of fullness or heaviness in abdomen/pelvis?
 Dyspareunia?
 Urinary troubles/defecation troubles?
 Weight change?
 Decrease in energy level?
 Family history?
 Meds?

Workup:

1. H & P
2. CBC, UA, hemocult, urine hCG
3. Pelvic ultrasound
4. Endometrial biopsy may be indicated if patient is having abnormal bleeding or has thickened endometrial stripe.

Management:

1. Observation for fibroids unless: AUB leads to anemia, severe pelvic pain, unable to evaluate adnexa, urinary tract/GI tract symptoms, increased size in uterus after menopause, rapid increase in size of uterus, infertility. (Twenty week size, if symptomatic, would not be observed)

2. **Medical:** Fibroids and endometriosis can be treated with OCP's/progestins, Danazol, or GnRH agonists. Endometrial hyperplasia can be treated with cyclic progestins for 3-6 months and then repeat endometrial bx.
3. **Surgical:** TAH or TVH. Myomectomy can be performed for fibroids and adenomyosis if fertility is desired.

19. Menorrhagia: 32yoF, G4 P4, presents at your office complaining of menstrual periods that last 14 days. Her cycles are irregular.

- 1) **Definition:** Menorrhagia, now referred to as heavy menstrual bleeding (HMB), is defined as regular menstrual blood loss greater than 80 mL or lasting longer than seven days.
 - a) Intermenstrual bleeding (IMB) is defined as irregular menstrual blood loss.
 - b) The average menstrual cycle lasts up to seven days and the amount of menstrual blood loss is 35-40 mL per cycle, but the range is wide.
 - c) The term HMB is applied variably to ovulatory or anovulatory uterine bleeding.

- 2) **Pathophysiology:** There are two types of HMB:
 - a) *Anovulation* is common among reproductive age women and this condition is often accompanied by heavy or prolonged uterine bleeding. In reproductive age women with regular periods (suggesting ovulatory cycles)-see below, heavy or prolonged uterine bleeding is usually due to distortion of the endometrial architecture.
 - i) For adolescents, anovulation and bleeding diatheses are likely more common causes of heavy bleeding than structural abnormalities. This diagnosis can be made only by excluding any pathology both by examination, US and by diagnostic curettage. Most anovulation will self resolve in 1-2 years after menarche once the hypothalamic-pituitary-ovarian (HPO) axis matures in this age group.
 - ii) Most commonly occurs in cases of chronic anovulation, as with polycystic ovary syndrome and around the time of menopause. The persistence of an unruptured follicular cyst in one ovary results in excessive estrogen production causing the endometrium to become greatly thickened and when it can no longer be sustained by the continuing high levels of estrogen, it eventually breaks down in a patchy fashion. Sometimes long periods of anovulation can predispose to cystic or adenomatous hyperplasia.
 - iii) In anovulatory patients sex steroids are produced but not cyclically therefore hormonal sloughing of the endometrium does not occur.
 - b) *Ovulation:* The pattern of the menstrual cycle and menstrual loss may be altered by defects of the corpus luteum or shortening of the follicular phase of development. Factors which affect the HPO axis will alter the periodicity of the menstrual cycle.
 - i) The follicular phase is shortened, but the luteal phase remains the same. Abnormalities of menstrual loss may occur on a regular cyclical basis. The number of days of bleeding may remain constant and the loss become heavy or the number of days of bleeding may become prolonged. This can be caused by defective corpus luteum formation or defective degeneration of the corpus luteum.

- 3) **Other etiologies:**
 - a) *Uterine leiomyomas* are the most common pelvic tumor in women and are a common cause of excessive bleeding. Other common causes include endometrial polyps, adenomyosis, or presence of a non-progestin intrauterine device.
 - b) *Adenomyosis* is associated with invasion of the myometrium by endometrial glands and may cause HMB and dysmenorrhea, but is not associated with any histological abnormality of the endometrium. Adenomyosis can only be diagnosed by pathology following a hysterectomy.
 - c) *Thyroid disorders* are another common etiology of uterine bleeding abnormalities.

- 4) **Management:** Risks associated with HMB or IMB include anemia, incapacitating blood loss, endometrial hyperplasia, and cancer.

- a) The primary goal of anovulatory uterine bleeding is to ensure regular shedding of the endometrium and consequent regulation of uterine bleeding. A progestational agent (progesterone) can be given for 10 days to mimic physiologic withdrawal of progesterone.
- b) OCPs can also be used as they suppress the endometrium and establish regular, predictable withdrawal cycles.
- c) If need to treat an acute heavy bleeding episode, focus treatment on: 1) control of the acute episode, and 2) prevention of future recurrences.
- d) Both high-dose estrogen (IV form if severe acute bleeding) and progestin therapy as well as combination treatment (high-dose OCP taper) can be used for management
- e) If heavy bleeding does not respond to medical therapy, consider surgery with D&C, endometrial ablation or hysterectomy, depending on etiology of the bleeding.

23. Pelvic Relaxation: 55 yo Amanda G5 P4014 c/o pelvic pressure symptoms. On exam you note her cervix is protruding from her vagina.

Pathophysiology:

Amount--

1st degree: descent limited to upper 2/3 of vagina: organ is prolapsed halfway to hymen

2nd degree: structure reaches introitus/hymen

3rd degree: prolapse through introitus: prolapse of organ halfway out of hymen

4th degree: total prolapse of organ (procedentia)

Kinds of prolapse/Differential Diagnosis:

Cystocele: herniation of bladder with associated descent of anterior vaginal segment

Cystourethrocele: cystocele combined with distal prolapse of the urethra with or without

Associated urethral hypermobility

Uterine prolapse: descent of uterus and cervix

Vaginal vault prolapse: descent of the vaginal apex following hysterectomy

Rectocele: herniation of the rectum with associated decent of the posterior vaginal segment

Enterocoele: herniation of the small bowel/peritoneum into the vaginal lumen

Risk Factors:

Multiparity

Operative Vaginal Delivery

Obesity

Advanced age

Estrogen Deficiency

Neurogenic Dysfunction of pelvic floor (ex. Diabetic Neuropathy)

Connective Tissue Disorder

Prior Pelvic Surgery with disruption of natural support

Chronically increased intraabdominal pressure (ex. Chronic cough)

Congenital Damage/Intrinsic Weakness

History:

Does pt. experience heaviness or pressure?

Is it worse late in day, after lifting, while standing?

Back pain?

Dyspareunia?

Urinary incontinence?

Dyschezia?

Difficulty emptying bladder?

Protrusion of tissue thru vagina?

Vaginal Bleeding?

Physical Exam:

Observe as patient strains (Valsalva), use a Sims speculum (1 blade). It may be necessary to examine the patient while she stands and strains.

Treatment:

1. Mechanical support (pessary)—if pt. is unfit for surgery or pregnant
2. Exercises to strengthen musculature "Kegel" exercises with possible physical therapy and behavioral modifications
3. Surgical repair
4. Estrogen replacement if post-menopausal
5. Also recommend weight reduction, treat chronic cough/infection, etc

25. Postmenopausal Bleeding: 58 year-old Minnie, G5 P3 Ab2, underwent menopause 7 years ago. She comes to your office complaining of vaginal bleeding for one week.

Definition: Bleeding 12 months after cessation of menses (often associated with genital malignancies).

Differential Diagnosis:

Exogenous estrogen
 Atrophic endometritis/vaginitis
 Endometrial cancer
 Endometrial or cervical polyps
 Endometrial hyperplasia
 Misc.(cervical ca, uterine sarcoma, urethral caruncle, trauma, fallopian tube ca)
 Infection
 Disease in adjacent organs: urethra (ex. Urethritis), bladder (ex. Cancer, UTI), bowel (ex. Inflammatory bowel disease, hemorrhoids)
 Anticoagulation therapy
 Post radiation therapy

History: Important questions to ask--

When did bleeding start?
 Any precipitating factors such as trauma?
 Nature of bleeding (temporal pattern, duration, postcoital, quantity)?
 Associated symptoms such as pain, fever, change in bowel or bladder function
 Associated discharge
 Past medical history (especially hepatic, renal, thyroid, or splenomegaly)
 Medications
 Personal or family history of a bleeding disorder

Physical Exam:

Abdominal exam - check for masses
 Pelvic exam - look for any visible lesions esp. exophytic, friable, or bleeding ones, uterine size may be normal. Determine bleeding site.

Workup: In this pt population mandatory to get histologic specimen because risk of endometrial cancer ~10-15%, but other causes are more common than cancer

- i) Transvaginal ultrasound - evaluate uterus, especially endometrial stripe. Generally a thickness of 4mm or less is reassuring.
- ii) Endometrial biopsy - often times first step due to logistics of getting an ultrasound
- iii) Dilation and curettage - with or without hysteroscopy. Can be used when unable to get an in-office endometrial biopsy due to cervical stenosis or patient discomfort. Also should be used if endometrial biopsy pathology is incongruent with clinical picture (i.e. highly suspicious for cancer, but non-malignant biopsy).

Management:

1. If malignancy is found, refer to Gyn/Onc
2. if 2nd to exog. estrogens - add progesterone or remove source
3. if 2nd to atrophy - consider hormone replacement and creams to help with symptoms, etc
4. if find polyps - removal and histologic evaluation of polyps
5. if endometrial hyperplasia - consider D&C if sample from endometrial biopsy as biopsy samples small percentage of endometrium, and can miss more advanced disease. Strongly consider hysterectomy for any post-menopausal patient with hyperplasia.

26. Postmenopausal Pelvic Mass: 60 year-old Lucinda, G3 P3, is in for an annual exam. She is 9 years postmenopausal (PM). You find a 5 cm solid mobile right adnexal mass.

Background:

1. First, note that ovaries should NOT be palpable in a postmenopausal (PM) woman (it should only be 2-3 cm), therefore any enlargement is abnormal. Any adnexal mass should be considered neoplastic until proven otherwise.
2. Malignant ovarian neoplasms may be entirely asymptomatic during the early and curable stages of the disease. 25% of genital cancers are ovarian, but they result in 50% of the deaths.
3. Every female has a 1/70 risk of developing ovarian malignancy during life.
4. Germ-cell tumors are typically more common in children and young women, whereas epithelial tumors are more common in older women. Mean age for ovarian cancer is 55-61. Whites are 50% more likely to develop ovarian cancer than blacks in the US.
5. Women with breast cancer have twice the risk of ovarian cancer. 25% of all ovarian tumors in PM women are malignant (only 10% in reproductive age women are malignant). These malignant tumors are typically (90%) of epithelial cell type. Other tumor types include germ cell tumors and stromal cell tumors.

Differential Diagnosis:

As Lucinda is PMP, physiologic cyst can be ruled out. The mass may be ovarian neoplasm, ovarian benign neoplasm, appendiceal abscess, diverticulitis abscess, pelvic adhesions, pelvic kidney, hydrosalpinx, ovarian torsion, fibroids, metastatic lesion from endometrium, breast, GI tract, TOA, fallopian tube cancer

Work-Up:

1. Very straightforward. Careful history taking, being sure to assess family history of breast/ovarian cancer, as both have familial components.
2. Early satiety may signal omental mets. Bloating and increased girth signal ascites.
3. Look for signs of virilization or hirsutism. Be sure of the date of menopausal onset; if the patient is within 3 years of natural menopause, the mass could be a residual functional cyst that has not regressed. This could drastically change patient management. However, in either case, ultrasound is warranted.
4. CA-125 should be measured, as it is elevated in 80% of epithelial cancers. CEA is often elevated in mucinous adenocarcinomas, and may be checked also. Also, careful physical exam or ultrasound may detect a mass in the other ovary, which drastically increases the odds of malignancy.

MANAGEMENT:

If the patient is within 3 years of menopause, and transvaginal ultrasound confirms a simple, unilocular cyst < 5 cm diameter, you may manage with serial pelvic and ultrasound exams. Other postmenopausal masses should be managed surgically. The presence of ascites on ultrasound is predictive of cancer. In fact, ascites and a pelvic mass should be considered ovarian carcinoma until

proven otherwise. Of course, specific patients may not warrant surgical treatment, such as extremely elderly patients, patients with a known lethal co-morbid condition, etc. Otherwise, our patient here should be taken to the OR.

Possible Findings And Treatment:

1. Benign epithelial neoplasms: Most common is serous cystadenoma (70% of serous tumors are benign). More common in PM women. 20% are malignant. Mucinous cystadenoma is the 2nd most common epithelial tumor, with a malignancy rate of 5%. 3rd most common are endometrioid tumors. Lastly, an uncommon epithelial tumor is a Brenner cell tumor; it is more common in the elderly.
2. Benign Germ Cell Neoplasms: Most common is the benign teratoma (dermoid cyst). Recall that a struma ovarii is a dermoid with functioning thyroid tissue. Though malignancy is <1%, treatment is surgical to prevent ovarian torsion. 10-20% of these cysts are bilateral.
3. Benign stromal cell neoplasms: May develop into primarily female cell type (granulosa theca cell tumors-produce estrogen) or primarily male cell type (Sertoli-Leydig cell tumors-produce androgens). These tumors often cause vaginal bleeding in the PM years. An ovarian fibroma occurs in 10% of patients with ovarian neoplasms, but does NOT produce sex steroids.

In general, benign ovarian neoplasms are--

- (1) more common than malignant in ALL age groups
- (2) chance for malignant transformation increases with age (10% Premenopausal, 25% after)
- (3) warrant surgical evaluation due to risk of malignancy
- (4) surgical treatment may be more conservative, particular if fertility is desired (obviously, not a consideration in this case). Also, in the case of benign neoplasms, it is advisable to remove BOTH ovaries to remove the possibility of future malignant transformation in the other ovary.
4. Malignant ovarian neoplasms: Typically spread by direct extension within the peritoneal cavity. May be classified as epithelial (most common), germ cell, and stromal.
 - (i) Epithelial types: 90% of all ovarian malignancies are epithelial in nature. Most common are serous tumors. There is also mucinous variety, which are among the largest of ovarian tumors. They are associated with thick mucinous ascites, termed pseudomyxoma peritonei. Next most common are the endometrioid epithelial cell tumors.
 - (ii) Germ cell tumors: Less than 5% of all ovarian malignancies. Most common are the dysgerminomas and immature teratomas. Also, there are mixed germ cell, endodermal sinus (aka yolk sac), and embryonal.
 - (iii) Stromal cell tumors: Make hormones. Most common is the granulosa cell tumor. May secrete a large amount of estrogen, which may cause endometrial hyperplasia or carcinoma. Sertoli-Leydig cell tumors usually occur in older patients, and should be suspected when patient presents with adnexal mass and hirsutism/virilization.

Management:

In short, this mass could be anything. However, workup would always begin with careful exam and ultrasound. This is almost always followed by surgical exploration, with staging if necessary. I'm not exactly sure what they expect for this clinical question, but I suspect they want to know

- (1) get an ultrasound
- (2) know that surgery is necessary
- (3) it's more likely to be benign
- (4) any palpable ovary in a PM woman is abnormal, with the possible exception of a PM woman < 3 years onset
- (5) you may want to obtain CA-125/CEA levels pre-surgical
- (6) ascites on ultrasound = bad thing
- (7) for this lady, surgical treatment would be TAH, BSO and possible debulking depending on pre-op and intra-op findings
- (8) malignant adnexal masses are often bilateral, hemorrhagic, necrotic, adherent, and solid with ascites, peritoneal studding. Based on just what is presented, and going with the "numbers", this mass is most likely a benign cystadenoma. Treatment is surgical removal, no further therapy.

30. Premenopausal pelvic mass: 25 year-old Betty, G1 P0 Ab1, presents at your office complaining of pelvic pressure symptoms. On pelvic examination you find she has a 5 cm cystic right adnexal mass.

Differential diagnosis: The most serious concern when an adnexal mass is discovered is possibility of malignancy. Characteristics that increase likelihood of malignancy include: prepubescent or postmenopausal female, complex/solid appearing mass, known genetic predisposition, known nongynecologic cancer (breast or gastric), ascites.

1. **Functional Ovarian Cyst:** not neoplasms but rather anatomic variations that arise as a result of normal ovarian function. Symptomatic or asymptomatic. They can be further divided into follicular cysts and corpus luteum cysts. Surgical excision indicated for cysts that are complex, symptomatic, increasing in size, or persisting for more than 4-6 months.
 - (i) *Follicular* cysts occur if a follicle fails to rupture. This lengthens the follicular phase and results in secondary amenorrhea. The cysts are lined by granulosa cells and contain fluid rich in estrogen. They are significant if they cause pain secondary to distention of the ovarian capsule or if they last longer than one menstrual interval. Ultrasound will show a smooth, thin walled unilocular simple cyst w/o evidence of blood or other soft tissues. They usually resolve spontaneously within 6-8 weeks. OCPs can be given to suppress gonadotropins, although this is better at preventing new cysts than fixing old ones. If it persists, suspect another type of cyst or a neoplasm. Rupture of the cyst can cause acute pelvic pain that can be managed conservatively. Laparoscopic cystectomy warranted if fluid-filled cyst that increases in size, is > 6cm, or causes persistent symptoms. Emergent surgery indicated for ovarian torsion (sx: sudden onset abdominal pain, nausea/vomiting, low-grade fever).
 - (ii) *Corpus luteum* cysts can either be just slightly enlarged corpus lutea, or rapidly enlarging luteal-phase cysts w/ spontaneous hemorrhage. The first type continues to produce progesterone longer than 14 days, resulting in delayed menstruation, giving pain and missed period as common complaints. Exam for the first will show enlarged, tender, cystic or solid, adnexal mass - in this case pregnancy test should be performed to rule out ectopic pregnancy. This first type may benefit from OCP's. The second, hemorrhagic type, may rupture in the luteal phase, resulting in acute pain. Depending on the extent of the bleeding, surgery may be warranted, whereas with mild bleeding analgesics are all that are required.
2. **Ovarian Neoplasm:** 25% of ovarian enlargements will turn out to be "nonfunctional ovarian neoplasms." In premenopausal women, 90% of these are benign - this decreases to 75% in postmenopausal women. Suspect neoplasm if complex appearing on ultrasound, increases in size, or persists despite OCPs and time. The most common tumor type is the benign cystic teratoma (dermoid), which can be diagnosed on u/s due to echogenicity of its internal contents (teeth, hair, etc). For more information, please see question specific to tumors of the ovary.
3. **Endometriosis:** This is responsible for the remaining 10% of adnexal masses. Key historical points to elicit are history of infertility, dysmenorrhea, deep thrust dyspareunia, abnormal bleeding, and pelvic pain. Remember, the only true diagnosis of endometriosis is histologic.
4. **Tubo-ovarian abscess:** Inflammatory mass involving fallopian tube, ovary, and occasionally adjacent pelvic organs. Typically result from infection of genital tract with gonorrhea, chlamydia, or trichomoniasis. Serious and life-threatening, requires antibiotics and occasionally surgery/drainage as rupture can result in peritonitis. Indications for antibiotic therapy only include hemodynamic stability, abscess < 9cm, adequate response to antibiotic treatment, and premenopausal. Surgery or minimally invasive drainage indicated for new/persistent fever or leukocytosis, worsening abdominal tenderness, enlarging mass, or signs of sepsis.

Another way to break down the differential is:

Extraovarian:

Ectopic pregnancy
Hydrosalpinx
TOA
Paraovarian cyst
Peritoneal Inclusion Cyst

Ovarian:

Simple or hemorrhagic physiologic cyst
(follicular, corpus luteum)
Endometrioma
Theca Lutein Cyst
Benign or malignant neoplasm

Pedunculated Fibroid
 Diverticular Abscess
 Appendiceal Abscess
 Fallopian Tube cancer

(epithelial, germ cell, sex-cord)
 Metastatic Cancer
 (breast, colon, endometrium)

31. Premenstrual Syndrome: 29 year-old Donna, G3 P3, presents to your office complaining of emotional lability, bloating and breast tenderness. The symptoms are so severe in the week prior to her menses she has difficulty functioning in the home and at work. She wonders if you can help her.

Background on PMS:

1. The syndrome consists of a constellation of symptoms including
 - (i) somatic sx (breast swelling/pain, bloating, headache, constipation or diarrhea, fatigue)
 - (ii) emotional sx (irritability, depression, anxiety, hostility, labile mood, easy crying)
 - (iii) behavioral sx (cravings, poor concentration, sensitivity to noise, decreased motor skills)
 - (iv) situational depression.
2. Criteria: Most women of reproductive age experience one or more mild emotional or physical symptom for 1-2 days before onset of menses. Clinically significant PMS includes at least one symptom associated with economic or social dysfunction that occurs during the five days before the onset of menses and is present in at least three consecutive menstrual cycles.
3. Incidence is between 10% and 90%, although severe PMS is in <10%.
4. Etiology is unknown. Psych, endocrine, diet, endorphins, serotonin, prostaglandin, fluid retention, and vitamins have been offered as explanations.

Differential Diagnosis:

1. Dysmenorrhea
2. Mood and Anxiety Disorders
3. Thyroid disorders
4. Substance Abuse
5. Menopausal transition
6. Migraine
7. Chronic Fatigue Syndrome
8. Irritable Bowel Syndrome (exacerbated just prior to/during menses)

Diagnosis:

Based on relating the patient's symptoms to the luteal phase with a menstrual diary. The key is a *documented symptom-free follicular phase*. Then, you have to rule out the above diagnoses with a good history/physical exam.

Have patient keep calendar for 2-3 months: should include complaints associated with PMS (somatic and emotional symptoms), daily weights, basal body temperatures to confirm pt is ovulating since ovulation is necessary to have the diagnosis of PMS.

Treatment:

Education of the patient is important. First line treatment includes SSRIs. Second line therapies include OCPs or GnRH agonists to suppress ovulation. Other therapies for symptomatic management include progesterone, NSAIDs, and diuretics. It's a mixed bag, and in serious cases requires time and an integrated, team approach.

Treatment can be broken up into:

1. Pharmacological: SSRI (mood and somatic complaints), oral contraceptives, GNRH analogues (somatic symptoms > emotional symptoms), mild diuretics (fluid retention), alprazolam (depression: need to consider addictive symptoms), calcium, vitamin E, vitamin B6
2. Non-pharmacological: behavior modification (eliminate caffeine, chocolate, alcohol, increase exercise), meditation, relaxation techniques, group therapy

33. Prepubertal Pelvic Mass: Prepubertal 8 yo Tamara is referred to you by her pediatrician with the findings of a 4 cm solid left adnexal mass.

Differential Diagnosis:

1. cystic teratoma (dermoid) #1 in all age groups
2. serous cystadenoma
3. follicular cyst - often in neonate #2
4. dysgerminoma (malignant)
5. GI neoplasm
6. Wilms tumor
7. neuroblastoma

History:

- ~Is there pain or cramping?
- ~Is there pelvic pressure?
- ~Is there any vaginal bleeding? vaginal discharge?
- ~Are there GI or urinary symptoms? eg. h/o UC, Crohn's dz
- ~Is there a history of pelvic kidney, ureterocele, carcinoma with poss. mets?
- ~Is there any increased abdominal girth?
- ~Is the pt having abdominal fullness/bloating?
- ~Is the pt having urinary frequency/retention?

Physical Exam:

- ~thorough pelvic exam for cervical motion tenderness, location of mass
- ~rectovaginal exam for cul-de-sac involvement
- ~assess for LAN (supraclavicular, axillary, inguinal)
- ~breast exam for presence of mass
- ~abdominal exam for masses, ascites
- ~lung exam for signs of effusion

Workup:

1. HCG, AFP, LDH are markers for germ cell tumor
2. CA-125 - 80% of epithelial ovarian cancer
3. CEA - colorectal cancer
4. LFTs - liver mets
5. CXR, CT scan (look for pleural effusion)
6. Pelvic US
7. IVP
8. Abd x-ray to look for calcifications assoc with benign cystic teratoma

Treatment Considerations:

- ~the only normal adnexal mass is a follicular cyst in a neonate secondary to maternal hormone stimulation of fetal ovaries
- ~most masses are benign, most should disappear
- ~aim to preserve fertility by cystectomy rather than oophorectomy - if ovary must be removed as in germ cell tumor, leave contralateral ovary and uterus (and use chemo rather than radiation, if indicated, as in lymph node spread)

38. Rape Victim: E.R. calls you to see 21 yo Ann, G0 P0, who states that was recently raped

Definition: Sexual assault is oral, manual, or genital contact against one's will. Rape is the coital form of sexual assault. Rape is the fastest growing violent crime in the US. It is estimated that 1 in 6 women will be raped in their lifetime, and many rapes are unreported because of victim's feelings of shame and guilt.

General:

The health care team has 3 tasks:

- (i) Care for the victim's emotional needs
- (ii) Evaluate and treat medically
- (iii) Collect forensic specimens

Consent for treatment is a legal requirement and an important aspect of the emotional care of the victim.

History: Necessary to gain medical and forensic information and an important therapeutic activity.

Hx should include the following:

1. Date and time of the assault; date and time of presentation
2. Physical surroundings and circumstances of the assault
3. Nature of the assault and associated pain experiences/any extragenital acts
4. Weapons and foreign objects used
5. Number of assailants
6. Actual acts that were committed
7. Whether or not ejaculation/orgasm occurred and whether or not a condom was used
8. Occurrence of vomiting or loss of consciousness
9. Whether or not the patient washed, wiped, bathed, douched, defecated, brushed teeth or changed clothes
10. Use of drugs, ETOH, or medications in proximity to the time of assault
11. Current meds/allergies
12. Date of last tetanus shot
13. Date and time of last consensual intercourse
14. Gravity, parity and menstrual hx
15. Contraceptive hx
16. General PMH as indicated

Physical Exam/Lab W/U: Obtain separate consent for examination and collection of evidence.

Explain to the pt what you are doing and why.

1. Note and record vital signs, general appearance
2. Examine clothing and skin for loose hair, stains, or other debris and collect as evidence
3. Inspect fingernails and preserve cleanings
4. Collect clothing
5. Comb pubic hair for loose strands and save
6. Clip and label samples of head and pubic hair for comparison with any loose strands found
7. Perform complete examination of head, body, and extremities; record injuries on body diagram
8. Inspect genitalia for lacs, abrasions, ecchymoses or hematomas, giving special attention to the posterior fourchette
9. Insert a speculum and examine internally; perform colposcopy if available to exclude lower reproductive tract trauma
10. Prepare GC Cx and appropriate smears for the detection of sperm
11. Obtain similar Cx from throat and anus if indicated
12. Collect blood for grouping, syphilis serology, pregnancy testing, drug and Etoh levels, and a reference saliva specimen to determine ABO secretor status of the victim, HIV, HepB, CMV, HSV, Hep C

Medical Tx:

1. All injuries should be appropriately tx (eg. Lacs)
2. Tetanus toxoid should be administered if pt >10yrs since last immunization
3. Prophylaxis for STDs should be offered. The currently recommended regimen is: 250mg IM Ceftriaxone plus 1000 mg of Azithromycin x1 dose (or 100mg of Doxycycline BID X 7 days)
4. Post coital (emergency) contraception should be offered (i.e Plan B: Levonorgestrel 0.75 mg one pill q12 hrs x2 doses). Prophylaxis can be administered for up to 72 hours after rape, but is most effective in first 24 hours. May include discussion regarding continuation of pregnancy if it has occurred.

Psychological Management:

1. The initial evaluation provides the opportunity to prepare the victim for the longer term psychological impact of the assault.
2. In the acute phase of adjustment, often irritability, tension, depression, fatigue, and persistent ruminations are seen.
3. Somatic sx of a general nature may occur such as HA and irritable bowel syndrome or specific sx such as vaginal irritation or discharge.
4. Behavioral problems may surface such as over-eating or substance abuse.
5. Flashbacks may occur in similar surroundings or other associated stimuli. Studies have found that avoiding such stimuli only exacerbates the reaction. Post-traumatic stress disorder is not uncommon.
6. Loss of libido, vaginal dryness and loss of orgasmic capacity are also common sequelae.

Follow Up:

1. Contact by phone or see within 24-48h. Refer to local rape crisis centers, encourage visit within 1-2 days.
2. Repeat tests for gonorrhea/chlamydia (2 weeks)
pregnancy, Trich, HPV, vaginismus (6 weeks)
Gonorrhea, chlamydia, HIV (3 months)
Hep B, HIV, RPR (6 months)

44. Sterilization: 20 year-old Tasha, G1 P1, comes to your office requesting permanent sterilization.**General:**

The permanency of surgical sterilization, either female or male, necessitates that extensive counseling and evaluation be done prior to any procedure. For tubal ligation, a 30 day interval between the signing of consent and the surgery is required by law. Also, pt must be 21 years old if Medicaid. The only time this may be waived to 72 hours is in the case of premature delivery or emergency abdominal surgery.

Types of Sterilization:

1. Vasectomy is the safest and simplest method. It causes no hormonal changes and if reversal is undertaken, no change in spermatogenesis will have occurred. Successful reversal can occur in over 60% of cases
2. Tubal Ligation: fatalities occur in 4 per 100,000 women being sterilized in the U.S. One ectopic pregnancy occurs per 15,000 sterilizations. Can be done 4-24 hours following delivery. Subtypes are:
 - a. Laparotomy
 - b. Laparoscopy
 - c. Mini-lap
 - d. Posterior colpotomy
 - e. Hysteroscopy
 - f. Blind cannulation of tubes via transcervical approach

Details of these surgeries can be found in Chapter 27 Sterilization from Beckman 7ed pp. 253-258. The take-home point is that they all tie off, burn off or scar off the fallopian tubes.

Patients must be counseled that there is a 1% failure rate with tubals, so if they miss a period, they should take a pregnancy test just in case. Risks include: bleeding, infection, ectopic pregnancy if pregnancy occurs.

Miscellaneous:

- *Can be done in the OR or in an outpatient center.
- *Occlusive devices (ie. Falope ring) are put at the junction of the isthmus and ampulla.
- *The Falope ring is more painful post-op because a loop of necrotic tissue remains.
- *Previous PID with adhesions may make laparoscopy hard.
- *Laparotomy or mini-laparotomy usually uses the Pomeroy technique (some exceptions) and are usually done within 48hrs postpartum.
- *Colpotomy is becoming obsolete because it is difficult to do and has higher infection rates.

47. Urinary Incontinence: 48 year-old Shirley, G5 P4 Ab1, comes to your office complaining of involuntary loss of urine.

Definitions/Causes:

1. Stress incontinence (SI): most common cause; loss of urine associated with coughing, lifting, exercise, etc.; seen most often in women, secondary to relaxation of pelvic floor following multiple deliveries, increased age or estrogen deficiency.
2. True incontinence (TI): Constant or periodic loss of urine without warning, caused by sphincter abnormality (.e.g. exstrophy of bladder) or urinary fistula secondary to sx or radiation.
3. Overflow incontinence (OI): Failure of bladder to empty properly; may be caused by bladder outlet obstruction, or detrusor hypotonicity or anything that causes hypotonicity, eg. DM. Have continual urine dripping or small amounts of leakage with minimal changes in intraabdominal pressure
4. Urge incontinence (UI): Loss of urine secondary to detrusor instability in patients with stroke, dementia, Parkinson's disease, etc. There is an abrupt onset of or increase in an overwhelming desire to void. Involuntary leakage accompanied by or immediately preceded by urgency.
5. Mixed incontinence (MI): Complaint of involuntary leaking associated with urgency and also with exertion, effort, sneezing, or coughing.

Workup:

- A. Detailed history:
 1. A urinary questionnaire, including presence of nocturia, urgency, precipitating events (medications, caffeine, alcohol, physical activity, cough, laughing, sound of water, placing hands in water), frequency of loss, type and severity of leakage.
 2. Voiding diary, to measure urine volumes and fluid intake during a 24 hour period.
 3. History of urinary tract infections
 4. Previous urologic surgery/gyn sx
 5. Obstetric history: parity, birth weights, mode of delivery; estrogen status
 6. Central nervous system or spinal cord disorders
 7. Use of medications, including diuretics, antihypertensives, caffeine, alcohol, anticholinergics, decongestants, nicotine, psychotropics
 8. Presence of other medical disorders (e.g. hypertension, hematuria)
 9. Bowel/sexual function
 10. Degree to which the incontinence affects patient's life
- B. Physical examination may detect:
 1. Exacerbating conditions, such as obstructive pulmonary disease, obesity, or intraabdominal mass
 2. Uterine descensus, vaginal prolapse
 3. Neurologic disorders
 4. On PE should perform: GU exam beginning with inspection, BME to rule out masses, exam with one blade of speculum looking for urethral hypermobility, cystocele, rectocele, rectal exam looking for masses/impaction
 5. Should also perform neurologic testing: perineal sensation, tone of anal sphincter, and bulbocavernosus reflex
- C. Diagnostic tests
 1. Midstream urine specimen for culture of infectious causes
 2. Urodynamic testing to determine:
 - a. flow rate of urine
 - b. residual urine volume of bladder
 - c. Cystometrics to determine bladder capacity, tone and dynamics, by filling bladder with water and saline to determine volumes when the desire to void were felt and to recreate situation in which incontinence occur (i.e. detrusor instability, or genuine stress incontinence)

- d. Q-tip test: measures the urethral axis. A Q-tip is inserted into the urethra with the patient in the lithotomy position. If the Q-tip moves more than 30 degrees from the horizontal with valsalva, there is abnormal urethral mobility consistent with pelvic floor relaxation in stress incontinence.

Management:

- SI: Pelvic Muscle exercise, bladder training, Bladder neck suspension, sling procedures, pessaries, estrogen therapy, alpha-adrenergic stimulation
- UI: Pharmacotherapy (anticholinergics, alpha-adrenergic agonists), bladder denervation, and augmentation cystoplasty, behavioral therapy (frequent voluntary voiding, training of CNS and pelvic mechanics to inhibit/ablate detrusor contractions), biofeedback therapy
- OI: Self-cath, surgical relief of obstruction; avoidance of indwelling catheters (reduce # of UTI's)
- TI: Appropriate surgical intervention, i.e. repair of fistula

49. Vaginal Discharge/Itching: 34 y.o. Heather, G4, P3 Ab1, comes to your office complaining of vaginal discharge and itching for the past 4 days.

Normal Vaginal Physiology: post pubertal

- pH 3.5-4.5
- 3-8 types of bacteria present with lactobacilli predominating

Differential Diagnosis:

1. Trichomonas
 - caused by the flagellated *Trichomonas vaginalis* which lives in vagina and male urethra
 - 25% infected females asymptomatic
 - vaginal discharge is bubbly and grayish green with a foul odor; strawberry cervix (petechiae) due to inflammation from infection
 - pruritis, burning, urinary frequency, dyspareunia
 - pH is 5 – 6 (remember pH >4.5)
 - pear shaped motile organism on wet mount
 - Tx: flagyl 500 mg bid X 7 days (partner also) or 2 g flagyl once, 7 day treatment leads to cure rates; however, if concerned about compliance, treat with one-time dosing. *Use clotrimazole (gyne-lotrimin) in 1st trimester because flagyl is teratogenic.
2. Bacterial vaginosis
 - caused by: *Gardnerella vaginalis* in the presence of anaerobes (*Bacteroides* and *Peptococcus*). Clinical syndrome resulting in replacement of the normal vaginal flora with anaerobic bacteria in high concentrations
 - profuse thin gray malodorous discharge that coats vaginal wall
 - vaginal fluid pH > 4.5
 - adding KOH produces fishy odor due to amines = (+) Whiff Test
 - see clue cells on wet prep; few WBCs
 - (+/-)itching
 - increases infectious morbidity following diagnostic/operative procedures, treat preoperatively if present
 - tx: flagyl same as for Trich
3. Molluscum contagiosum
 - caused by a growth stimulating virus
 - usually asymptomatic or mild pruritis
 - red to yellow umbilicated papules,
 - tx: carbonic acid / trichloroacetic acid / silver nitrate and manually express caseous content of lesions (material if very infectious, so be cautious)
4. Candidiasis
 - vaginal discharge with cottage cheese appearance
 - 20% asymptomatic

- pruritis, burning, dyspareunia, erythema
- ph is 4.5
- hyphae / spores on KOH prep
- Tx: Miconazole (Monistat) / Clotrimazole (Gyne-Lotrimin) / Butoconazole (Femstat) / fluconazole 150 mg po (Diflucan)

History:

- Pruritis, dyspareunia, burning?
- Urination troubles?
- Describe discharge. (color, consistency, amount, odor)
- Exposure to allergies
- Abdominal pain
- Exposure to new sexual partner
- When did symptoms start in relation to menses
- Hygienic practices
- Meds used (OCPS, abx?)

Physical Exam/Workup:

- wet prep
- KOH prep if suspect candidiasis

Treatment: as above. Don't forget the partners in cases of Trichomas. Also in cases of Trichomonas also ask if they desire testing for Hep B, Hep C, HIV, RPR as this is considered STI.

50. Vulvar Lesions: 57 year-old Lottie, G5 P3 Ab2, comes to your office complaining of vulvar itching for 6 months. On exam you find a 6 x 10 mm white lesion on the right labia majora.

Differential Diagnosis:

1. **Vulvar Intraepithelial Neoplasia (VIN):** presenting complaints include vulvar pruritus, chronic irritation, and a development of raised mass lesions. Normally, the lesions are fairly well isolated and are raised above the normal epithelial surface and have a *whitish cast or hue*. As with other vulvar lesions, *diagnosis by biopsy is mandatory*. Microscopically, the lesions mimic intraepithelial neoplasia elsewhere, including mitotic figures and pleomorphism, with loss of normal differentiation of the lower one-third to one-half of the epithelial layer. The goal of treatment is to quickly and completely remove all areas of involved skin. Most isolated and limited VIN-I (mild dysplasia) and VIN-II (moderate dysplasia) lesions may be removed by local excision, cryocautery, electrodesiccation, or laser cautery. VIN-III (carcinoma in situ) is best treated by wide local excision with or without combination laser ablation to ensure no progressive disease or vulvar carcinoma.
2. **Vulvar Cancer:** typically affects postmenopausal women (65-70 years), with *vulvar pruritus* being the most common presenting complaint. In addition, patients may notice a *red or white* ulcerative or exophytic lesion arising most commonly on the posterior two-thirds of either labium majus. A thorough biopsy (usually multiple biopsies are taken) is mandatory. These tumors account for 4% of all gynecologic malignancies, and 90% are of the squamous cell variety. It spreads in a predictable fashion to the regional (including inguinal and femoral) lymph nodes, and lesions in the anterior one-third of the vulva may spread directly to the deep pelvic nodes. Staging is clinical, with an overall 5-year survival rate of 70% (but only 20% if the deep pelvic nodes are involved). The mainstay of treatment is surgical.
3. **Paget's disease (of the vulva):** a rare (0.5% of vulvar CA) intraepithelial adenocarcinoma that often appears as a velvety red lesion with areas of superficial white coating ("cake-icing" effect). Noninvasive lesions are treated with wide excision, while invasive lesions may be treated with a radical vulvectomy. Often associated with underlying adenocarcinoma. May also associated with GI neoplasm.
4. **Lichen sclerosus (et atrophicus):** a slowly developing, chronic, localized lesion of unknown etiology which often has the appearance of parchment paper or cigarette paper although

thickened hyperplastic areas are not uncommon. Most patients are 50 years or older, and have involvement on both sides of the vulva, with the most common sites being the labia majora, labia minora, the clitoral and periclitoral epithelium, and the perineal body [can also involve the neck, shoulders, and forearms]. *Chronic vulvar pruritus* normally occurs, and inspection of the vulva reveals an ivory white, smooth surface. The treatment of choice is superpotent topical corticosteroids (Clobetasol). *Microscopic confirmation via biopsy is mandatory.*

5. Hyperplastic Vulvar Dystrophy: usually produces a white or reddish area on the surface of the vulva; will likely need to be confirmed via biopsy. Initial treatment with fluorinated topical steroids relieves pruritus; follow-up examinations with constant search for progressive change and possible malignancy are essential.
6. Lichen planus: may have areas of whitish, lacy bands of keratosis near the reddish ulcerated-like lesions characteristic of the disease. Complaints include chronic vulvar *burning* and/or pruritus and *insertional dyspareunia* and a *profuse vaginal discharge*. Biopsy may be warranted to confirm the diagnosis in some patients. Not malignant or premalignant; treatment consists of topical steroids.
7. Lichen Simplex Chronicus: secondary to an irritant dermatitis, which progresses to lichen simplex chronicus as a result of the effects of chronic mechanical irritation from scratching and rubbing. Inspection usually shows diffusely reddened areas with occasional hyperplastic or hyperpigmented plaques of red to reddish brown; biopsy of patients with these characteristic findings is usually not warranted. Treatment includes Benadryl and topical steroid creams.
8. Psoriasis: may involve the vulva, with lesions typically slightly raised round or ovoid patches with a silvery scale appearance atop an erythematous base. Pruritus is usually *not* marked, and the diagnosis is generally known because of psoriasis elsewhere, obviating the need for biopsy.

Workup and Management:

The major symptoms of vulvar disease include pruritus, burning, nonspecific irritation, and/or appreciation of a mass. Further history will be of limited value in these patients, but questions concerning associated local symptoms (e.g., vaginal discharge) and constitutional symptoms (e.g., weight loss) may be helpful. On physical exam, be sure to look/palpate for enlarged/tender groin lymph nodes.

The **need for a thorough biopsy is near-universal** in the workup for vulvar disease, if in doubt, biopsy!. Management will depend upon the findings, as described with each item in the differential diagnosis.

51. Preventative Care and Routine Screening: A 60 y.o. G4 P4 patient presents for annual exam. What should this include? How would this list change if patient was 40 y.o. or 20 y.o.?

60 year old:

- cholesterol screening first at 20 yo then q5 years (q 3-4 years if >65)
- rectal/hemoccult q1y >50y.o.
- sigmoidoscopy q3-5 y >40
- colonoscopy >50yo, then q10years if no hereditary genetic disorder or strong familial history
- Pap/pelvic exam >21yo, **See ASCCP guidelines or Case 2-
- breast exam, may be done with annual well-woman exam
- MMG baseline at 40yo q2y <50; annually if >50yo or strong suggestive history,
**MMG earlier if hereditary or familial breast cancer history
- dT q10 yrs.
- measles booster if born after 1956
- rubella vaccine if reproductive age without proof of immunity or MMR postpartum if found nonimmune after prenatal care
- influenza vaccine annualy
- Pneumovax x1 >65
- TSH start screeing at 25yo, then q3-5 yrs

- TB skin testing for health professional workers or living in high prevalence area or +exposure
- HRT after menopause / oophorectomy for symptoms control (lowest dose possible for shortest time possible)
- UA done at every prenatal visit
- Fasting glucose every 3 years
- Bone density screening at 65yo

Section II: Endocrinology and Fertility

15. Hirsutism/Virilism: 18 year-old Marla, G0 P0, comes to your office complaining of excessive dark, coarse hair growth on her face, chest, and pubic area.

Definition:

Hirsutism- excessive body hair. Development of androgen dependent terminal body hair in women
Virilism- masculinization: deepening voice, male body habitus, temporal balding, clitoromegaly

Differential Dx:

- (i) Polycystic Ovary Disease (PCO)
- (ii) Congenital Adrenal Hyperplasia
- (iii) Idiopathic/Genetic
- (iv) Ovarian Cancer
- (v) Hyperthecosis
- (vi) Adrenal Tumor
- (vii) Cushing's Syndrome
- (viii) Drugs
- (ix) Hyperprolactinemia

Work Up:

1. labs: total testosterone, free testosterone, SHBG, TSH, Prolactin, 17-OHP
2. Previously, cut off for concern for ovarian malignancy was test > 2 ng/nL and DHEAS of > 700 microg/dL, however these are not sensitive or specific for possible malignancy.

Pathophysiology of PCOS:

In this patient, PCOS is the most likely etiology of hirsutism. Insulin resistance has been known to play a large role in PCOS and causes decreased levels of SHBG as well as hypothalamic effects that cause more bioavailable circulating androgen and anovulation.

PCOS is diagnosed based on 2/3 criteria (Rotterdam): clinical findings consistent with

hyperandrogenism- acne, hirsutism; 'string of pearls' on TVUS, and history of anovulation or oligomenorrhea. Insulin resistance, although central to syndrome, is not part of the criteria for diagnosis. Hyperthecosis is a more severe form of PCOS, with a marked elevation of testosterone and symptoms of virilization.

Treatment:

In this case, the first line of treatment should be a combined OCP, which will suppress LH production by the pituitary and suppress androgen secretion/circulation by increasing SHBG. For women that desire to conceive, the recommendation is clomiphene or letrozole. Insulin-sensitizing agents such as metformin have also been used to treat PCOS given the insulin-resistance mechanism of the syndrome.

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18. MENOPAUSE: 51 year-old Hattie, G3 P3, has had increasing irregular menses. Her last period was 3 months ago. She has been experiencing sudden onset of profuse, embarrassing diaphoresis and sensation of heat. She finds her emotional state increasingly labile.

- 1) **Definition:** Menopause is the permanent cessation of menses after significant decrease of ovarian estrogen production.
 - a) 12 consecutive months with no menstrual bleeding. One sees increased menstrual irregularity and varying decreases in menstrual flow, hot flashes, nervousness, mood changes, and decreased vaginal lubrication, tissue atrophy and aging from decreased production of estrogen and other hormones. The result is cessation of menses and thus cessation of fertility.
 - b) Median age = 51. Range = 45-55, <40 is considered premature ovarian failure.
 - c) Associated with a high serum FSH level, low AMH and inhibin B levels.

- 2) **Pathophysiology:** Basically menopause is the depletion of ovarian follicles.
 - a) The ovaries can not respond to gonadotropins and thus decrease production of estrogens, progesterone, and androstenedione.
 - b) The process begins slowly and before actual menopause, and women will have oligo-ovulation or anovulation. The quality of ova and fertility decrease and pregnancies occur less frequently and result in more chromosomal anomalies.
 - c) Decreased progesterone causes shorter more irregular menstrual bleeding, among other things. Women have elevated gonadotropins and decreased sex hormones such that FSH gets 10-20x normal limit and LH 3x normal limit. FSH >40mlu/ml is diagnostic of menopause.

- 3) **Clinical Manifestations:**
 - a) Vasomotor - hot flashes in 75% (relative decrease in estrogen)
 - b) Genital Atrophy - dryness, irritation, dysuria, vaginitis (dec. estrog.). Atrophy also leads to dyspareunia and vaginal bleeding, urethral support weakens and increases risk for stress incontinence.
 - c) Osteoporosis - Ca is lost primarily from trabecular bone i.e. vertebrae and femoral neck; women can shrink 2.5 inches in height secondary to vertebral fractures.
 - d) CV disease - cholesterol, LDL, triglycerides all increase and HDL decreases leading to significant increase in CV disease.
 - e) Emotions - insomnia, poor memory, mental confusion, lethargy, irritability, nervousness, fatigue, dizziness, inability to cope, decreased libido, depression, sleep disturbance.

- 4) **Management:**
 - a) You must patiently listen to pt's history and discuss the normal aspects of menopause with her, explaining therapy to decrease symptoms when applicable.
 - b) Hormone replacement therapy can be used to help with vasomotor symptoms, vaginal atrophy, osteoporosis,
 - c) To prevent osteoporosis, hormone therapy and 1000mg of Calcium is proven beneficent (1500mg Ca is needed without hormone replacement.)
 - d) Emotional concerns should be dealt with on individual basis depending on the specific combination of symptoms is each pt.
 - e) WHI trial showed:
 - i) slight increase in MI with combination estrogen/progesterone therapy
 - ii) no change in MI risk with estrogen therapy alone
 - iii) ↑risk of stroke with combination therapy or estrogen therapy alone
 - iv) ↑risk of DVT/PE with combination therapy or estrogen therapy alone
 - v) ↑risk of breast cancer with combination therapy
 - vi) slight ↓risk of breast cancer with estrogen therapy alone
 - vii) ↓risk of osteoporotic fractures with combination therapy or estrogen therapy alone
 - viii) ↓risk of colorectal cancer with combination therapy

- ix) no change in risk of colorectal cancer with estrogen therapy alone

28. PRECOCIOUS PUBERTY - 5 year-old Lucy is referred to you by her pediatrician with the findings of breast development along with pubic and axillary hair.

Definition:

Recall that the usual sequence of puberty is

- (1) Thelarche (breast development) at 9.8 years
- (2) adrenarche (pubic and axillary hair development) at 10.5 years
- (3) maximal growth spurt at 11.4 years, and
- (4) menarche (onset of menses) at 12.8 years.

If physical signs of secondary sexual development appear before the age of 8 years, you should consider the diagnosis of precocious puberty (PP). This condition is more common in females. It also has no serious pathology; it simply causes an advance in sexual maturation and carries the risk of short stature because of premature closure of the epiphyseal plates. Not associated with premature menopause or infertility.

Differential Diagnosis:

- A. **Gonadotropin Dependent Precocious Puberty (GDPP):** early activation of the hypothalamic-pituitary-gonadal axis. PP recapitulates normal pubertal development, but at an earlier age. GnRH agonist therapy typically effective. Ex. Idiopathic (80%), CNS problems, primary hypothyroidism.
 1. CNS lesions - Hamartomas in hypothalamus, astrocytomas, ependymoma, hydrocephalus, craniopharyngioma, CNS infections (meningitis, encephalitis), abnormal skull development due to rickets.
 2. Primary hypothyroidism - Typically in children with longstanding primary hypothyroidism. Present with early breast development, galactorrhea, and menstrual bleeding. Thyrotropin releasing hormone becomes elevated, which elevates TSH. Overlap of TSH with hCG receptor elevates FSH and LH. Always assess thyroid function in PP patients. With thyroid replacement, pubertal development will stop and even regress.

- B. **Gonadotropin Independent Precocious Puberty (GIPP):** sexual maturation may be due to peripheral source of gonadal hormones. More likely to display deviations from normal sequence and pace of puberty (Ex. progression to menstrual bleeding within one year of onset of breast development, likely ovarian disease). GnRH agonist therapy is ineffective. Ex. Ovarian cyst or tumor, McCune-Albright syndrome (4%), Adrenal feminizing, ectopic gonadotropin production.
 1. McCune-Albright syndrome - (i.e., polyostotic fibrous dysplasia) defined as triad of cafe-au-lait spots, multiple disseminated cystic bone lesions, and precocious puberty. H/O bone fractures and PP. PP is a result of somatic mutation and autonomous early production of estrogen by ovaries: FSH/LH levels are low and respond poorly to GnRH stimulation and there is an absence of nocturnal gonadotropin pulsation
 2. Ectopic gonadotropin production - Less than 0.5% of cases. Tumors implicated are dysgerminomas and chorioepitheliomas of the ovary and hepatomas of the liver. Presence of abdominal tumors or ascites is a clue.
 4. Ovarian
 - (i) Follicular cysts: Most common cause of GIPP in girls. Present after episode of vaginal bleeding. Typically regress spontaneously and treatment is conservative management. Large cysts may predispose to ovarian torsion.

- (ii) Tumors: Rare causes. Most common of these is Granulosa cell tumors which secrete estrogen and cause isosexual PP (phenotypically appropriate secondary sexual characteristics).
5. Adrenal
- (i) Defects in adrenal steroid biosynthesis: The most common cause of this is congenital adrenal hyperplasia 21-hydroxylase type. Recall that 21-hydroxylase converts progesterone to desoxycorticosterone. Obviously, there is a deficit of cortisol in the body. However, there is also a build-up of adrenal androgens, which results in precocious puberty. In girls, there is premature development of pubic hair followed by axillary hair. Breast development either does not occur or is incomplete for the stage of sexual development. In males, there is premature enlargement of the phallus and the appearance of axillary and pubic hair. However, the testicles remain small because the source of androgens is the adrenal gland rather than the testicles.
 - (ii) Adrenal tumors are not common, though an adrenal carcinoma may secrete estrogen and cause PP.
- C. **Incomplete Precocious Puberty:** early development of secondary sexual characteristics and usually is a variant of normal puberty.
1. Premature thelarche - relatively common, probably secondary to increased sensitivity of the breast tissue to estrogen, so that lower levels of the hormone stimulate breast growth. Typically follow at 6 month intervals.

History:

Careful evaluation warranted in children with secondary sexual development younger than age eight in girls. The progression of menarcheal events in PP may be confused and are often slower than normal. Evaluate height, as these patients are usually tall for their age. However, due to premature epiphyseal plate closure, their eventual height may be sub-average. (1/2 of these patients will be less than 5 feet tall.) NOTE: Onset of dental eruption is more closely related to chronological age than skeletal age. Do not forget drug ingestion - ingestion of exogenous estrogenic meds may cause a darker pigmentation of the areola and nipples. Assessment should include record of growth/height/weight, pubertal staging, and bone age with radiographic assessment of bone age (bone age > chronological age = further evaluation). Further labs/imaging includes:

1. Thyroid studies - Can easily rule out primary hypothyroidism.
2. Measure adrenal androgens - Basal LH and LH following GnRH agonist to differentiate GDPP (LH/FSH increase) vs GIPP (LH/FSH do not increase).
 - GDPP: Brain imaging, estradiol, testosterone, thyroid studies.
 - GIPP: testosterone, estradiol, LH, FSH, cortisol (drawn in afternoon, test for Cushings), DHEA, DHEAS, 17-hydroxyprogesterone
3. Pelvic US - evaluate for pelvic masses/tumors.
4. Head CT - evaluate for tumors of the hypothalamic-pituitary stalk.

Treatment:

- If PP is within a few months of the expected time of normal puberty, it is appropriate to let it progress without further evaluation.
- If puberty is advanced by several years, it should be stopped. The use of GnRH agonists in a continuous fashion will block the periodic secretion of GnRH and suppress pituitary gonadotropin secretion. This will eliminate menses, delay closure of the epiphyses, and inhibit the development of secondary sexual characteristics.
- Do not neglect psychological support.
- If specific etiology for precocious puberty is identified, treatment is aimed at curing the underlying disorder

This Case:

- As breast development IS occurring, you could probably rule out congenital adrenal hyperplasia.

- Estrogen production by ovarian tumor typically causes breast development *and* skeletal growth, but *not* hair growth, so this could probably be ruled out.
- It seems that puberty is developing early, but following the *normal* steps. This would suggest a GDPP cause such as *pituitary-hypothalamic stalk lesion* or *primary hypothyroidism*.
- A history of broken bones, or cafe-au-lait spots on exam could suggest McCune-Albright syndrome.
- Suggest work-up would be *thyroid studies*, thorough *physical exam* with pelvic, good *neurological exam* paying attention to visual field limits. Further studies would include head CT. Given young age and likely GDPP, should be responsive to GnRH treatment.

35. Primary Amenorrhea: 19 year old Rhonda G0 P0, presents at your office stating she has never had a menstrual period.

Definition:

- complete absence of menstruation in a woman of reproductive age who has **never** had a period
- the diagnosis of primary amenorrhea is made when no spontaneous bleeding has occurred by the age of 16 ½ years.
- work up is instituted earlier if patient presents with no breast development by age 15 or who has failed to menstruate spontaneously within 2 years of the onset of breast development (thelarche) and pubic or axillary hair development (adrenarche).

Pathophysiology: normal menstruation requires the following components:

- patent outlet (normal vagina and cervix)
- a uterus that responds to estrogen and progesterone stimulation
- ovaries that respond to gonadotropins with estrogen and progesterone production
- the pituitary and hypothalamus, which sense the hormonal milieu and respond with release of gonadotropins

Injury or other pathology to any of these components can cause amenorrhea. The anatomical existence and normality of the female organs deserve special attention when evaluating primary amenorrhea.

Differential Diagnosis:

Pregnancy
 Hypogonadotropic hypogonadism
 Kallman's syndrome
 Gonadal dysgenesis
 Androgen insensitivity
 Congenital absence of the uterus
 17,20 desmolase deficiency
 17 α hydroxylase deficiency with either 46XX or 46 XY
 Prolactinoma
 Polycystic ovary
 hypothalamic dysfunction
 Hypothalamic-pituitary failure
 ovarian failure
 Weight loss/anorexia
 Hypothyroidism
 Mullerian anomalies/agenesis
 Turner's syndrome

Differential can also be broken up into compartments:

Compartment I: Problem with uterus/cervix/vagina

- Asherman's syndrome – intrauterine adhesions

- Mullerian anomalies – imperforate hymen, obliteration of vaginal orifice, vaginal septum, or absent cervix/uterus
- Androgen insensitivity – genetically male with female characteristics

Compartment II: Problem with the ovary

- Turner's syndrome
- Mosaicism
- XY gonadal dysgenesis
- Gonadal agenesis
- Premature ovarian failure

Compartment III: Problem with the pituitary

- Prolactinomas
- Sheehan's syndrome
- Thyroid dysfunction

Compartment IV: CNS disorders

- Hypothalamic amenorrhea
- Anorexia
- Exercise
- Kallman's syndrome

History:

- Determine if this is primary or secondary (i.e. has the pt **ever** had a menstrual period)
- Determine past medical history since other abnormalities (cardiac or renal) are associated with anomalies of gonadal failure or gonadal agenesis/dysgenesis
- Determine past surgical history to conclude if any gonadal tissue has been removed
- Determine nutritional status since anorexia and stress can cause amenorrhea
- Determine athletic status since high performance athletes (gymnasts) are often amenorrheic
- Take a sexual history and include any contraceptive methods currently used (some women can be pregnant if they had sex during ovulation of their very first period)
- Take a family history since if mom was late, the daughter will probably be late

Physical Exam:

Perform a complete physical exam (cardiac, renal, olfactory included) and pelvic and breast exam as indicated by pt's age and history.

Breast exam: assess development and tanner stage

Pelvic exam: assess the presence of any pubic hair and tanner stage. Assess the presence of the hymen, and the uterus.

Also need to assess prepubertal development along with current height, weight, and arm span

Labs:

- hCG
- FSH, TSH, PRL
- GnRH test if indicated (see below 1.)
- Testosterone level as indicated (see below 2.)
- Karyotype if in question as stated above

Workup and Management:

Management will vary widely depending on the abnormalities found. If normal female external genitalia are present, one can divide primary amenorrhea into four general categories--

1. Patient with no breast development and uterus present

2. Patient with breast development and no uterus present
3. Patient with no breast development and no uterus present
4. Patient with breast development and uterus present

1. Patient with no breast development and uterus present:

Differential includes:

- (i) hypogonadotropic hypogonadism (hypothalamic or pituitary failure)
 - FSH levels are low or low normal
- (ii) gonadal dysgenesis
 - Causes include 45 X (Turner's); structurally abnormal X chromosome; mosaicism with or without a Y chromosome; pure gonadal dysgenesis 46XX and 46 XY; and 17 α hydroxylase deficiency with 46 XX (patients will also have HTN and hypokalemia)
 - FSH levels are elevated (in the menopausal range)
 - Patients with elevated FSH and primary amenorrhea require a karyotype to establish the diagnosis of ovarian failure and determine the presence of Y chromosome
 - These patients are sterile and can carry a pregnancy only if a donor egg is used and transferred to the uterus

Work-up:

- (i) Hypogonadotropic hypogonadism is the most common cause in this group of patients.
 - To differentiate between hypothalamic or pituitary origin perform a GnRH test- if there is an appropriate LH response following the administration of exogenous GnRH the diagnosis of hypothalamic failure to produce or secrete adequate GnRH is made. If no response after priming the pituitary with a 10-day course of GnRH the diagnosis of pituitary failure is made.
 - Some patients may have amenorrhea with anosmia (*Kallman syndrome*)
 - Coffee, tobacco, orange, and cocoa can be used to assess the integrity of the olfactory system
 - Rarely a craniopharyngioma may present with amenorrhea. In this case a CT or MRI is necessary to assess the hypothalamic-pituitary axis
- (ii) Gonadal dysgenesis pts have hypergonadotropic hypogonadism caused by a genetic or enzymatic abnormality that results in failure of gonadal development or abnormal functioning ovary.

Management :

- (i) Evaluate for intracranial tumors by checking thyroid function and levels of GH, prolactin, and cortisol. Skull X-rays of the sella turcica and CT of the pituitary region are also recommended
- (ii) Patients with gonadal dysgenesis should have a CXR, EKG, IVP, and thyroid function tests to evaluate the common associated problems
- (iii) All patients should be treated with estrogen-progestin replacement to induce breast development, cyclic menstrual bleeding, and to prevent osteoporosis and coronary heart disease

2. Patients with breast development and no uterus present

Differential includes:

- (i) Androgen insensitivity (testicular feminization syndrome)
- (ii) Congenital absence of the uterus (these patients have ovaries)

Work-up:

to differentiate, test for ovulation or testosterone. Androgen insensitive patients have normal male levels, and congenital absence of the uterus have normal female levels

Management:

- (i) Androgen insensitivity
 - a. Androgen insensitive patients are XY genotype but are phenotypically female because an androgen intracellular receptor is not functioning (a maternal X-linked recessive gene). The Wolffian system does not develop despite normal male levels of

testosterone. The MIF is still present so the mullerian system does not develop. These patients have *large breasts* with *immature nipples*, but no axillary or pubic hair.

- b. These males should be karyotyped to establish the diagnosis. The testicles should be removed to prevent malignant transformation and the patient should be treated with estrogen
- (ii) Congenital absence of the uterus
 - a. These patients have sexual hair and mature nipples; 40% have associated renal anomalies so an IVP or an US should be performed to establish renal function
 - b. These pts require no HRT since they have functioning ovaries. These patients cannot conceive or carry a pregnancy unless the patient with an absent uterus undergoes IVF with embryo transfer to a surrogate mother

3. Patients with no breast development and no uterus

Differential includes:

- (i) 17,20 Desmolase deficiency
- (ii) agonadism (vanishing testicles syndrome)
- (iii) 17 hydroxylase deficiency with 46XY karyotype
 - These patients are rare and often have a male karyotype (46XY), elevated gonadotropins, and serum testosterone level within the normal female range

Work-up and management:

- (i) 17,20 desmolase deficiency: diagnosed by incubation studies with a portion of gonadal tissue. 17,20 Desmolase prevents the formation of estrogen and testosterone, but not aldosterone, cortisol, or progesterone. Therefore there is a deficiency of sex hormones. These patients have no breast development. They should have any gonadal tissue removed and treated with estrogen replacement to prevent osteoporosis and CVD
- (ii) Agonadism: suspected by a lack of testosterone response following the daily administration of hCG and confirmed by laparotomy.
- (iii) 17 hydroxylase deficiency with 46Xy karyotype: may have elevated BP and hypokalemia secondary to the increased aldosterone. If gonadal tissue is present remove to prevent malignant transformation and treat with HRT to induce breast development and prevent osteoporosis and CVD

4. Patients with breast development and uterus present

Differential includes:

- (i) Polycystic ovary disease
- (ii) Hypothalamic dysfunction
- (iii) Hypothalamic pituitary failure
- (iv) Ovarian failure
- (v) Prolactinoma

Workup and Management:

- (i) 25% of these patients have an elevated prolactin level with no galactorrhea, and radiographic abnormalities of the sella turcica suggestive of a pituitary adenoma, therefore r/o prolactinoma
- (ii) If prolactin is normal: same differential as secondary amenorrhea, so both groups of patients undergo similar systemic evaluation (Please see chart attached).

Another way to look at workup:

Check TSH, PRL, give progesterone challenge after negative UCG

If TSH is increased: Hypothyroidism

If PRL is increased: Hyperprolactinemia → possibly get MRI of head

If + withdrawal bleed with nl PRL, FSH → anovulation

If no withdrawal bleed with nl PRL, FSH → give estrogen for 21 days followed by Provera

If + bleed → check FSH/LH assay

If low or nl → MRI of head → if nl: hypothalamic amenorrhea

If high → ovarian failure

If no bleed → deficit in endometrial/outflow tract

36. Primary Infertility: 30 year-old Marsha, G0 P0, has been married for 5 years. In spite of not using any contraception she has been unable to get pregnant. She desperately wants a child and comes to your office.

Definition:

- Infertility is defined as the inability to conceive after 1 year of unprotected intercourse of reasonable frequency
- The incidence of pregnancy after 2 years of regular, unprotected sex is 93%. Obviously, this couple is infertile, a condition affecting 10-15% of US couples. You may also tell her that 80% of infertile couples will conceive with proper treatment.
- Generally agreed upon that an infertility evaluation should be considered in any couple that has failed to conceive in 1 year.

History:

- Menstrual History: Determine the regularity, frequency, duration of pt's cycles, or recent change in interval or duration of her cycles. Irregularity could signal anovulation, and points to a female cause of infertility. Also ask about prior contraceptive use and duration of infertility.
- Regular cycles could lead you to look to the male partner in greater detail. Specifically, decreased sperm production could be caused by thermal shock, such as hot tub use, tight clothing that pulls the testicles too close to the body, prolonged sitting which could cause poor heat dispersion. Recall that sperm production occurs at a temp approximately 1 degree F lower than body temp.
- Has the male ever fathered a child in a previous relationship? Has the female?
- Hx of recurrent ovarian cysts, endometriosis, leiomyomas, STDs, or PID?

Workup:

1. First, evaluate for ovulation.
 - The cheapest and simplest way is by temperature chart. The characteristic biphasic temp shift occurs in more than 90% of ovulating women. Ovulation results in a rise in BBT due to progesterone. 13-14 days post-ovulation, the temp falls and menses begins within 24-36 hrs.
 - A temp elevation of more than 16 days suggests pregnancy.
 - Ovulation detection kits, which test for urinary LH, are available and relatively inexpensive.
2. A normal semen analysis excludes a male cause for infertility in more than 90% of couples.
 - This test examines *quantity* and *quality* of seminal fluid:
 - a. Sperm count per mL
 - Normal fertile > 20,000,000
 - Subfertile between 5,000,000 and 20,000,000
 - Infertile < 5,000,000
 - b. Normal Volume \geq 1.5 mL
 - c. Viscosity: full liquefaction within 60 min
 - d. Motility: 50% motile within 4 hr of collection; higher motility suggests higher fertility
 - e. Differential: < 25% abnormal forms
 - The test is relatively cheap and is indicated as an early part of an infertility exam.
 - On physical exam, look for varicocele or signs of infection as a cause for oligospermia.
3. A hysterosalpingogram (HSG) is an x-ray study in which radiopaque dye is injected through the cervix into the uterus. Evaluates shape and size of the uterine cavity, in addition to defining tubal status. The dye SHOULD fill the uterus, tubes, and ultimately spill into the peritoneal cavity and pool in the cul-de-sac.
 - This test will detect congenital anatomical abnormalities from a simple septum to a complete reduplication of the reproductive organs.
 - Perform this test between days 5 and 10 of the cycle, as the test could interfere with a possible pregnancy event.

- If performed during menses, retrograde menstrual flow could be increased. This test may also be therapeutic, in that it may unclog a blocked tube.
- 4. Diagnostic laparoscopy allows visualization of the reproductive organs; direct inspection provides the most accurate assessment of pelvic pathology. This could reveal tubal damage from a previous infection (i.e. gonorrhea or chlamydia). Endometriosis, which can cause scarring and adhesions that immobilize the tubes, could also be evaluated. This method is complementary to HSG, not a substitute.
- 5. Blood tests for FSH, LH, prolactin, androstenedione, testosterone, TSH, T4, and progesterone may be indicated. Immunologically, the presence of anti-sperm antibodies in the male or female may be tested for.
- 6. A post-coital test may be performed. Here, you sample the cervical fluid on the day of ovulation about 2 - 8 hours after the couple has sex. This allows evaluation of coitus, ejaculation, sperm pickup, motility, storage, and cervical mucus.

Treatment:

1. Male factors: 40% of infertility
 - If the problem is *environmental*, behavioral counseling may be necessary. Discontinue hot tub use or activities calling for prolonged sitting. Get rid of the tight jeans.
 - Oligospermia due to hormonal abnormalities does not respond well to induction of spermatogenesis.
 - There is no known treatment for men with anti-sperm antibodies.
 - Varicoceles may be surgically repaired.
 - Note that marijuana use may cause decreased sperm production.
2. Female factors: 60% of infertility
 - Anatomic problems may be fixed surgically (30% of *all* infertility)
 - Anovulation is initially treated with clomiphene. This drug is a SERM that blocks estrogen receptors in the hypothalamus, thus inducing an increase in FSH release from the pituitary. Clomiphene (typically 50-100 mg/day) is begun on day 5 of menses, and given for 3-9 days. Ovulation should occur 14 days after the first day of clomiphene. This drug is effective and cheap. Letrozole (an aromatase inhibitor) has also been studied and has been determined to be first line for patients with PCOS. It is dosed at 5 mg given over the same period of time as clomid.
 - If oral agents fail, you may try administering FSH directly. Pergonal, a purified preparation of gonadotropins from the urine of postmenopausal women, is given parenterally. You **MUST** monitor serum estradiol carefully, and obtain frequent US of the ovaries.
 - Complications occur relatively frequently, and include preterm delivery, hyperstimulation of the ovaries, and multiple gestations
 - Assisted reproduction, such as egg/sperm donation, IVF, GIFT, etc, may be performed, but usually only by a reproductive endocrinologist.

Order Of Tests:

The following order is a general rule, but should be modified appropriate to individual circumstances:

1. BBT (basal body temperature) chart for ovulation. Possibly use of ovulation detection kit.
2. Serum levels of FSH, LH, TSH, prolactin, etc.
3. Semen analysis.
4. Post-coital test.
5. HSG.
6. Diagnostic lap.

41. Secondary Amenorrhea: 24 year-old Debra, G2 P1 Ab1, has not had a menstrual period since her last pregnancy 15 months ago.

Definition: failure to menstruate for a period of *6 months* in a woman of childbearing age who has previously menstruated *regularly*; >12 months in a woman with a h/o oligomenorrhea, or, the absence of menses for a total of three previous cycle intervals (for irregular menstruation).

Incidence is approximately 0.7%.

Oligomenorrhea: a reduction of menses, with the interval > 40 days but < 6 months.

Hypomenorrhea: a reduction in the number of days or the amount of menstrual flow.

Pathophysiology: normal menstruation requires the following components:

- (i) patent outlet (normal vagina and cervix)
- (ii) a uterus that responds to estrogen and progesterone stimulation
- (iii) ovaries that respond to gonadotropins with estrogen and progesterone production
- (iv) the pituitary and hypothalamus, which sense the hormonal milieu and respond with release of gonadotropins

Injury or other pathology to any of these components can cause amenorrhea.

Differential Diagnosis:

More Likely Causes in this patient (related to pregnancy and childbirth)--

- (i) Pituitary infarction (Sheehan's syndrome) due to postpartum hemorrhage; a > 75% destruction is usually required for a patient to be symptomatic. These patients may present with a *failure to nurse* and a loss of pubic/axillary hair; they may also have other symptoms of pituitary insufficiency. Rare
- (ii) Destruction of endometrium and uterine scarring (Asherman's syndrome). Causes include D&C (or any uterine surgery that interferes with endometrial cavity) due to retained products of pregnancy and *infection* of the uterine cavity.

Less Likely Causes--

- (iii) Pregnancy (*the* most common cause of amenorrhea, possible but less likely with this patient)
- (iv) Breastfeeding (usually only about 10 months amenorrhea)
- (v) Hypothalamic-pituitary-ovarian (HPO) dysfunction other than Sheehan's syndrome (includes weight loss, excessive exercise, obesity, drugs [marijuana, tranquilizers], neoplasms, chronic anxiety, anorexia, head injury, stress, prolactinoma, thyroid disease)
- (vi) Ovarian dysfunction (Savage syndrome, premature menopause, autoimmune, alkylating chemotherapy)
- (vii) Other (Cushing's disease, hypothyroidism, etc.)

History:

What was the outcome of her last pregnancy 15 months ago? was it successful?

Did she most recently have an abortion or miscarriage? Was a D&C necessary?

Were there any other complications of the pregnancy, delivery, or puerperium?

Was she able to nurse post-partum? Is she still nursing?

Has she experienced hot flushes in the last 15 months?

What is her menstrual history (regularity, etc.)?

The most important question, and will guide you through the rest of the history.

The patient has had 1 abortion, although it could have been with the earlier pregnancy. A recent D&C suggests endometrial scarring and compromised outflow tract (Asherman's syndrome)

Possibilities include postpartum hemorrhage w/ pituitary infarction (Sheehan's syndrome); uterine infection w/ scarring (suggests Asherman's syndrome); choriocarcinoma w/ alkylating chemotherapy (ovarian failure)

Failure to nurse w/ breast involution suggests a pituitary origin. If she is *still* nursing at 15 months, physiologic suppression is a possibility, but further workup is still necessary.

Estrogen deficiency caused by ovarian failure causes hot flushes, whereas estrogen deficiency caused by hypothalamic-pituitary dysfunction does not.

Establish a baseline (maybe she only menstruates every 15 months...)

Is she sexually active? Does she have a Hx of STD's?	Sexual Hx may give a hint of prior infections.
Does she use birth control? If so, what?	"Post pill" amenorrhea is generally < 6 months, so is <i>not</i> in the differential for this patient.
Does she have any other significant medical conditions? What medications is she on?	Antipsychotics, tricyclic antidepressants, antihypertensives [reserpine and methyldopa], anti-anxiety agents, Reglan, opiates, barbiturates, and estrogens can cause amenorrhea.
Does she have any significant family history of diseases?	A family Hx of pituitary, pancreatic, and parathyroid tumors (MEN-I) would suggest considering pituitary causes.

In the event the above history is non-contributory, it will be necessary to gather more detailed information, especially relating to illegal drug use, weight loss, exercise, mood/sleep changes, visual field changes, vaginal dryness, dyspareunia, hair growth, voice changes, etc

Physical exam:

Check for the presence of normal female anatomy and signs of pregnancy; anorexic vs. obese; hirsutism vs. loss of pubic hair; clitoromegaly (excess androgens); smooth vagina with dry endocervix (estrogen deficiency); galactorrhea (elevated prolactin, but could be normal if nursing). Also need to check BMI

Workup:

1. hCG level to rule out pregnancy (regardless of sexual Hx)
2. Thyroid function tests (T₄ and TSH) to rule out rare cases of asymptomatic hypothyroidism; a *low* TSH with *low* T₄ suggests pituitary insufficiency.
3. Serum prolactin levels; if positive a CT scan of the head should be performed
4. Serum FSH and LH to determine if there is primary ovarian failure (high values) vs. hypothalamic-pituitary dysfunction (low values)
5. Progestin administration to assess the level of endogenous estrogen and the competence of the outflow tract; if there is no withdrawal bleeding, the test may be repeated.
6. Specialized tests depending on the history (e.g., for a woman with a prior D&C, a hysterosalpingogram or hysteroscopy might be used instead of progestin administration to check for a competent outflow tract).
7. Other testing (e.g., adrenal function) as necessary

Management:

1. If outflow tract obstruction due to endometrial scarring is suggested (Asherman's syndrome), surgical correction is generally successful. Hormonal (estrogen) therapy may also be used to help the endometrium cover up the scarring.
2. If pituitary infarction (Sheehan's syndrome) is suggested, ovulation can be induced by exogenous administration of FSH and LH (e.g., Pergonal). However, women with this syndrome will exhibit pan-hypopituitarism and require continuous hormone replacement therapy (esp. estrogen and cortisone).
3. If the secondary amenorrhea is due to an underlying chronic disease (e.g., hypothyroidism), this disease should be treated first, as the menses usually return when the condition is corrected.
4. If primary gonadal failure is indicated (e.g., by elevated FSH and LH), estrogen replacement therapy will be necessary.

42. Secondary Infertility: 30 year-old Joyce had a successful term pregnancy 3 years ago. In spite of not using any contraception she has been unable to get pregnant again. She desperately wants a child and comes to your office.

Definitions:

- (i) *Infertility* is a couple's failure to conceive after 1 year of unprotected intercourse. This happens to around 15% of reproductive-aged couples in the US.
- (ii) *Primary* infertility means the couple has never conceived [see case 36 for more details]
- (iii) *Secondary* infertility means they have in the past, they just can't now (with the obvious question being "what changed?")

Approach:

- START SIMPLE: approach infertility by saying there could be something wrong with the ovary, the egg, the tubes, the uterus, or the sperm.
- Divide it into issues with anovulation, anatomical defects in the female genital tract or abnormal spermatogenesis.

Workup

- A. Initial evaluation includes:
 - 1) History, looking for any obvious cause (PID, tubes tied, etc.), always ask of male has fathered any children (FOB hx is also very important here, 50% due to male infertility issues), can help with initial w/u
 - 2) basal body temperature chart (rarely used now)- the temp will rise around 1 degree with ovulation (due to progesterone), then drop during menstruation. Serum progesterone can also be checked during the luteal phase to check for ovulation.
 - 3) Hysterosalpingogram (HSG) - Done in the radiology suite. Dye is squirted into the uterus, fluoroscopy is performed and pictures are taken, look for uterine abnormalities (septate or bicornuate or unicornuate or fibroids, etc) and for patent fallopian tubes ("fill (of the uterus) and spill (of the dye out of the ends of the tubes)"). Incidentally, HSG's themselves actually are supposed to increase fertility, apparently they "blow open" the tubes, making it easier for the egg to make it.
 - 4) Semen analysis - the least popular part of the workup for the men; however, simplest and cheapest to perform, can save women going through "million dollar" invasive workup. Looking for adequate volume of ejaculate, good numbers of sperm, with good motility. (like to have >20 million/mL w/ at least 60% motile sperm)
- B. If all of these are normal other tests can be performed, including exploratory laparoscopy, looking for endometriosis/adhesions/ anything else that might be wrong. More advanced testing includes postcoital cervical mucous testing, though less used now

Management:

- A. Anovulation -
 - Ovulation may be induced. Clomiphene citrate (CC), an antiestrogen at the hypothalamic and pituitary levels that induces increased FSH, is usually first option. CC leads to increased follicular activity.
 - If this doesn't work, FSH (expensive, commonly used for IVF) can be given. Both of these increase the risk of multiple gestation and ovarian hyperstimulation syndrome which is serious and requires hospitalization and close monitoring.
- B. Anatomic
 - Adhesions, blocked tubes, and uterine abnormalities can, at times, be corrected surgically. IVF and other advanced fertility techniques are also an option.
 - If hydrosalpinx present, reduces chance of pregnancy by 50%! Pathogenesis thought to be due to inflammatory fluid retrograde flow into uterus causing uninhabitable environment for implantation. Necessitates salpingectomy, if both tubes affected, patient will need bilateral salpingectomy and likely IVF to achieve pregnancy
 - *Keep in mind, no need for salpingectomy if tubes scarred but no evid of hydrosalpinx i.e. no fluid.*
- C. Spermatogenesis
 - Clomiphene can help 20% of the time.

- If unsuccessful, artificial insemination with ICSI or donor sperm or assisted techniques (such as GIFT and IVF) can be tried.

Section III: Gynecologic Oncology

2. Abnormal Pap Smear: Your office nurse shows you the PAP smear report on 40 year-old Harriet, G3 P3. It is consistent with moderate dysplasia.

Definitions:

1. PAP smear: Developed in 1940 by George Papanicolaou to examine single-cell morphology based on an exfoliative cell specimen scraped from the cervix at the time of routine pelvic exam. Its accuracy depends on the following:
 - (i) the degree of cervical inflammation and concomitant infection (which may obscure dysplastic changes)
 - (ii) adequacy of the specimen obtained (need endocervical cells)
 - (iii) expeditious fixation of the smear to avoid drying artifact.
 - (iv) The most accurate samples are obtained by using both the spatula and endocervical brush
2. Cervical carcinoma: considered a “controllable” cancer because--
 - (i) it has an identifiable precursor lesion (CIN) that may (but not always) progress to invasive cancer
 - (ii) there is an inexpensive and noninvasive screening test (Pap smear) and follow-up diagnostic procedure (colposcopy)
 - (iii) there are simple and effective treatments of the precursor lesion (cryotherapy, laser ablation, LEEP excision, and cold knife cone biopsy) with high cure rates.
 - (iv) It is also one of only a few cancers for which a vaccine exists that have a significantly impact on reducing an individual's risk.

Pathophysiology:

- **Cervical cancer and CIN are caused by HPV. (High risk types – 16,18,31,33 etc)**
- The histology of cervix is complex. Cervical epithelium is of two types: columnar (glandular) and stratified nonkeratinizing squamous epithelia.
- The area where the two type of epithelia meet is called the squamocolumnar junction (SCJ)
- The SCJ is clinically important because it is the site where over 90% of cervical neoplasias arise.
- As the uterus and cervix grow during puberty and adolescence, the SCJ everts from its position just inside the cervical os to become visible on the cervical surface. This area is called the transformation zone (TZ)
- The cells within the TZ represent the newest and least mature cells in the cervix, and it is thought that they are most vulnerable to oncogenic changes.
- HPV may or may not result in neoplastic change – Most HPV infections are transient. If HPV DNA is integrated into the host DNA, the expression of cell's regulatory genes may be altered, leading to transformation of the cells into intraepithelial lesions or cancer.

Epidemiology and Screening:

- (i) In the 1930's, the death rate for cervical CA was ~6x that for ovarian CA. With the advent of the PAP smear, this has steadily fallen, and the death rate from Cervical CA is now less than that for Ovarian CA.
- (ii) Risk factors for cervical neoplasia:
 - **cigarette smoking (counsel pts on this modifiable risk!)**
 - Early intercourse
 - Multiple sex partners
 - Early childbearing
 - HPV (types 16,18,31,33)
 - immunocompromise
 - high-risk' sex partners
 - intrauterine DES exposure
 - socioeconomic status, race

- venereal infection, HIV
- (iii) The average age at diagnosis for the 16,000 new cases annually is 50 years old.
 - It is presumed that the precursor CIN precedes invasive CA by about 10 years, but in some patients, precursor CIN did not exist at all.
 - 85% of cervical CA is squamous cell, 15% is adenocarcinoma (arising from the endocervical glands)
 - Other rare types: clear cell CA (in utero DES exposure), sarcoma, and lymphoma.
- (iv) Current guidelines for routine screening (Routine screening is for patients with normal Pap smears):
 - Start screening at age 21. NO EXCEPTIONS!
 - From 21-29, routine cytology every 3 years.
 - Cytology with HPV co-testing (tests for high-risk HPV subtypes) at age 30. If HPV co-testing is NEGATIVE, increase screening interval to every 5 years.
 - If prior screening has been normal, can discontinue screening at age 65 or at time of hysterectomy

Management:

A. PAP Smears

1. Atypical Squamous Cells of Undermined Significance (ASCUS)
 - Requires reflex HPV testing (except for ages 21-24, repeat cytology in 12months is preferred*)
 - If HPV negative, continue routine screening (considered normal Pap)
 - If HPV positive, management depends on age:
 - 21-24: repeat cytology in one year (2nd acceptable option to above)
 - If >25: colposcopy with directed biopsies +/- endocervical curettage (ECC)
2. Atypical Squamous Cells, cannot r/o high grade lesion (ASC-H)
 - Colposcopy with directed biopsies +/- ECC regardless of age.
3. Low-Grade Squamous Intraepithelial Lesion (LGSIL)
 - If age 21-24: repeat cytology in 1 year
 - If >25, colposcopy
3. High-Grade Squamous Intraepithelial Lesion (HGSIL)
 - Colposcopy with endocervical curettage (ECC) and directed biopsies regardless of age

Or

 - Immediate loop electrosurgical excision "See and treat." Under new guidelines, "see-and-treat" is not acceptable for patients age 21-24.
4. Atypical Glandular Cells of Undetermined Significance (AGCUS)
 - More likely to indicate endocervical or endometrial pathology
 - Management options--
 - (i) Colposcopy with sampling of endocervical canal (MUST do ECC)
 - (ii) Endometrial biopsy in women over the age of 35 with unexplained VB or in women with significant risk factors for endometrial cancer or hyperplasia (obesity, chronic anovulation, etc)
 - (iii) Cone biopsy

***Please refer to ASCCP guidelines for details.

Procedures:

1. Colposcopy: (diagnostic)
 - A colposcope is a sophisticated binocular stereomicroscope that can view small, often subtle dysplastic change on the cervix. During colposcopy, acetic acid is placed on the surface of the cervix to make dysplastic areas turn white.
 - Criteria such as white epithelium, abnormal vascular patterns, and punctate lesions help identify suspicious areas that may then be biopsied.
 - After sampling the colposcopically identified lesions, ECC is performed where a sample of the endocervix is taken and evaluated for lesions. ECC will be positive for dysplasia in 5-10% of women with a dysplastic Pap.

2. Cervical conization: (diagnostic and potentially therapeutic)
 - This involves taking a cone shaped biopsy of the cervix for either diagnostic or therapeutic purposes.
 - Two types:
 - 1) Cold knife cone (CKC) *advantage of being able to analyze margins
 - Uses a scalpel
 - Has to be done in OR with anesthesia
 - Higher blood loss
 - Usually performed to adequately diagnose cervical cancer if present to decide on radical hysterectomy vs. primary radiation (increased morbidity, decreased mortality if both done)
 - 2) Loop electrosurgical excision procedure (LEEP) *advantage of outpatient procedure
 - Usually done in office with local anesthesia (cervical block)
 - Uses a wire loop and monopolar cautery
 - Lower blood loss
 - Disadvantage is that cautery artifact can make it difficult to interpret margins
 - Some situations mandate diagnostic conization:
 - 1) Unsatisfactory colpo--cannot visualize the entire SCJ
 - 2) Positive ECC mandates conization with clear margins
 - 3) Discrepant Pap smear and biopsy results
 - 4) Microinvasion/CIS on biopsy
 - 5) Adeno CIS
 - 6) Persistent abnormal paps
3. Cryocautery: (therapeutic)
 - Used to treat low grade CIN, it uses a mushroom tipped stainless steel probe supercooled with liquid N₂. It involves a 3-min freeze, a 5-min thaw to allow edema to set in, and a second 3 min freeze to extent the damaged area deeper.
 - Cure rates for low grade CIN = 90%
 - Disadvantage: no tissue for pathology
4. Laser therapy: (therapeutic)
 - Can also be used for high-grade lesions as well as low grade, but it has cure rates similar to cryo.
 - Disadvantage: no tissue for pathology

Cervical Carcinoma

Cancer Staging

2. Cervical Carcinoma: Clinical staging involves histologic assessment of tumor sample, physical exam, and lab studies (IVP, cystoscopy, proctosigmoidoscopy, barium enema, LFTs, renal function)
 - Stage I: CA is strictly confined to the cervix
 - 1A: microinvasive
 - 1a1: measured stromal invasion <3.0mm in depth and extension of <7.0mm
 - 1a2: Measured stromal invasion of > 3.0 mm and <5.0mm with an extension of not >7.0mm
 - 1B: Clinically visible lesion limited to cervix
 - 1b1: clinically visible lesion <4.0 cm in greatest dimension
 - 1b2: clinically visible lesion >4.0 cm in greatest dimension
 - Stage II: CA extends beyond cervix but has not extended to pelvic wall; or, involves vagina but not as far as lower third
 - II_A Involves upper 2/3 of vagina
 - II_B Parametrial involvement
 - Stage III: CA has extended to pelvic wall; lower third of vagina; hydronephrosis
 - III_A Extends to distal 1/3 of vagina
 - III_B Extension to pelvic wall, hydronephrosis

Stage IV: CA has extended beyond true pelvis or involves bladder or rectal mucosa.

IV_A Bladder or rectal involvement.

IV_B Distant metastasis

Treatment

- (i) Stage 1a1 – treatment with excisional procedure of the cervix or simple hysterectomy
- (ii) Stage 1a2: modified radical hysterectomy with lymph node dissection
- (iii) Stage 1b1 (and select 1b2 and 2a, but rare): radical hysterectomy with lymph node dissection
- (iv) Bulky 1b2 and greater: External beam and brachytherapy radiation and concurrent cisplatin-based chemotherapy.

22. Ovarian Cancer : 54 yo G2 P2, comes to your office complaining of abdominal enlargement and bloating. Abdominal exam reveals shifting dullness, pelvic exam reveals diffuse masses.

Incidence:

1. Ovarian CA is the leading cause of death attributable to GYN cancers in the US
2. 12/1000 women will develop the disease, only 2-3 of the 12 will be cured
3. Incidence rises in the 5th decade and continues until the 8th decade. The postmenopausal pt is at greatest risk
4. Ovarian CA is silent in its early development. In 70% of the cases, the dz has spread beyond the pelvis by the time the dx is made
5. There is NO dependable screening test. CA125 CANNOT serve as a screening test.
6. Patients must have biannual pelvic exams during the postmenopausal years in order to detect ovarian enlargement.

Risk Factors:

1. white
2. nulliparous
3. late menopause
4. family hx
5. prolonged intervals of uninterrupted ovulation
6. low parity
7. decreased fertility
8. delayed childbearing if no OCPs used
9. BRCA I/II mutations

Pathophysiology:

1. Categorized according to site of origin
 - a. Epithelial (85%) - most common is *serous* cystadenoma; bilateral in 35-50% of cases
 - b. Sex cord stromal
 - c. Germ cell
 - d. Non-specialized stromal
 - e. Metastatic
2. Modes of spread
 - a. primarily via seeding through the peritoneal cavity by direct extension due to sloughing from the ovarian surface
 - b. distribution can follow circulatory path of flow (posterior cul de sac - paracolic gutters- R. hemidiaphragm - liver capsule - omentum)
 - c. lymphatic dissemination to pelvic and periaortic nodes in advanced disease
 - d. blocks diaphragm lymphatics causing ascites
 - e. As a terminal event, bowel obstruction caused by massive serosal involvement is common
 - f. Death usually occurs as a result of progressive encasement of abdominal organs causing anorexia, vomiting, and inanition.

Differential Diagnosis:

1. ovarian cancer
2. other malignancy (breast, liver)

3. benign cyst/benign ovarian neoplasm
4. tubo-ovarian abscess
5. endometriosis
6. pelvic or horseshoe kidney
7. Inflammatory or neoplastic disease of the bowel
8. Ectopic pregnancy

History:

- symptoms/signs are often nonspecific
- H/O?
 - 1) irregular menses
 - 2) mass effects of the bladder or rectum such as urinary frequency or constipation
 - 3) lower abdominal or pelvic fullness - usually a late manifestation caused by the tumor or ascites
 - 4) dyspareunia/urinary frequency
 - 5) pain(rare) secondary to torsion, rupture, hemorrhage
 - 6) abdominal distention is often the presenting c/o (caused by ascites)
 - 7) weight loss
 - 8) increased satiety

Physical Exam:

- Early detection requires frequent pelvic exams, especially after 40yo; solid, fixed pelvic masses are suggestive.
- If ascites and upper abdominal masses are present, ovarian CA is most likely

Workup:

- (i) Pap smear, endocervical curettage, possible endometrial Bx to R/O other malignancies
- (ii) Abdominal X-ray to R/O calcification of benign cystic teratoma - common in pt < 25yo
- (iii) Barium enema to R/O colon CA with ovarian mets
- (iv) Mammogram to R/O primary breast CA
- (v) Pelvic US to characterize the mass
 - a. uniloculated usually functional cysts, multiloculated usually CA
 - b. 95% of ovarian CA are >5cm
 - c. Multicystic with solid components and free fluid in the cul de sac are suggestive of CA
- (vi) CA125 levels- elevated in 85% of the patients with ovarian CA - used to follow course of dz
- (vii) Abdominopelvic CT and CXR are helpful in evaluating the extent of the disease
- (viii) Surgical Evaluation:
 - a. Exploratory laparotomy through a vertical abdominal incision allowing an evaluation of the upper abdomen.
 - b. Peritoneal washings from the pelvis and upper abdomen
 - c. Inspection of all peritoneal and diaphragmatic surfaces
 - d. Sampling of pelvic/obturator and para-aortic lymph nodes
 - e. Omentectomy
 - f. A wedge biopsy of the contralateral ovary to exclude occult disease in young women who wish to preserve fertility and who have an ovarian cancer apparently confined to one ovary

Staging:

1. Stage I: Limited to the ovaries
 - a. Stage 1A
 - Limited to one ovary; capsule intact; negative washings
 - b. Stage 1B
 - Limited to both ovaries; capsules intact, negative washings
 - c. Stage 1C (1-3)
 - Tumor either stage 1A or 1B but with
 - 1C1: surgical spill
 - 1C2: capsule rupture before surgery or tumor on surface
 - 1C3: malignant cells in ascites or washings
2. Stage II: Involvement of one or both ovaries with pelvic extension or primary peritoneal cancer

- a. Stage IIA: Extension or metastases to the uterus or tubes or both
- b. Stage IIB: Extension to other pelvic tissues
3. Stage III: Involvement of one or both ovaries extension into the peritoneal cavity and/or (+) retroperitoneal or inguinal nodes; superficial liver mets; tumor limited to the true pelvis but histologically proven malignant extension to the small bowel or omentum.
 - a. IIIA: Retroperitoneal nodes only
 - IIIA-1: Pelvic mets < 2cm
 - IIIA-2: Microscopic extrapelvic peritoneal involvement +/- retroperitoneal nodes
 - b. IIIB: Extrapelvic peritoneal mets < 2cm; +/- nodes, includes extension to liver capsule
 - c. IIIC: Mets > 2cm
4. Stage IV: Involvement of one or both ovaries with distant metastases
 - a. IVa: Pleural effusion with + cytology
 - b. IVb: Distant mets outside pelvis

Treatment:

1. Stage 1a : limited resection with staging biopsies
2. > Stage 1a:
 - a. TAH/BSO/infracolic omentectomy/ascitic fluid or peritoneal washings/peritoneal bx
3. Advanced stage:
 - a. Surgery: Remove as much tumor as possible (debulking). Goal is no residual disease (NRD) or at least an optimal debulking (< 1cm disease at each location)
 - b. Chemo Tx: Usually follows debulking surgery for advanced stage and early stage dz with poorly differentiated (grade 3) tumors, though more are performing neo-adjuvant chemo with surgery to follow.
 - Standard is cis-platinum and cyclophosphamide and/or taxol (Paclitaxel)
 - Carbo-platinum if renal neurotoxicity are too great from cisplatinium
 - Usual duration of tx is 6 courses, 3 weeks apart.

Prognosis:

1. stage 1 - 80-95% 5 yr. survival
2. stage 2 - 70% 5 yr. survival
3. advanced stage - 20% 5 yr. survival

46. Trophoblastic Disease: You recently performed a D&C on 28 year-old Darlene, G2 P1 now Ab1, 10 weeks gestation by dates. The gross findings were consistent with a molar pregnancy. The path report confirms your suspicion.

Definitions:

1. Gestational trophoblastic disease (GTD) is characterized by tumors that arise from the proliferation of placental trophoblast. It produces a distinct hormone marker, human chorionic gonadotrophin (hCG). It is the first solid tumor to respond to chemotherapy, and the cure rate approaches 100%.
2. Classification--
 - (i) Hydatidiform mole (molar pregnancy)
 - a. Complete, or classic
 - b. Incomplete, or partial
 - (ii) Invasive/persistent gestational trophoblastic neoplasia
 - associated with antecedent pregnancy (SAB, term, molar)
 - (iii) Choriocarcinoma
 - (iv) Placental site trophoblastic disease

Pathophysiology:

1. Benign Gestational Trophoblastic Disease:
 - (i) Complete (classic) mole:
 - Accounts for 95% of hydatidiform moles

- 20% of complete moles will lead to persistent disease.
 - 46, XX karyotype with both genes being of paternal origin as a result of duplication of a 23 chromosome haploid sperm in an empty ovum.
 - 3-13% of complete moles are 46, XY from *dispermic* fertilization of an empty ovum.
 - A 46, YY conceptus is not viable.
 - Dispermic complete moles has a 4-fold increase in residual gestational trophoblastic disease compared with monospermic moles.
 - Uterine size usually greater in size than expected by dates
- (ii) Partial moles:
- 5% of hydatidiform moles
 - Commonly have a triploid (69-chromosome) karyotype.
 - A normal haploid (23, X) ovum undergoes dispermic fertilization to form a 69, XXY (70%), 69, XXX (27%), 69, XYY (3%) conceptus.
 - 5% of partial moles will lead to persistent disease.
 - usually associated with an embryo—usually dies by 9 weeks but may survive to term
2. Malignant Gestational trophoblastic neoplasia (GTN)
- (i) malignant GTD, which arises from trophoblastic elements of the developing blastocyst, retains the invasive tendencies of the normal placenta, and remains able to secrete hCG.
- (ii) GTN can be either metastatic or nonmetastatic.
- These include invasive moles, placental trophoblastic tumors, and choriocarcinoma.

Incidence:

1. Benign GTD occurs in 1 of 1200 pregnancies in the U.S. and up to 1 of 120 pregnancies in other parts of the world (e.g. East Asia).
2. Malignant GTD, develops in 20% of moles, occurs in 1 of 20,000 pregnancies in the U.S. and may follow:
 - a. Normal pregnancy (50%)
 - b. Hydatidiform mole (25%)
 - c. Spontaneous abortion or ectopic pregnancy (25%)

Risk factors:

1. Maternal age
 - Increased risk in women over age 35
 - Risk is **5X greater** in women over age 40
 - Risk may be increased in teenagers
2. Previous molar pregnancy: 10X increase in risk of having a subsequent mole.
3. Paternal age: increased risk if father is over age 45.
4. Nulliparity

Signs and symptoms:

1. *Gestational hypertension* in the first-half of pregnancy is virtually diagnostic of a mole.
2. *Hyperthyroidism* is secondary to the high level of hCG, which behaves like TSH.
3. *Bleeding* usually occurs in the first trimester and may be accompanied with the *passage of vesicular tissue*.
4. *Uterus is often larger* than expected in terms of the last menstrual period.
5. *Nausea and vomiting* occur in about 1/3 of pts, very common for these patients to have hyperemesis gravidarum (due to high levels of HCG).
5. *Abdominal pain* secondary to theca-lutein cysts is found in 15% of pts because the molar pregnancy produces excessive hCG, which stimulates excessive growth of the ovaries.
6. *Vaginal passage* of hydropic vesicles
7. *B-HCG* greater than expected

Workup:

1. Complete history and physical exam
2. Ultrasound (should see a “**snowy field**” or “**snow storm**” appearance if molar pregnancy)
3. Measurement of serum hCG level (>100,000 mIU/ml for molar pregnancies)

4. Hepatic, renal, and thyroid function tests

Treatment:

1. Benign Disease: (Complete/Partia)
 - (i) Preferred method of treatment is evacuation of the uterus by suction and curettage. Hysterectomy is an alternative in selected patients.
 - (ii) Follow-up:
 - a. Weekly measurements of serum hCG levels until levels are normal and then monthly for 6 consecutive months.
 - b. If levels plateau or rise during the 6 month interval, patient should be evaluated for metastasis (Virtually all episodes of malignant sequelae occur within 6 months of evacuation).
 - c. Patient must use effective contraception for the entire interval of hormonal follow-up.
2. Gestational Trophoblastic Neoplasia (GTN)
 - (i) Invasive/Persistent hydatidiform mole: has features of hydatidiform mole, but edematous chorionic villi persist with invasion into the myometrium and continue to produce hCG. Rarely metastasize. Diagnosed when serum BHCG plateaus, rises, or persistence of detectable HCG for more than 6 months after molar evacuation
 - a. First-line therapy is methotrexate. Since MTX is secreted by the kidney, urine creatinine levels must be normal before each treatment. Patients whose levels of hCG plateau or rise during therapy should be switched to alternative therapy.
 - b. Alternative therapy: actinomycin-D or etoposide
 - c. Early hysterectomy shortens the duration and amount of chemotherapy needed to produce remission.
 - d. Failure of alternative therapy or the appearance of new metastasis mandates the use of multiagent chemotherapy (MTX, actinomycin-D, cyclophosphamide, vincristine).
 - (ii) Choriocarcinoma/Placental site trophoblastic disease:
 - assign risk from WHO score
 - Low risk: single agent chemotherapy
 - High risk: multiagent chemotherapy
 - (iii) Risk for choriocarcinoma is 2-19% for women with a molar pregnancy.
 - (iii) Diagnostic Evaluation for metastatic disease: (performed if hCG levels either plateau or continue to rise)
 - a. Chest X-ray
 - b. Ultrasound or CT of abdomen and pelvis
 - c. Measurement of hCG levels in CSF
 - d. Angiography of selected pelvic organs
 - (iv) Common sites of metastasis:

- Lung:	80%
- Vagina:	30%
- Pelvis:	20%
- Brain:	10%
- Liver:	10%
- Bowel, kidney, spleen:	< 5%
- Other:	10%
 - (v) Staging of GTN:
 - Stage I: limited to uterus (100% cure rate)
 - Stage II: extends outside the uterus, limited to the genital structures (88% cure rate)
 - Stage III: extends to the lungs (90% cure rate)
 - Stage IV: all other metastatic sites (40% cure rate)

Section IV: Infectious Disease

40. Salpingitis: E.R. calls you to see 21 year-old Michelle, G0 P0 complaining of severe pelvic pain. She has a 103 °F fever with exquisite tenderness to cervical motion.

Definition:

- Salpingitis is an inflammation of the fallopian tubes.
- PID makes up a spectrum of inflammatory disorders of the upper genital tract, including salpingitis, endometritis, tubo-ovarian abscess and pelvic peritonitis.

Pathophysiology:

- Sexual activity is responsible for moving organisms from the lower genital tract to the upper genital tract. Current evidence supports a multibacterial etiology of Acute PID.
- Organisms often involved are *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, *Mycoplasma hominis*, *Urea urealyticum*, *Actinomyces israelii* (especially if an IUD has been present several years-rare but pathognomonic), anaerobic bacteria and facultative gram-negative rods.

Differential Diagnosis:

1. Acute Appendicitis
2. UTI
3. Adnexal torsion
4. Endometriosis
5. Bleeding corpus luteum
6. Ectopic pregnancy
7. Ruptured ovarian cyst
8. Inflammatory bowel disease
9. Degenerating fibroids
10. Spontaneous abortion
11. Diverticulitis

History:

- The usual history as for any STD is useful. Know that acute PID can be aggravated by menses, sexual intercourse, strenuous physical activity and even a pelvic exam.
- Common Presenting Complaints:
 - 1) Lower quadrant pain, often bilateral
 - 2) Recent onset of menses (esp. with chlamydial and gonococcal infections)
 - 3) Dysuria
 - 4) Purulent vaginal discharge
 - 5) Nausea and/or vomiting
 - 6) Fever and shaking chills

Physical Exam:

- Patient is usually febrile and tachycardic with normal BP. There is generalized lower abdominal tenderness w/o palpable masses.
- On spec exam, there may be purulent discharge and inflamed cervix
- On bimanual exam, *cervical motion tenderness* and *bilateral adnexal tenderness* are present without masses.

Workup:

- 1) Pregnancy test - r/o ectopic
- 2) CBC - neutrophil leukocytosis indicates acute infection (not totally reliable since less than 50% of cases will have WBC > 10,000)
- 3) ESR – elevated, nonspecific
- 4) Urinalysis - r/o UTI
- 5) Cervical culture - esp. for Chlamydia and Gonorrhoeae
- 6) Culdocentesis - secondary test; if purulent fluid obtained, culture will assist in choice of abx.
- 7) Pelvic Ultrasound - may help define adnexal masses, identify an intrauterine or ectopic pregnancy or help locate/confirm IUD
- 8) Laparoscopy - if dz. Process is unclear, it is the ultimate way to establish diagnosis though not necessary in PID, especially if pt is improving on abx

Management:

- A. Hospitalization for acute salpingo-oophoritis (PID) is indicated in these situations:

- 1) Dx is uncertain
 - 2) Surgical emergencies (i.e. Appendicitis or ectopic) are to be ruled out
 - 3) Pelvic abscess is suspected
 - 4) Severe illness precludes outpatient management
 - 5) Patient is pregnant
 - 6) Patient is unable to tolerate or follow outpatient management
 - 7) Patient failure to respond to outpatient management
 - 8) Clinical follow-up after 48-72 hr. of antibiotic therapy cannot be arranged. *If patient shows no response in this time frame, surgery must be considered.*
 - 9) HIV +
- B. Outpatient Treatment Options:
- 1) Cefoxitin 2.0 gm IM, with probenecid 1gm PO
 - 2) Ceftriaxone 250 mg IM
 - 3) Equivalent cephalosporin plus Doxycycline 100 mg PO bid for 10-14 days
- C. Inpatient Treatment Options:
- 1) Cefotetan 2gms IV q12hours plus Doxycycline 100mg po/IV Q12hours
 - 2) Gentamycin/Clindamycin

43. Sexually Transmitted Diseases: 21YO Trudy, G0 P0, presents to your office complaining of exquisitely tender vulvar lesions. On pelvic examination you confirm her findings. You also note periurethral, vaginal, and cervical ulcerative lesions. Inguinal nodes are palpable and tender bilaterally. Temperature is 101.2 F.

Differential Diagnosis: consists of STDs that cause genital lesions

Most likely cause--

1. **Herpes genitalis** (85% HSV2, HSV1 usually oral; however, increased prevalence of genital HSV1 among adolescents)
 - a. Symptoms:
 - (i) prodromal phase of mild paresthesias and burning in affected areas several days before outbreak of vesicles
 - (ii) dysuria from exquisitely painful vulvar lesion may cause urinary retention
 - b. Signs:
 - (i) painful vesicular lesions, that lyse and progress shallow, painful ulcers with a red border found on vulva, vagina, cervix, perineal, and perianal skin that resolve within 5 to 10 days.
 - (ii) Primary infections also characterized by malaise, low grade fever, and inguinal adenopathy in 40% of pt's
 - c. Dx:
 - (i) viral cultures taken by swab of a lesion, is most sensitive, comes back in < 48hrs
 - (ii) smears with Wright's stain to see giant cells with acidophilic intranuclear inclusion bodies
 - d. Management:
 - (i) directed towards management of local lesions and symptoms
 - (ii) Sitz baths, diluted Burow's solution, and topical anesthetics may be used to symptoms
 - (iii) topical abx for secondary (Neosporin) infections
 - (iv) oral Acyclovir or Valtrex can be used for therapy (initial outbreak, recurrent outbreaks, suppression)
 - (v) hospitalization for IV Acyclovir may be required for severe outbreak immunocompromised pt's/unable to urinate

- (vi) warn pt of need for c/s in case of active, p lesions during delivery, to prevent perinatal infection of baby
- (vii) 30% of pt's develop recurrences, but are usually milder and of shorter duration

Other possible causes--

2. Chancroid (*Haemophilus ducreyi*)

- a. Symptoms:
 - (i) painful soft chancres, foul smelling with grayish base (papule/pustules) on vulva
 - (ii) usually 1-3 in number
 - (iii) duration of weeks
- b. Signs: tender lymphadenopathy
- c. Dx: cx and gram stain smears
- d. Tx: Erythromycin 500mg QID for 10 days

3. Primary Syphilis (*Treponema pallidum*)

- a. Symptoms/lesion:
 - (i) a single, *usually painless*, chancre appears at site of primary entry of organism 10-60 days after infection (@ vulva, vagina, cervix, anus, rectum, pharynx, lips, fingers), healing spontaneously within 3-9wks)
 - (ii) Signs: firm nontender adenopathy
- b. Dx:
 - (i) Spirochetes seen on darkfield microscopy
 - (ii) Serology VDRL, RPR, usually negative during primary infection
- c. Tx:
 - (i) PCN G (preferred even in pts with PCN allergy, try to sensitive pts first!)
 - (ii) Other options: Tetracycline, or Erythromycin (pregnant pt's if can't use PCN)

4. Granuloma inguinale

- a. Symptoms/signs:
 - (i) single or multiple red papules with pseudoadenopathy that ulcerate
 - (ii) rare to cause pain
 - (iii) advanced stage characterized by fibrosis, scarring, and keloid formation
- b. Dx:
 - (i) by tissue smears. Donovan bodies (=encapsulated bipolar staining bacterium of reddish color found within large mononuclear cells) seen with Wright or Giemsa stain
- c. Tx: Tetracycline 500mg q6 for 3wks

5. Lymphogranuloma venereum (*Chlamydia trachomatis*)

- a. Symptoms/Signs:
 - (i) generalized malaise, HA, and fever
 - (ii) painless vulvovaginal vesicle/ulcer, progresses to bubo
 - (iii) tender, suppurative nodes
- b. Dx: clinical, complement fixation test for antibodies
- c. Tx: Tetracycline 500mg q6 for 3wks

6. Molluscum contagiosum (*Poxviridae*)

- a. causes raised papules with waxy core, dx by presence of inclusion bodies
- b. treated with dessication, cryotherapy, curettage

7. Parasites (Scabies)- can cause genital lesions

- a. causes intense itching especially around areas of skin folds (wrists, underarms, etc)
- b. treated with Lindane 1%

8. HPV- painless condylomas, treated with cryotherapy, or trichloroacetic acid

History:

- take thorough sexual history
- ask about signs and symptoms listed above, ask about symptoms of vaginal discharge as relates to Chlamydia, Gonorrhea, Candida, Trichomonas etc.
- 20-50% of pt's have at least one more coexisting STD infection

P.E. & Work Up:

1. do thorough pelvic exam, look for lesions, vaginal discharge. Inspect perineum and perianal areas, inspect inguinal region for rashes, lesions, and adenopathy; for completeness inspect oral cavity and cervical nodes.
2. obtain cultures (for GC and Chlamydia) and smears!
3. wet prep (KOH whiff test +, and clue cells for BV), KOH prep of Candida hyphae

Management:

1. treat underlying causes, as stated above
 - (i) Flagyl for concomitant Trichomonas or Bacterial vaginosis
 - (ii) Ceftriaxone/or Doxycycline for Gonorrhea
 - (iii) Miconazole/Clotrimazole/or Butoconazole for Candida.
2. As with any STD, explain to pts the importance of safer sex, assess if their current practices have put them at increased risk for other STDs such as HIV, HepB, and HepC, (and recommend that they be tested for these); also emphasize the communicable nature of these diseases, and that it is imperative that any of their *partners* must also be treated to break the cycle of reinfection

Section V: Prenatal Care**3. Anemia in Pregnancy: 19 year-old Anna, G2 P1, at 15 weeks gestation is found on routine prenatal CBC to have: hemoglobin 9.0, hematocrit 26.3, MCV 75, RDW 18.**

Definition: Anemia in pregnancy is generally defined as a hematocrit less than 30% or a hemoglobin less than 10.0 g/dL.

Pathophysiology:

1. During the course of pregnancy, there is a significant expansion of plasma volume more so than RBC mass. On average, there is a 1000 mL increase in plasma volume, but only a 300 ml increase in red cell mass. Thus, the HCT demonstrates a 'physiologic' decrease, but it is not actually an anemia. However, due to the monthly blood loss prior to pregnancy, and current dietary practices, women enter pregnancy on the verge of iron deficiency. When faced with plasma expansion plus the fetal nutritional requirements, mothers frequently fall into iron-deficiency anemia (over 90% of the anemias seen in pregnancy). Because it is so common, a trial of iron therapy is given to all anemic mothers prior to extensive workup.
2. Other causes of anemia in pregnancy include folate deficiency (due to nutrition or medications like dilantin, nitrofurantoin, pyrimethamine, or trimethoprim); mixed iron and folate deficiency; vitamin B12 deficiency (rare, but usually seen in women with malabsorption secondary to sprue, pancreatic disease, Crohns, ulcerative colitis, or surgical resection); hereditary hemolytic anemias (spherocytosis, glucose 6-phosphatase deficiency, pyruvate kinase deficiency); hemoglobinopathies such as sickle-cell and the thalassemias.

Workup:

1. Things to look for in the history:
 - a. nutrition
 - b. evidence of pica (ingestion of nonedible substances like starch, ice, dirt; more common in African-Americans)
 - c. a family history of hemolytic anemia or hemoglobinopathies.
2. Laboratory tests: Evaluation should begin with Hgb electrophoresis, CBC with diff and Ferritin. Can also consider B12/Folate levels

CBC with diff.

-Note the WBC and platelet count. Pancytopenia is suggestive of a bone marrow disorder
-MCV

Mean Corpuscular Volume (MCV)

Microcytic anemia (MCV < 80): Iron deficient, thalassemia, anemia of chronic disease, and lead poisoning

Normocytic anemia (MCV 80-100): Hemorrhagic, early iron deficiency anemia, anemia of chronic disease, endocrine dysfunction, hereditary spherocytosis, paroxysmal nocturnal hemoglobinuria

Macrocytic anemia (MCV >100): Folic acid deficiency, B12 deficiency, drug induced hemolytic anemia, reticulocytosis, liver disease

Lab values associated with diseases:

- a. Iron deficiency:
 - (i) microcytic, hypochromic, low MCV, low serum iron
 - (ii) increased TIBC, low serum ferritin
- b. Folate deficiency: hypersegmented neutrophils, high MCV
- c. B12 deficiency: high MCV as well
- d. Mixed Iron/Folate deficiency: normocytic/normochromic
- e. Hereditary hemolytic anemias: look for spherocytes, etc.
- f. Hemoglobinopathies:

- (i) Thalassemia trait = microcytic, hypochromic, but normal iron and TIBC, high HbA2.
- (ii) HbSS/SC/Thalassemias = look for sickle cells, target cells, diagnosis requires electrophoresis.

Management of Anemias:

Microcytic Anemia

1. Iron deficiency: Primary cause of Anemia in pregnancy.
 - Oral Iron: First line therapy. (325 mg FeSO4 bid)
 - Parenteral Iron Therapy: For severe iron deficiency when non-compliant or abnormal absorption. Usually as inpatient setting (Iron Sucrose vs Iron dextran)

Macrocytic Anemia

1. Folate deficiency: Treated with 1 mg folate qd; or removal of competing medications.
2. B12 deficiency: Treated with IM B12 q month.

Hemoglobinopathies

1. Hemoglobinopathies: Conservative management (hydration, oxygen, analgesia)
 - Transfusions are reserved for complications of hemoglobinopathies (congestive heart failure, sickle-cell crises, and severely low levels of hemoglobin). It should also be noted that women with sickle-cell disease are at higher risk to develop UTIs, so watch for these.

6. Discrepant Fundal Size: 38 year-old Emma, G5 P1 Ab3, is referred to you for evaluation at 32 weeks gestation by dates. (a) Her fundal height is 27 cm. (b) Her fundal height is 40 cm.

A. 27 cm FH @ 32 weeks gestation.

Definition:

- Intrauterine growth restriction (IUGR) is fetal or neonatal weight below the 10% for a given gestational age of AC lag of more than 4 weeks.
- These infants are at an increased risk for perinatal morbidity and mortality including meconium aspiration, asphyxia, polycythemia, hypoglycemia, and developmental delay

Etiology:

1. Causes
 - a. **Maternal factors:**
 - poor nutrition
 - tobacco use
 - substance use
 - cyanotic heart disease
 - pulmonary insufficiency
 - severe anemia
 - sickle cell disease
 - auto-immune diseases
 - toxins (warfarin, anti-convulsants, folic acid antagonists)
 - radiation exposure
 - uterine malformations (didelphys)
 - multiple gestations
 - b. **Placental factors (leading to placental insufficiency)**
 - chronic hypertension
 - chronic renal disease
 - gestational hypertension/pre eclampsia
 - single umbilical artery
 - velmaentous cord insertion/marginal cord insertion
 - placental hemangioma
 - c. **Fetal inadequate usage of substrate**
 - intrauterine infection (rubella, toxo, CMV, varicella, etc)

- congenital anomalies
- 2. Symmetric IUGR
 - a. occurs before 16 weeks and involves inadequate growth of **both** the head and the body.
 - b. most commonly associated with infections or congenital fetal anomalies including trisomies and NTD, also heavy drug use.
- 3. Asymmetric IUGR
 - a. occurs later in pregnancy after 32 week.
 - b. Brain size is spared so the head size is **proportionally larger** than the abdominal size. BPD is normal.
 - c. caused by uteroplacental insufficiency
 - maternal factors: gHTN/preE, renal or cardiac disease, hemoglobinopathies, lupus
 - uterine factors: morphologic abnormalities
 - placental factors: infarcts, thrombosis, partial abruption, previa, or multiple gestation

Diagnosis:

- The first step in diagnosis recheck dating, confirm LMP
- It is also important to know her previous fundal heights to note a change
- If the fetus is still small for dates the next step would be an ultrasound.
- Ultrasound is indicated whenever the fundal height lags more than **3cm behind** a well established gestational age, or whenever the mother has a well established high risk condition.

Management:

1. If IUGR is diagnosed efforts should be taken to modify associated factors such as cessation of smoking and improved nutrition.
2. Serial assessment:
 - a. Regular fetal monitoring with BPP's q weekly, dopplers at diagnosis. Fluid and growth starting at 28 weeks.
 - b. Continue the pregnancy as long as testing as above is reassuring/
 - c. If the BPP is non-reassuring, consider delivery or admission for betamethasone.
 - d. Delivery should be individualized, and are dependent on GA, AFV, fetal testing and cervical exam.
 - e. The gestational age of the fetus should always be considered when making the decision to deliver early (i.e. the complications of prematurity with GA < 32 weeks may be worse than the current poor intrauterine environment).
3. Delivery:
 - a. During labor these high risk patients must be monitored to detect earliest evidence of distress, since the fetoplacental unit does not have a normal reserve.
 - b. In the presence of recurrent abnormal fetal heart rate patterns, which are unresponsive to traditional treatment, delivery by C-section is indicated.
 - c. After birth the infant should be examined to rule out anomalies and infection.

B. Large for gestational age:

Definition: > 90% for gestational age

Grade I: 4000-4499g

Grade II: 4500- 4999g

Grade III: > 5000g

Differential Diagnosis:

- Poor dating
- Excessive maternal weight gain
- Macrosomia
- Polyhydramnios
- Multiple gestation
- Molar pregnancy

Management:

1. Poor Dates
 - As always the first step is to verify dates
 - An ultrasound should be done next and would differentiate between other causes.
2. Macrosomia
 - Fetus weighing more than 4000g or is above the 90th percentile is considered to be excessive in size.
 - It may result from genetic determinants, maternal diabetes, or post-term gestation.
 - Consider delivery via c-section based on extent of macrosomia .
3. Polyhydramnios
 - AFI > 25 cm. Detected by US
 - Complications include increased risk of pre-term labor, maternal respiratory discomfort, umbilical cord prolapse at rupture, and fetal malpresentation.
 - Causes include fetal anomalies like anencephaly, duodenal atresia, and tracheoesophageal fistula. (these impair fetal swallowing ability and ↓ uptake of fluid).
 - Hydrops: the fetus and placenta become edematous as a result of fetal CHF, hypoproteinemia, or hypoalbuminemia, resulting in transudation of placental fluid and possible increased production of fluid.
4. Multiple Gestation
 - Detected by ultrasound
 - patient should be seen weekly starting during the mid-second trimester
5. Molar Pregnancy
 - Usually presents with bleeding and a greatly elevated beta-HCG.
 - By ultrasound one would see a snowstorm effect or vesicular pattern.

11. Fetal Demise: 28 year-old Mary, G2 P1, at 30 weeks gestation (confirmed by a 15 week ultrasound) comes to L & D due to no fetal movements for 2 days.

Definition: fetal death prior to labor *after 20wks gestation or fetal weight >350g* if GA unknown. Complicates 1 in 160 pregnancies in the US.

Etiology/Risk factors: *Most prevalent risk factors are non-Hispanic black race, nulliparity, AMA, & obesity*

1. Idiopathic
2. Congenital & karyotypic abnormalities
3. Growth restriction/placental abnormalities
4. Maternal DM, SLE, renal dz, thyroid dz, & cholestasis
5. HTN/PreE
6. Infections like parvovirus B19, syphilis, streptococcal infection, listeria
7. Smoking
8. Multiple gestation
9. Cord accidents
10. Antiphospholipid antibodies
11. AMA >35yo

Workup:

- i) high clinical suspicion when pt reports no fetal movement, especially if uterus is small for dates
- ii) no fetal heart tones by Doppler
- iii) ultrasound confirms no movement or FHT's, collapse of fetal body with overlapping of cranial bones (Spalding's sign) b/c of brain liquefaction

Management:

- i) watchful expectancy- 80% of pt's have spontaneous labor w/in 2-3 wks of demise

- ii) induction of labor- indicated b/c of emotional burden of carrying dead fetus, possible infection, and risk of DIC if fetus is carried for >5wks.
- iii) 12-24wks- use vaginal misoprostol v. high-dose oxytocin infusion for induction of labor
- iv) >24wks with favorable cervix- IV oxytocin (use of PGE2 carries risk of uterine rupture).
- v) >24wks with unfavorable cervix- use of cervical foley before oxytocin infusion may enhance cervical ripening.
- vi) monitor for coagulopathy- check weekly fibrinogen; fibrinogen <300mg/dl indicates consumptive coagulopathy.
- vii) emotional support
- viii) determine cause individualized but consider -TORCH studies; listeria cx; anti-cardiolipin ab; maternal drug screen; fasting blood sugar; for congenital abnl get chromosomal analysis, total body radiography, and autopsy. Amniocentesis prior to induction of labor provides the best chance of obtaining viable tissue for genetic testing.
- ix) subsequent pregnancies are managed as high risk

13. First Trimester Bleeding: 22 year old Sally, G1 P0, at 10 weeks gestation by dates comes to the ER complaining of vaginal bleeding.

Definitions:

Abortion termination of a pregnancy <20 weeks or a fetal weight of <500gms (this includes spontaneous and elective abortion)

Threatened Abortion Uterine bleeding without cervical dilatation with evidence of living fetus (+CA), <20 wks.

Inevitable Abortion Uterine bleeding with cervical dilatation. No expulsion of tissue at <20wks

Incomplete Abortion Passage of some products of conception through the cervix at <20 wks, cervix still dilated on exam.

Complete Abortion Spontaneous expulsion of all products of conception from the uterus at <20 wks, cervix closed on exam. Prior documentation of IUP now with nothing visualized in uterus.

Missed Abortion Fetal death at <20 weeks without expulsion of tissue (i.e. no CA seen on TVUS with IUP), cervix closed on exam.

Induced Abortion Intentional termination of pregnancy at <20 wks

Pathophysiology:

1. Approximately 20% of women bleed during the first trimester with a wide variation in the DDx.
2. Approximately ½ to 2/3 of women who bleed from the uterus in the first trimester will miscarry or abort the fetus.
 - a. Fetal Factors that increase spontaneous abortion
 - Genetic abnormality of the conceptus (**most common cause for first trimester loss**)
 - b. General maternal factors that increase spontaneous abortion risk
 - (i) Infections- rubella, Listeria monocytogenes, CMV, Treponema pallidum, Mycoplasma, and Toxoplasmosis
 - (ii) Environmental exposure- >20 cigarettes /day, and >7 standard alcoholic drinks per week
 - (iii) Psychological Factors
 - (iv) Systemic Disorders- DM, hypothyroidism, and SLE
 - (v) Local maternal factors-uterine abnormalities such as cervical incompetence, congenital abnormalities of the uterine fundus, and acquired abnormalities of the uterine fundus (submucosal fibroids)

Differential Diagnosis:

1. Different types of Abortion/miscarriage
2. Ectopic pregnancy (usually presents with pain)
3. Vaginal and cervical lesions (vaginitis or cervicitis)
4. Increased friability of cervical tissue – i.e. s/p cervical exam or sexual intercourse

5. Molar pregnancy
6. Cervical/vaginal neoplasm

History:

- 1) Quality of bleeding
- 2) Quantity of bleeding (spotting vs. soaking)
- 3) Onset and duration
- 4) Pelvic pain
- 5) Fever
- 6) Drug history
- 7) Smoking history
- 8) Alcohol history
- 9) Sexual history
- 10) Uterine surgeries
- 11) Uterine abnormalities
- 12) Incompetent cervix (in some patients it is the result of trauma; also, prior cervical surgery such as conization or LEEP)
 - * The history given is inadequate since we know nothing about the bleeding or the duration. We should complete a complete sexual history including the date of last intercourse. A history of any STDs would be helpful as would any PMH available as well as social and family history.

Physical Exam:

- 1) Assess hemodynamic status – vital signs
 - a) Heart rate, BP, color, skin turgor, skin temperature (all associations of shock)
- 2) Complete PE – cardiovascular, abdominal
- 3) Pelvic Exam Bleeding from cervical os (actively bleeding, brisk/slow, amount)
 - a) Cervical dilatation
 - b) Cervical discharge
 - c) Cervical erosions
 - d) Bimanual exam: uterine tenderness and adnexal tenderness
 - * All of the above would be necessary for this patient

Work-up:

- 1) Serial HCG to determine pregnancy vs. molar pregnancy vs. abnormal gestation (levels of hCG should rise ~ 53% in 48 hrs in a normal viable intrauterine pregnancy for the first 7-8 wks after the LMP; with abnormal gestation, the levels rise more slowly, plateau or decline)
- 2) CBC with diff
- 3) TVUS
- 4) Cervical Cultures for GC, Chlamydia...
- 5) Rh status
- 6) Type and screen for PRBC
 - * All of the above would be necessary for the above patient.

Management:

1. Threatened abortion: given bleeding precautions, outpatient follow up
 - a. If Rh-, Rhogam administration needed
2. Inevitable or Missed Abortion: dx via US (absence of FHR and/or declining serial hCG levels)
 - a. Counsel regarding surgical vs medical vs expectant management
 - b. If medical route, can give Mifepristone (PGF₂) or Misoprostol (PGE₂) suppository vaginally to induce uterine ctx /expulsion
 - c. If surgical route: D&C
 - d. May give doxycycline pre- and postoperatively for antibiotic ppx
 - e. f/u pathology
 - f. If expectant route: follow up in clinic for documentation of passed pregnancy (i.e. neg UPT, TVUS)
3. Incomplete abortion: remove product of conception in cervical canal

- a. Suction D&C if unable to remove all products or if patient is actively bleeding
4. Complete Abortion: Follow patient expectantly with serial hCG until 0
 - a. Rh- Rhogam
5. Ectopic pregnancy: diagnosed with aid of quantitative HCG and TVUS
 - a. laparoscopic surgery to remove or methotrexate in appropriate patients
 - 1) Candidates for methotrexate:
 - (a) Reliable patient
 - (b) B-hcg <5,000
 - (c) Hemodynamically stable with no concern for rupture
 - (d) No fetal cardiac activity
6. Cervicitis or vaginitis: treat the infection with Flagyl, doxycycline, Erythromycin...
7. Molar pregnancy: D&C for pathology. Be careful of bleeding—can manage with oxytocin or other agents such as methergine/hemabate.
 - a. F/U with serial hCGs and prevention of pregnancy with birth control
 - b. Chemo with methotrexate or actinomycin D is controversial, since only about 20% require chemo and the cure rate is almost 100% when adequate F/U is given
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14. Glucose Intolerance in Pregnancy: 22 year old Carol, G1 PO, at 23 wks gestation by dates is referred to you with the following 3 hour 100g OGTT results: F 102; 1 hr 195; 2 hr 180; 3hr 140.

Epidemiology:

1. Diabetes should be strongly suspected in women who have:
 - a) A strong family history of diabetes
 - b) Previously given birth to large (i.e. macrosomic) infants
 - c) Persistent glucosuria
 - d) A history of unexplained miscarriages
2. Risks
 - a) Age > 25
 - b) obesity
 - c) family hx DM
 - d) previous macrosomic infant
 - e) previous stillbirth
 - f) previous infant with congenital anomaly
 - g) previous polyhydramnios
 - h) h/o recurrent abortions

Screening:

1. Glucosuria during pregnancy - should be investigated, even though the presence of glucosuria does **not** always reflect hyperglycemia from impaired glucose tolerance, but may reflect a lower renal threshold for glucose, which may be induced by a normal pregnancy.
2. Glucose Testing - should be done at 24-28 weeks when insulin requirements of pregnancy are maximal. High risk patients should be screened at 1st visit if the visit is prior to 24 weeks.
 - a. Screening tests - *screening* tests for high-risk patients are performed before and after a 50g/75g glucose load. There are three acceptable screening tests. An abnormal test necessitates a standard glucose tolerance test. Abnormalities are reflected by the following plasma glucose levels:
 - a) One hour- 135 mg/dl or above (50g load)
 - b) Two hour – 92 (fasting)/180 (1 hr) /153 (2 hrs) (75g load)
 - b. Standard glucose tolerance test is a 3 hour test with periodic blood determinations after a 100g glucose load is ingested. This test is done if any of the three above screening test results are abnormal or borderline. Abnormal test is defined as when **two or more** plasma glucose levels equal or exceed the following:

- a) 95 mg/dl (fasting)
- b) 180 mg/dl (1 hour)
- c) 155 mg/dl (2 hour)
- d) 145 mg/dl (3 hour)

Classification: (White's Classification of Diabetes in Pregnancy) – gives prognostic indication – the higher the class, the higher the risk of pregnancy-related complications

Class A: Gestational diabetes only, no history of DM outside of pregnancy

A1: managed with ADA diet alone

A2: requires medication, either oral hypoglyemics or insulin

Class B: diagnosed at >20yrs old and duration <10yrs

Class C: diagnosed at age 10-19 yrs or 10-19 yrs duration

Class D: diagnosed <10yrs or >20 yr duration w/ benign retinopathy or HTN

Class F: nephropathy (> 300 mg protein/24 hr urine or elevated Cr)

Class R: proliferating retinopathy or vitreous hemorrhage

Class H: Ischemic cardiovascular Disease

Class T: prior renal transplant

*Patients may have combinations of classes, for example, if a patient has both proliferative retinopathy and diabetic nephropathy, they would be a Class RF diabetic.

Complications:

1. Effect of pregnancy on diabetes

- a. The diabetogenic properties of pregnancy are reversible but still may induce abnormalities in glucose tolerance in women who have no evidence of diabetes.
 - (i) Insulin antagonism is due to the action of human *placental lactogen* and the steroids estrogen and progesterone.
 - (ii) *Placental insulinase* accelerates insulin degradation.
- b. control of diabetes may be more difficult in pregnancy.
 - (i) Insulin shock can result from nausea and vomiting (due to the patient's lack of sustenance).
 - (ii) Insulin resistance and ketoacidosis can result from infection.
- c. Insulin requirements in chemical and overt diabetics decrease rapidly after delivery because of the disappearance of *placental lactogen and insulinase*, as well as the reduction in estrogen and progesterone.

2. Effect of diabetes on pregnancy

- a. Mother - There is an increased likelihood of:
 - (i) Preeclampsia and eclampsia
 - (ii) Infection, which can be severe
 - (iii) Macrosomic infant, which can present problems with delivery, such as shoulder dystocia
 - (iv) C/S delivery due to macrosomia
 - (v) Polyhydramnios
 - (vi) Postpartum hemorrhage
 - (vii) IUGR (with more advanced stages of DM and vascular involvement)
- b. Fetus - there is an increased likelihood of :
 - (i) Perinatal mortality, especially when the pregnant diabetic is not managed appropriately
 - (ii) Perinatal morbidity from birth injury (often due to macrosomia with accompanying shoulder dystocia and brachial plexus injury) and preterm delivery
 - (iii) Perinatal hypoglycemia and hypocalcemia
 - (iv) Congenital abnormalities, such as neural tube and heart defects
 - (v) Diabetes in the infant's offspring

Management:

1. Preconception and prenatal care: A patient with GDM needs Rx to lower perinatal & maternal risks. The mainstay of therapy is dietary modification to lower fat. (30-35 kcal/kg/d =1800-2800cal ADA diet) Along with regular daily exercise.
 - a. Hemoglobin A1c determination at the patient's first visit provides an assessment of her prior diabetic regulation.
 - b. Strict glucose control prior to and during early pregnancy is thought to reduce the risk of severe malformations, such as neural tube defects, which are seen in fetuses of poorly controlled diabetics. The maternal glucose level should be kept as close to normal as possible.
 - (i) This may involve one or more antepartum hospitalizations for glucose control.
 - (ii) The pregnancy should continue until the fetus is mature unless the intrauterine environment has deteriorated to the point at which fetal well being is threatened.
 - c. Determination of the precise fetal age is important in a diabetic woman.
 - (i) Ultrasound evaluation is used in conjunction with the last menstrual period (LMP) to date the pregnancy.
 - (ii) A well established EDD is necessary to assess the following accurately:
 - Macrosomia
 - Polyhydramnios
 - Intrauterine growth retardation, which is *seen in diabetics with vascular disease/pregestational diabetes*
 - (iii) Regular ultrasound examinations are performed to monitor fetal growth Q 3-4 wks at ≥ 28 wks. A targeted u/s exam is performed at 18-20 wks and fetal ECHO is performed at 20-22 wks to evaluate for fetal cardiac anomalies
 - d. Goal for insulin use is euglycemia (FG<95;2^{hr} pp<120)
 - (i) dose according to body wt. & increase with pregnancy progression as indicated by patterned BS.
2. Third Trimester and delivery management:
 - a. *Class A diabetes* - treated with diet alone along with weekly monitoring of fasting blood glucose levels. If patient has gestational diabetes and does not require insulin, her fetus can be delivered at term; there is no need for early delivery.
 - b. Overt insulin dependent diabetes
 - (i) Fetal testing should be initiated by 32 weeks. Pts at OBCC receive a biophysical profile, which includes the following:
 - NST
 - fetal breathing
 - fetal tone
 - fetal motion
 - AFI (greatest vertical pocket)
 - (ii) Method of Delivery
 - (a) Induction of labor may be attempted if the fetus is not excessively large and if the cervix is capable of being induced (i.e. if the cervix is soft, appreciable effaced, and somewhat dilated)
 - (b) C/S is commonly used to avoid the trauma of a delivery of a large infant and to avoid the stress of labor for the fetus that has shown signs of distress. ABOG guidelines: c-section can be performed for > 5000g for nondiabetic patient and > 4500 g for diabetic patient

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16. Hypertension in pregnancy: 16 year old Tiffany, G1 P0 at 35 weeks gestation comes to your office for a regular prenatal visit. BP is 150/90.

Definition:

- A. An absolute BP > 140/90 is abnormal because the resting arterial pressure is lower in pregnancy. An increase of 30mmHg systolic or 15 mmHg diastolic also represents pathology.
- B. There are 5 classifications of hypertensive disorders of pregnancy:
 1. Pre-eclampsia → Eclampsia
 2. Gestational Hypertension
 3. Chronic hypertension
 4. Chronic hypertension with superimposed pre-E
 5. HELLP

Pathophysiology:

- A. Pre-eclampsia
 1. Epidemiology:
 - primarily confined to a young woman in her first pregnancy, commonly occurring during the last trimester of pregnancy (if it arises in the early second trimester (14-20 weeks) a hydatidiform mole or choriocarcinoma should be considered).
 - *Eclampsia is the addition of grand mal seizures to either the mild or the severe pre-E syndrome. 25% of eclampsia occurs before labor, 50% during labor and 25% after delivery.*
 2. Etiology:
 - unknown, but the pathophysiologic abnormality is a generalized arteriolar constriction or vasospasm secondary to abnormal placentation, likely at the time of trophoblastic invasion.
 - In general, the CO in a pre-E does not differ significantly from normal pregnant subjects, but the systemic vascular resistance is significantly elevated in the pre-E (secondary to abnormal placenta)
 - The Renal blood flow and GFR in pts with pre-E is significantly lower than in normal pregnant subjects.
 - The cerebral vascular resistance is always high in pts with pre-E and eclampsia
 3. Diagnosis: based on elevated BP > 140/90 and associated proteinuria (\geq 300mg / 24 hrs) at > 20 wks gestation. Urine protein/creatinine ratio of 0.3 or greater has been used to extrapolate to a 24 hr urine collection of > 300mg in situations where delivery is necessary.
- B. Chronic Hypertension: BP > 140/90 diagnosed < 20 weeks gestation. It is not uncommon for the physiologic stress of pregnancy to bring to clinical attention previously unapparent or subclinical vascular or renal disease.
- C. Chronic Hypertension with superimposed pre-eclampsia: The diagnosis should be reserved for those with chronic hypertension who have a marked increase in pre-existing proteinuria during pregnancy or have proteinuria for the first time in the latter half of pregnancy. (need a baseline 24 hr urine and baseline creatinine in the first trimester to compare to later values)
- D. Gestational Hypertension > 20 wks, BP >140/90 without significant proteinuria or evidence of end organ damage (low platelets, Cr elevation, etc).
- E. Severe PreEclampsia: Only one of the following is necessary for this diagnosis: BP >160/110, >5g protein on 24 hr urine collection, impaired liver function, progressive renal insufficiency, pulmonary edema, new onset cerebral or visual disturbances
- F. HELLP: hemolysis, elevated liver enzymes, low platelet count: This condition is associated with significant maternal and fetal morbidity.

Physical Exam:

- A. Vital signs with attention to the BP with serial sitting BPs. Note temp, HR and RR to r/o infection. The DBP should be noted since it more accurately assesses peripheral resistance.
- B. All should receive a complete PE with concentration on the following to r/o pre-E:
 1. Eyes (funduscopic exam to note any hypertensive changes and record a baseline)
 2. BP taken in both arms to r/o aortic coarctation
 3. CV and lungs to assess pulmonary edema
 4. Abdominal exam to assess RUQ pain
- C. Extremity exam to assess edema (particularly of face and hands) and cyanosis

- D. Neuro exam to assess headache, altered consciousness, hyperreflexia and irritability of reflexes (worrisome of CNS involvement)
- * Our patient is worrisome because of her age (16) her nulliparity and because she is in her third trimester. Her BP of 150/90 is alarming on first glance, but we must take a complete history and also assess BPs on separate occasions.
- Has she been having headaches?
 - Has she had any recent weight gain?
 - Any problems with her vision?
 - Any recent abdominal pain in her RUQ?
 - Any recent fevers or infections?
 - Any history of any previous elevated BPs before pregnancy?

Work-up:

- A. Labs: Cr, Platelet count, Liver function studies, PCV, Spot urine protein/CR ratio and/or +/- 24-hr protein, and 24-hr creatinine
- B. Ultrasound: asses fluid and growth of the fetus—pre-eclampsia is associated with placental insufficiency and fetal intrauterine growth restriction

Management:

- A. Pre-E and Superimposed PreE:
1. Admission to high risk obstetric service
 2. Management/decision to deliver varies depending on gestational age, fetal status (fetal testing results, amniotic fluid volume, fetal growth), degree of blood pressure elevation and cervical examination
 - i. All patients who develop evidence of severe disease (e.g. BP \geq 160/110, lab abnormalities, symptoms, pulmonary edema) are delivered
 - ii. Consider delivery in patients with mild disease if they are \geq 37 wks
 - v. Intrapartum fetal monitoring is mandatory (bi-weekly modified BPPs vs BPPs)
 - vi. Anticonvulsant (magnesium sulfate) is used for seizure prophylaxis in all pre-E during L&D and for 24hrs after delivery
 - vii. The ultimate management is delivery as the condition is cured with delivery of the baby and the placenta.
- B. Chronic Hypertension
1. Continue all previous meds
 2. Serial ultrasonic examinations starting at 28 wks q3-4 wks to detect IUGR
 3. Fetal testing-weekly BPPs at 32 weeks to ensure fetal well being
 4. Watch closely for evidence of superimposed preeclampsia
- C. HELLP
1. Deliver and monitor for return of labs to baseline postpartum
- D. Gestational Hypertension
1. Delivery if term (\geq 37 wks)
 2. Can manage blood pressure with agents such as procardia or labetalol as long as no evidence of proteinuria or other lab abnormalities
 3. Special care must be taken to not overlook possibility of PreEclampsia

** Task Force Report : Hypertension in Pregnancy, November 2013***

17. Isoimmunization: 31 year-old Charlotte, G2 P1, was seen at your office for the first prenatal visit at 12 weeks gestation by dates. Her prenatal laboratory panel reveals a blood type of AB negative. (a) Her atypical antibody screen is positive. (b) Her atypical antibody screen is negative.

- 1) **Definition:** "Isoimmunization refers to the development of antibodies to RBC antigens following exposure to such antigens from another individual." For our purposes the other individual is the growing baby, 50% of whose genetic make-up is different from the mother's.
- 2) **Pathophysiology:**

- a) If mom is exposed to baby's RBCs anytime during pregnancy (which is highly likely as only a tiny amount of blood is sufficient) she may develop antibodies to the baby's red blood cell antigens.
 - i) Later in that pregnancy or even more likely, in a subsequent pregnancy, mom's antibodies can cross the placenta and destroy fetal RBCs leading to fetal anemia, etc.
 - ii) Though baby has a huge capacity to manufacture RBCs, this capacity has its limits.
- b) RBCs have many surface antigens, however the most frequently involved group is called Rhesus (Rh) system (a complex of five antigens → C, c, D, E, e).
 - i) Of the Rh system, the D antigen is most commonly associated with hemolytic disease.
 - ii) 15% of Rh - moms with Rh+ babies develop antibodies.
 - iii) During the first pregnancy the baby usually has no complications. In the next pregnancy passage of even tiny quantities of blood (even <0.1mL) can evoke significant maternal antibody production.
 - iv) In the case of the Rh antigen, IgG which easily crosses the placenta, is produced. The antibody binds fetal RBCs--->hemolysis--->increase bilirubin--->anemia, jaundice, etc.
 - v) In the first baby this may be mild, but in later pregnancies, the transfer of IgG may be accelerated and lead to serious anemia outstripping liver capacity for RBC production and decrease the amount of other proteins produced.
 - vi) Therefore you get anemia (which if severe, can lead to high output CHF), and decreased oncotic pressure causing fetal ascites and edema--->hydrops fetalis.
- 3) **History and Workup:**
 - a) Evaluation of Rh status is conducted on every mother by analysis of blood type.
 - b) Routine antenatal labs also check maternal blood for the presence of a variety of antibodies.
 - i) Significant ones are further evaluated for strength of antibody response.
 - ii) Anti-D titers of 1:16 or greater are considered critical values and warrant further evaluation.
- 4) **Management:** (of Rh- moms)--Positive Titers:
 - a) Mildly + (< 1:16) requires review of chart to see if pt ever given RhoGAM (e.g. with previous pregnancy), ask about prior history of transfusions. Follow titers regularly (e.g. monthly) and check antigen status of the father of the baby. If the father does not express the antigen to which the mother is producing antibodies, regardless of the titer, the fetus will not be affected.
 - b) Strongly + indicates need for further eval of fetus including possible amniotic fluid assessment and ultrasound (as well as typical NST, etc later in pregnancy.)
 - i) Amniotic fluid is checked by amniocentesis for level of bilirubin which accurately reflects the fetus's condition. Bili levels decrease during nl pregnancy on a determined rate and degree of deviation is referred to as change in optical density-- OD450. Markedly elevated OD450 values indicate severely affected fetuses (see Liley curve in text).
 - ii) The current trend in management is the measurement of the peak velocity of the middle cerebral artery (MCA) flow using Doppler ultrasound. The velocity of flow through the MCA is related to the viscosity of the blood. In the setting of fetal anemia, the blood is less viscous due to fewer cells, and, therefore, the velocity of flow increases. Gestational age-specific peak velocity normal curves have been derived and correlate with the fetal Hct.
 - iii) Ultrasound assessment of the fetus also helpful in finding severe signs of hemolysis that have resulted in profound anemia, such as subcutaneous edema, pericardial and pleural effusions, and ascites
 - iv) If baby found in severe cond., an infusion of Rh- RBCs can be given by percutaneous umbilical blood sampling (PUBS) and intrauterine transfusion.
 - c) Negative Titers: Negative on initial screen needs to be rechecked at 28wks, if still negative, RhoGAM is given prophylactically. If the baby is born Rh-, no more indicated, but if the baby is Rh+, another 300microgm of Rh immunoglobulin (RhoGAM) is given to the mother within 72hrs of delivery. Subsequent risk of complications is decreased from 16% to 2%.
 - d) Other indications for RhoGAM administration include: at time of amniocentesis, after + Kleihauer-Betke test, after an ectopic pregnancy, after spontaneous or induced abortion after abdominal trauma, after vaginal delivery or cesarean section.

20. Multiple Gestation: 21yo G1 P0, at 15 weeks gestation has a uterine fundus palpable at the umbilicus. An ultrasound examination shows twin gestation with a single placenta but no septum was visualized.

Etiology and Epidemiology:

1. The overall incidence of twins at delivery is approximately 1%.
 - a. There are 2 types of twins, depending on how many ova are released: monozygotic and dizygotic types.
 - i. Dizygotic twins: two separate ova fertilized by two separate sperms
 - ii. Monozygotic twins: result from division of one fertilized ovum *after* conception
 - b. Monozygotic (identical) twinning is a chance occurrence and is rarely affected by other parameters. It occurs approximately 3-4 out of 1000 births throughout the world.
 - i. Rates increase slightly with delayed implantation, as occurs with in vitro fertilization.
 - c. The frequency of dizygotic (fraternal) twinning does vary throughout the world and has several factors affecting its incidence
 - i. Rates: 7-10 per 1000 among Caucasians, 10-40 per 1000 among Africans, and 3 per 1000 among Asians.
 - ii. Heredity and the use of certain drugs in the preovulatory phase of the cycle increases the frequency of dizygotic twinning.
2. Placentation:
 - a. In dizygotic twinning, division of the zygote happens within 0-4 days of fertilization; two individual placental units are produced, and the membrane between these two has amnion and chorion layers from each infant.
 - i. The central membrane (septum) between the infants has two amnion layers and two chorion layers ("twin peak" or lambda sign), a situation always seen with dizygotic twins.
 - b. In monozygotic twins, the placentation depends on the time at which the twin division occurs, because the amnion and chorion form at different times in gestation.
 - i. Monochorionic/diamniotic : The chorion forms by day 3; if the division occurs between days 4 and 8, the placenta has two amnions (T-sign in dividing membrane) and only one chorion, and the central membrane between the infants is thin → this is called a monochorionic placenta ()
 - ii. The amnion forms by day 8; if the division occurs between day 8 and day 13 of gestation, no central membrane develops, and a monoamniotic monochorionic twin gestation occurs.
 - iii. If the division occurs after day 13, the result is a physical attachment of the twin bodies producing conjoined twins.

Risks:

1. Since no septum was visualized on ultrasound, Maggie is most likely to have monoamniotic monochorionic placenta.
 - a. Monoamniotic twinning is uncommon, occurring in approximately 1% of monozygotic twins or 0.3% of all twin gestations.
 - b. A risk in these pregnancies is cord entanglement with fetal movement, which can lead to obstruction of blood flow and fetal death.
 - c. A risk that occurs in monochorionic twins is twin-twin transfusion syndrome, which occurs in approximately 2 to 6 percent of monoamniotic pregnancies, but more commonly in monochorionic diamniotic pregnancies. Rates in the latter mentioned pregnancy type are approximately 9 to 15 percent. One twin becomes hypovolemic (donor twin) and the other hypervolemic (recipient twin). This condition can lead to a marked discrepancy in twin size and amniotic fluid volume, and can ultimately lead to hydrops or death in one or both of the twins.
 - d. Perinatal mortality caused by this complication approaches 50%; most of the fetuses that die are less than 32 weeks of gestation.

2. The diagnosis can be suspected by being unable to find a septum on the ultrasound scan.

Physical Exam:

- A. The clinical exam usually reveals a uterine fundal height growing at a rate that is greater than expected for a singleton pregnancy.
- B. With a singleton pregnancy, after 20 weeks of gestation the fundus should be palpable at or near the umbilicus.
- C. Since Maggie is carrying twins, a palpable uterine fundus at 15 weeks is not unusual.

Management:

- A. If monoamniotic monochorionic twins are diagnosed, fetal heart rate testing should be done starting at 28 weeks gestation, with special attention to identifying cord compression patterns. Many patients are monitored inpatient for daily fetal heart rate testing, as often as two to three times per day.
 - a. Delivery is affected as soon as fetal lung maturity is diagnosed
- B. Cesarean delivery is performed for monoamniotic twins due to the risk of cord entanglement.

32. Prenatal Diagnosis: Naomi is a 42 yo G1 P1 who comes in for her first prenatal visit at 8 wGA. She had a previous Down's baby with spina bifida. She asks if you can help identify if her present fetus is normal.

History:

- Age of mother
- Child or family history of birth defects, genetic disorders, etc.
- Previous OB history, including #fetal losses, #preterm births, etc.
- Past or present exposure to teratogenic agents such as thalidomide, alcohol, antibiotics, etc.

Indications for prenatal diagnosis:

1. Age greater than or equal to 35
2. Previous child or family history of birth defects, mental retardation, chromosomal abnormality, or known genetic disorder.
3. Multiple fetal losses.
4. A baby who died in the neonatal period.
5. Maternal conditions predisposing the fetus to congenital abnormalities.
6. A current pregnancy history of teratogenic exposure.

Note: Screening for aneuploidy can be offered to all women who present for prenatal care prior to 20 weeks regardless of maternal age.

Risk:

1. 1/1000 incidence of neural tube defects (3% for couples with previous child with NT defect)
2. 1/800 incidence of Down Syndrome (1/300 for women 35-39, 1/80 for women 40-45)

Tests:

1. First Trimester Screening (10 – 14 wGA)
 - ~Screens for Trisomy 18/21 and neural tube defects (NTD)
 - ~Measures nuchal translucency (NT) alone, or NT as well as PAPP-A and b-HCG
 - ~NT alone has a 64-70% chance of detecting Trisomy 21 (T21)
 - ~NT combined w/ PAPP-A and b-HCG has an 82-87% chance of detecting T21
 - ~If the NT is ≥ 3.5 mm then offer a targeted scan
2. Second Trimester Screening (15 – 20 wGA)
 - ~Screens for Trisomy 21/18 and NTD
 - ~Consists of triple screen OR quad screen

- Triple screen is MSAFP, hCG, and estriol (69% detection rate for T21)
 - Quad screen is triple screen plus inhibin A (81% chance of detecting T21)
 - MSAFP alone can detect 80% of neural tube defects (NTD) as well as ventral wall defects
 - ~MSAFP is **increased** in NTDs, ventral wall defects (as well as multiple gestations, fetal demise, or inaccurate gestation ages)
 - ~MSAFP is **decreased** in association w/ T21 (detects ~20% alone)
3. Integrated Screening & Sequential Screening
- ~Integrated screening tests (for Trisomy 21/18 and NTD) has a 94-96% detection rate for T21
 - ~PAPP-A and NT in 1st Trimester
 - ~Quad screen in 2nd trimester
 - ~Don't evaluate results of 1st TM screen until after 2nd TM screen completed
 - ~Sequential Screening tests (contingent or sequential tests for Trisomy 21/18 and NTD)
 - ~Contingent has an 88-94% detection rate for Trisomy 21
 - 1st TM screen (NT, PAPP-A, and b-HCG)
 - If the screen is positive then a diagnostic test is offered (i.e. Amniocentesis)
 - If the screen is negative then no further screening offered
 - If the screen is indeterminate then a 2nd TM screen is offered
 - ~Sequential has a 95% chance of detecting Trisomy 21
 - 1st TM screen (NT, PAPP-A, and b-HCG)
 - If the screen is positive then a diagnostic test is offered (i.e. Amniocentesis)
 - If the screen is negative then a 2nd TM screening test is offered
4. Amniocentesis (diagnostic)
- ~performed at 16-20 wks
 - ~detects chromosomal disorders and NTDs (~99% accuracy for chrom. disorders)
 - ~about 20 ml of amniotic fluid is aspirated - takes about 10-14 days for chrom. analysis
 - ~"early" amniocentesis (less than 15 wks) may be done if CVS cannot be done
5. Chorionic Villous Sampling (CVS)
- ~performed at 9-12 wks (transabdominal or transcervical)
 - ~direct study of the dividing cells can detect chrom. abnorm. within 48 hr
 - ~can also detect biochemical genetic disorders such as Tay-Sachs, Gaucher, etc
 - ~risk of miscarriage about 1% higher than normal 1st trimester risk
 - ~CANNOT measure AFP by this method
6. Percutaneous Umbilical Blood Sampling (PUBS)
- ~performed in second or third trimester
 - ~used to confirm chrom. abnormalities suggested by US, amnio, or CVS
 - ~rapid fetal karyotype (48 hrs)
 - ~procedure relate loss rate higher (1%) than with amnio (1/200)
7. Ultrasonography (US)
- ~used to identify structural abnormalities (craniospinal, GI, renal, skeletal, heart)
 - ~transvaginal US used in 1st trimester to assess fetal viability
 - ~echocardiograms can delineate congenital heart defects in high risk women
8. Non-invasive Prenatal Screening (NIPS)
- ~evaluation of maternal serum for free fetal DNA
 - ~evaluates the maternal serum for cell-free fetal DNA
 - ~not indicated for sex analysis
 - ~per ACOG should only be offered for the following high risk situations:
 - Advanced maternal Age (AMA)
 - Positive screening results

- Prior affected pregnancy
 - Anomaly noted on ultrasound
 - Prior known translocation
- ~a **screening tool**, not a diagnostic tool

45. Third Trimester Bleeding: 32 year-old Elsie, G4 P3, at 31 weeks gestation comes to L&D with complaints of painless vaginal bleeding for the past hour. On exam her perineum is grossly bloody but there is no active bleeding.

Differential Diagnosis:

1. Contact Bleeding - cervical or vaginal lesions/lacerations (ie. caused by intercourse)
2. Cervical Inflammation - ie. infection
3. Labor (term or preterm)
4. Placenta Previa
5. Abruptio placentae
6. Uterine rupture
7. Coagulation disorder
8. Fetal Vessel Rupture
9. Cervical Cancer

Etiology and Pathophysiology:

1. Placenta Previa:
 - a. Comprises 20% of all antepartum hemorrhages.
 - b. defined by a placenta which precedes the baby to the cervical os
 - i. complete (covering the entire os)
 - ii. partial (covers part of the os)
 - iii. marginal (only touches the edge of the os)
 - iv. Don't confuse this with a low-lying placenta, where the placenta implants on the lower third of the uterus. Low-lying placentas generally don't cause bleeding, if they due this normally occurs in 2nd or early 3rd trimester; however placenta normally migrates away from os as pregnancy progresses.
 - c. Predisposing Risk Factors for Previa:
 - i. Multiparity
 - ii. Increasing maternal age
 - iii. Prior Previa (4-8% risk of recurrence)
 - iv. Multiple gestation
 - d. Diagnosis is made by transvaginal ultrasound (can see on abdominal, but TVUS is confirmatory)
 - e. Placenta previa may also be associated with abruption or labor, so contractions don't rule out PP.
 - i. This is also associated with placenta accreta (condition of abnormal placental adherence).
 - ii. Maternal mortality is less than 1% and the risk to the fetus is associated with preterm delivery.
 - f. Management of PP:
 - i. If bleeding is not excessive, manage with bedrest/pelvic rest.
 - ii. Follow maternal Hct and ensure blood available iron supplementation.
 - iii. Asses fetal lung maturity (L/S ratio) at 36 wks and delivery by cesarean section.
2. Abruptio Placentae:
 - a. Occurs in 1/120 births
 - b. Defined by premature separation of placenta from the uterine wall.
 - i. This separation can be initiated by a hemorrhage into the decidua basalis and cause formation of a decidual hematoma.

- ii. Placental abruption is the most common cause of DIC in pregnancy, secondary to release of thromboplastin from the disrupted placenta into maternal circulation.
 - iii. DIC occurs in 20% of cases.
 - Hypovolemic shock and acute renal failure may be seen with abruption in these cases.
 - Perinatal mortality rate is 35%.
 - c. Predisposing factors to AP:
 - i. Hypertension
 - ii. Trauma
 - iii. Polyhydramnios with rapid decompression on membrane rupture
 - iv. Cocaine or tobacco use
 - v. Preterm PROM
 - vi. Short umbilical cord
 - d. Diagnosis of AP: Made largely on presentation including:
 - i. Uterine tenderness
 - ii. Uterine hyperactivity
 - iii. Increased tone
 - iv. Vaginal bleeding
 - iii. Maternal tachycardia or hypotension
 - iv. Nonreassuring fetal heart rate tracing (e.g., tachycardia, late decels)
 - e. Management: Deliver as soon as possible and monitor Mom and fetus as with a previa.
3. Uterine Rupture:
- a. Is defined by complete separation of the uterine musculature through all of its layers, with all or a part of the fetus sticking out of the uterine cavity.
 - b. Overall incidence is 0.5 %.
 - i. A prior uterine scar is associated with 40% of cases.
 - ii. Risk with a vertical (classic) c-section is 10 times that of a low transverse.
 - c. Factors assoc. with rupture in an unscarred uterus are:
 - i. injudicious use of oxytocin
 - ii. grand multiparity
 - iii. marked uterine distension
 - iv. abnormal fetal lie
 - v. cephalopelvic disproportion
 - vi. external version/extraction
 - vii. shoulder dystocia
 - viii. midforceps delivery
 - ix. uteroplacental pathology
 - x. trauma
 - d. Diagnosis:
 - i. Rupture is classically associated with acute onset of severe abdominal pain and a nonreassuring fetal tracing.
 - ii. Impending rupture may be preceded by hyperventilation, restlessness, agitation and tachycardia. Vaginal bleeding may be present or absent. Loss of fetal station may be seen.
 - e. Management:
 - i. If there is a high degree of suspicion, immediate laparotomy is required.
 - ii. Usually total abdominal hysterectomy is the treatment of choice, but repair of the rupture site can be considered if the site is small and the woman desires future fertility.

General Principles Of Managing A Third Trimester Bleed:

1. Assess hemodynamic stability of mother - pulse, BP, skin color, mentation. If these are not satisfactory, more drastic treatments are required.
2. Establish fetal heart tone monitoring.
3. Volume replete with fluids and transfusion if necessary.
4. If fetus is in distress or unstable, c-section immediately.

- In the case of placental abruption, use oxytocin to assist in vaginal delivery. DIC should resolve once the patient is delivered.

48. UTI In Pregnancy: 21 year-old Rochelle, G2 P1, at 30 weeks gestation presents to your ER with 103.5 fever, right flank tenderness, and dysuria.

Background:

- UTI is common in pregnancy.
 - 9-11% of ALL women will have an asymptomatic infection with >100,000 CFU's on a midstream culture.
 - Untreated, 25% will develop symptomatic UTI.
- Asymptomatic bacteriuria is more likely to become symptomatic in the pregnant female.
 - This is likely due to pregnancy-induced urinary stasis (progesterone decreases ureteral tone and motility) and glycosuria (common in pregnancy).
 - Also, urinary pH is increased due to increased bicarb secretion which can cause increased bacterial growth.
- Acute cystitis occurs in 1% of pregnancies.
- Pyelonephritis occurs in 1-2% of all pregnant patients, and is one of the most common complications requiring hospitalization.
 - These patients will be acutely ill, with fever, costovertebral tenderness, general malaise, and often dehydration.
 - * This case description might suggest pyelo so ensure you have fully worked this pt up and that she has no signs of sepsis, if +sepsis likely pyelo!

History/Exam:

- It is standard to obtain a urine culture at the onset of prenatal care and treat asymptomatic bacteriuria, typically with ampicillin, sulfisoxazole, or nitrofurantoin, as the bug is usually *E. coli*.
- Suppressive therapy with nitrofurantoin (100 mg nightly-you want abx to concentrate in urine at night, as this is time urine is most stagnant during the day leading to increased risk of infection) is indicated with repetitive UTI's in pregnancy, or following pyelonephritis in preg.
- Treat cystitis identically. Pyelo is described above. Blood cultures are a good idea if you suspect pyelo and the patient is ill appearing.

Treatment:

- For UTI, ampicillin (500 mg qid) for GBS, Bactrim DS (1 tab BID) or nitrofurantoin (100 mg qid) for 7-10 days is usually sufficient. Shorter (3d) courses may be acceptable as well; however, pregnancy is considered complicated UTI, therefore, longer courses preferred.
 - In the late 3rd trimester (when delivery is imminent), sulfas should be used with caution as they compete with bilirubin for albumin-binding sites, and may cause hyperbilirubinemia in the newborn.
 - Nitrofurantoin should be avoided in late pregnancy because of the risk of hemolysis as a result of deficiency of erythrocyte phosphate dehydrogenase in the newborn.
 - Suppression therapy with nitrofurantoin as above when indicated.
- For pyelo, IV hydration and antibiotics, usually a first- or third generation cephalosporin or ampicillin/gentamicin.
 - Uterine contractions may be seen, and preterm labor could develop.
 - Also, *E. coli* may produce phospholipase A, which could promote prostaglandin synthesis, which could increase uterine activity.
 - Fever is known to produce contractions so any temp over 100 °F should be treated with antipyretics.
 - Sepsis occurs in 2-3% patients with pyelo, so careful management is key. Pulmonary edema/ARDS may be seen.
 - If acute pyelo does not respond to antibiotics, you must suspect obstruction or a paranephric abscess, and consider imaging studies (U/S, IVP).

Analysis:

- Though the given case states *UTI in pregnancy*, a patient with this history in the ER may have indication for hospitalization.
- Certainly, antipyretics and antibiotics should be given promptly after cultures are obtained.
- However, I think the most reasonable approach would be admission for IV hydration and antibiotics as these patients may acutely decompensate quickly.

Section VI: Obstetrics**1. Abnormal Labor: L & D notifies you that 32 year-old Georgia, G4 P3, at 41 1/2 weeks gestation in active labor has been 5 cm dilated for the past 3 hours.**

Definition: Abnormal labor, or dystocia ("difficult labor or childbirth"), results when anatomic or functional abnormalities of the fetus, the maternal bony pelvis, the uterus and cervix, and/or a combination of the above interferes with the normal course of labor and delivery.

Pathophysiology: In order to diagnose abnormal labor, the normal stages of labor must first be considered:

1. Labor = the process by which products of conception (fetus, placenta, cord, membranes) are expelled from the uterus. It is defined as the progressive effacement and dilation of the uterine cervix as a result of rhythmic contractions of the uterine musculature.
2. It is further divided into stages:
 - a. **First stage** = interval between the onset of labor and full (10 cm) dilation.
 - (i) *latent phase* = cervical effacement and dilation <4 cm.
 - (ii) *active phase* = rapid cervical dilation, beginning at 4 cm, ends at 10 cm
 - b. **Second stage** = delivery of the infant through a completely dilated cervix.
 - c. **Third stage** = begins after delivery of infant, ends with delivery of placenta.
 - d. **Fourth stage** = first hour after delivery of placenta.
3. Abnormal labor patterns:
 - a. Prolonged latent phase
 - (i) No progress from latent to active phase of labor
 - (ii) >20 h for nulligravidas
 - (iii) >14 h for multiparas
 - b. Prolonged active phase of labor such that
 - (i) Cervical dilation proceeds at
 - <1.2 cm/hr for nulligravidas
 - <1.5 cm/hr for multiparas
 - (ii) Descent of the presenting part proceeds at
 - <1 cm/hr for nulligravidas
 - <1.5 cm/hr for multiparas

Causes and evaluation of abnormal labor:

1. Remember the three basic components of labor and delivery (The 3 P's):
 - a. the power (uterine contractions and maternal effort)
 - b. the passenger (the fetus)
 - c. the passage (maternal bony pelvis).
2. Monitoring progression of labor
 - a. **Vaginal exams** (dilation/effacement/station of presenting part/presence of caput or molding/position of presenting part)
 - b. **Assessment of uterine contractions** using a tocodynamometer or IUPC (intrauterine pressure catheter)
 - c. **Pelvimetry** (to evaluate the maternal pelvis)

Stage 1 Arrest

- a. **Prolonged latent phase:**
 - abnormal fetal position
 - unripened cervix when labor starts
 - excessive anesthesia
 - fetopelvic disproportion
 - dysfunctional or ineffective contractions or **FALSE LABOR** (keep in mind)
- b. **Prolonged active phase:**
 - fetal malposition
 - fetopelvic disproportion

- excess sedation
- inadequate contractions
- rupture of membranes before active phase

Stage 2 Disorders**Second Stage Protraction**

- With regional anesthesia: >3 hrs
- No regional anesthesia: >2 hours

Second Stage Arrest

- No descent after 1 hr pushing
- Reasons for 2nd Stage Arrest
 - fetopelvic disproportion
 - fetal malposition
 - small or abnormally shaped pelvis
 - inadequate contractions

(Again- Remember Three "P" – Power, Passenger, passage)

Risks of prolonged labor:

1. Maternal risks:
 - Cesarean section
 - infection
 - exhaustion
 - lacerations
 - uterine atony with possible hemorrhage.
2. Fetal risks:
 - asphyxia
 - trauma from difficult deliveries
 - infection
 - meconium aspiration syndrome (airway obstruction and chemical pneumonitis)

Management of abnormal labor:

1. Induction and augmentation with oxytocin (Pitocin)
 - a. By using the Bishop score (a scale of cervical 'ripeness') the decision whether to induce or augment can be made.
 - b. Augmentation of labor can be done in a prolonged latent phase, active phase (after considering fetal malposition), or with secondary arrest of dilation.
2. Cervical ripening
 - a. intravaginal prostaglandin gel
 - b. laminaria (hygroscopic rods made from seaweed inserted into the internal os so they can expand)
 - c. Cervical foley – foley balloon inserted into cervix and inflated to 30cc
3. Amniotomy
 - artificial rupture of the membranes using an amniohook can help speed up a prolonged latent phase.
4. Forceps/vacuum delivery
 - these tools can aid in the descent of the fetal head
5. Cesarean section
 - a. the decision on when to do a c-section is debated. An IUPC should be used to ensure the contractions are adequate. In the past, a 2 hour second stage (3 h epidural in place) in the face of adequate contractions has been considered an indication for c/s.

Breech presentation:

1. occurs in about 2-4% of singleton deliveries at term; more frequently preterm.
2. associated factors:
 - multiple pregnancy
 - polyhydramnios

- hydrocephaly
 - anencephaly
 - uterine anomalies
 - uterine tumors.
3. Three types of breech presentation:
 - a. frank = feet up by the head, butt first.
 - b. complete = feet sitting 'Indian-style'
 - c. incomplete = one foot kicking down, like the baby's going to hop out on one foot.
 4. Correction of a breech:
 - a. external cephalic version--turning the baby around from the outside can be done if the fetus is normal with reassuring heart tones, adequate amniotic fluid, the presenting part is not in pelvis, there are no operative scars on the uterus, and the woman is NOT in labor.
 - b. Risks include abruption, cord accident, and uterine rupture. External version is more successful in parous women.
 - c. Criteria for vaginal delivery of a breech:
 - normal labor curve
 - fetal weight between 2000-4000 g in frank or complete breech
 - reassuring fetal heart tracing
 - adequate maternal pelvis by clinical pelvimetry
 - normally flexed fetal head
- ***Proven Pelvis aids in improved success

12. Fetal Distress: L & D nurse calls you in a panic regarding 18 year-old Peggy, G1 P0, 39 weeks gestation in active labor. The fetal monitor which was initially normal now shows FHR baseline at 70/min. FECC is in place.

Definitions:

1. **Fetal distress:** also known as non-reassuring fetal heart tones (NRFT)
2. **Baseline fetal heart activity:** baseline characteristics of fetal heart rate in the between uterine contractions. Normally 110-160 beats/min.
3. **Periodic fetal heart rate activity:** characteristics of fetal heart rate that are associated with uterine contractions.
4. **Fetal bradycardia:** Baseline rate < 110 beats/min for at least 3 min (preferably 10 min, to distinguish it from prolonged deceleration)
 - Mild: 100-110 beats/min
 - Moderate: 80-99 beats/min
 - Severe: < 80 beats/min

Pathophysiology: Bradycardia is the initial response of the fetus to acute hypoxia. The extent of bradycardia depends on the degree of fetal hypoxia.

Differential Causes: The asphyxic stimulus may be caused by:

- 1) decrease in maternal oxygen tension
 - ex: during apnea of seizure
- 2) decrease in uterine blood flow
 - a. excessive uterine contractions
 - b. maternal hypotension due to:
 - epidural analgesia
 - compression of vena cava by uterus
 - uterine rupture
- 3) decrease in umbilical blood flow
 - cord compression (against head of fetus)
 - cord knot
 - cord prolapse (through cervix or uterine rupture)
- 4) loss of placental area (i.e. abruptio placentae)

- 5) fetal hemorrhage (rare, i.e. tearing of vasa previa)

History: (Things to ask the nurse or find in the chart)

What are the mother's vital signs?

-rule out maternal hypotension or apnea

Does the mother appear to be in hypovolemic shock?

-rule out placental abruption or uterine rupture

Does the mother appear to be in an excessive amount of pain?

-pain may be associated with hyperstimulation of uterus, placental abruption, or uterine rupture.

Does the patient have medical conditions such as hypertension, diabetes mellitus, or collagen-vascular disorders that can cause placental dysfunction?

Has there been evidence of intrauterine growth restriction?

Physical Exam:

1. Check the fetal heart rate strip, and determine the patterns of acceleration/deceleration, as well as beat to beat variability, and frequency of uterine contractions.
2. Determine how long the bradycardia has been present.
3. What is the quality and frequency of the mother's contractions?
4. Is there excessive vaginal bleeding or meconium passage?
5. Palpate the abdomen (Tender in placental abruption)
6. Palpate the uterus (Placental abruption, hyperstimulation, or uterine rupture causes tenderness, irritability, or hypertonus)
7. How much is the patient's cervix dilated and how close is the patient to delivery? (This will determine if a rapid delivery will be vaginal or cesarean)

Management:

1. Reposition the patient.
2. Administer supplemental oxygen
3. Decrease uterine contractions:
 - a. discontinue oxytocin
 - b. administer a tocolytic agent if excessive uterine activity is present
 - Terbutaline sulfate 0.25 mg SQ once
 - MgSO₄ 2g IV over 10 min
4. Correct maternal hypotension
 - a. increase IV infusion rate
 - b. give ephedrine sulfate 25-50 mg IM or IV.
5. If above steps do not resolve bradycardia, plans should be made to proceed with delivery.

Prolonged End-Stage Bradycardia

1. This term refers to a prolonged deceleration, generally late in the second stage of labor, in the presence of otherwise normal FHR tracing (quite likely to be a vagal response to head compression as the head traverses the depths of the pelvis).
2. The current recommendation is that if the bradycardia is persistent and FHR variability decreases, the baby should be delivered as rapidly as possible.
 - However, if beat to beat variability is retained, efforts should be made to abolish the bradycardia or effect a spontaneous delivery.
 - It is unusual for prolonged bradycardia to result in absence of FHR variability and fetal decompensation in less than 10 minutes if the FHR is above 60 beats/min.

21. Operative Obstetrics: 28 year old Sybil, G1 P0, 41 weeks gestation has been in the second stage of labor for the past four hours. She is exhausted and has not been pushing effectively. The fetus is cephalic presentation. Fetal position is right occiput transverse. Station is +1. The fetal head has molding and also caput formation. You recommend a cesarean. Sybil asks is a trial of vacuum extractor or forceps might be safer.

Definition:

- **Second stage of labor:** The interval between full cervical dilatation and delivery of the infant.
 - *Arrest of descent* is one problem associated with the second stage of labor. This disorder requires prompt re-evaluation of uterine contractility, maternal and fetal well-being, and cephalopelvic relationships.
 - Obvious problems such as hypotonic dysfunction, over distended bladder, conduction anesthesia, or ineffectual bearing down should be treated appropriately with a high expectation of success.
 - In the absence of such factors, however, very careful judgment is required. Estimation of fetopelvic relationships, including station, caput formation, molding, palpation of the fetal head above the symphysis, and malrotation, is mandatory.

Classifications: Forceps deliveries are classified according to the station of the fetal head at the time of application

1. **Outlet forceps:** application of forceps when the scalp is visible at the introitus without separating the labia, the fetal skull has reached the pelvic floor, the fetal head is at or near the perineum, and the angle between the AP line and the sagittal suture does not exceed 45 degrees.
2. **Low forceps:** application when the leading point of the skull is at station +2 or more, subclassified as to whether the angle between the sagittal suture and AP exceeds 45 degrees.
3. **Mid-forceps:** application of forceps when the head is engaged but the presenting part is above station +2 (ie. -3 to +1). We don't really do this anymore.
4. **Vacuum Extraction:**
 - The classic instrument consists of a disk-shaped cup through which a vacuum of up to 0.8 kg/cc² is applied to the fetal scalp.
 - This suction induces a caput succedaneum (chignon) within the cup to which traditional force is applied during uterine contractions.

Randomized studies comparing forceps with vacuum have not shown a significant difference in success rates or complications (though the complications associated with each are different), and the choice of instrument appears to remain one of operator preference.

Indications and Contraindications for Forceps/Vacuum Delivery:

1. The major controversy surrounds the mid-forceps delivery.
2. ACOG has suggested that that outlet forceps may be used to shorten the second stage of labor when it is in the best interest of the mother or fetus.
3. More difficult forceps delivery (low or mid forceps) may be considered when the second stage is prolonged, for fetal distress, or for maternal indications such as cardiac disease or exhaustion.
4. In a recent survey of residency programs in the U.S. and Canada, outlet and low forceps were used at all institutions, but 14% of the programs had abandoned the use of midforceps delivery.
5. Occiput Transverse Positions:
 - Forceps delivery from the occiput transverse position is best accomplished with the use of specialized forceps. The instruments (Kielland, Barton) require considerable skill and experience, and their use has decreased greatly in recent years.
6. The indications and contraindications to vacuum extraction are essentially the same as those for forceps delivery.

Prerequisites for Forceps Delivery:

1. The membranes must be ruptured.
2. The cervix must be fully dilated.
3. The operator must be fully acquainted with the use of the instrument.
4. The position and station of the fetal head must be known with certainty.
5. Adequate maternal anesthesia for proper application of the forceps must be present.
6. The maternal pelvis must be adequate in size for atraumatic delivery.
7. The characteristics of the maternal pelvis must be appropriate for the type of delivery being considered.
8. The fetal head must be engaged.

Management:

- Cesarean delivery is employed when labor is contraindicated or vaginal delivery is unlikely to be accomplished safely or within a time frame necessary to prevent the development of fetal and/or maternal morbidity in excess of that expected following vaginal delivery.
- In Sybil's case, most physicians would recommend a cesarean section, as hers would be a very difficult mid-pelvic delivery.

24. Post Dates: 24 year-old Liza, G3 P1 Ab2, saw you for the first time 6 weeks ago. By dates, she is now 42 1/2 weeks gestation

Definition: Prolonged or post term pregnancy is one that persists > 42 weeks (294 days) from the first day of the last menstrual period.

Incidence: ~10%; occurs more frequently in women who are younger or older than average childbearing age and in grandmultiples (women who have had 5 or more pregnancies resulting in viable fetuses)

Etiology: unknown in majority of cases, most common known cause – *inaccurate dating*.

Other causes:

4. Deficiency of ACTH in the fetus
5. Placental sulfatase deficiency
6. Ectopic (eg. abdominal) pregnancy
7. Associated with anencephaly due to decreased fetal production of estriol precursors that are normally secreted from fetal adrenals (anencephalics have hypoplastic adrenals)

Effects On Fetus: Morbidity and mortality rates for mother and fetus increase seven-fold. Increased risk to fetus and neonate can be attributed to the development of:

- 1) Dysmaturity syndrome
 6. occurs in **up to 20%** of postterm pregnancies
 7. related to aging and infarction of the placenta, which results in placental insufficiency w/ impaired oxygen diffusion & decreased transfer of nutrients to the fetus
 8. prenatal mortality factor increased w/ intrauterine hypoxia (meconium staining of umbilical cord, fetal membranes, skin, nails)
 9. fetus typically has loss of subcutaneous fat, long fingernails, dry cracked wrinkled skin, abundant hair and unusual degree of alertness
 10. Increased incidence of non-reassuring fetal testing
- 2) Macrosomia (>4500 gm birth weight)— occurs in **2.5 to 10%** of postterm pregnancies. Macrosomia can result in:
 - a. Abnormal labor
 - b. Shoulder dystocia
 - c. Birth trauma
 - d. Increased C/S rate
- 3) Meconium aspiration syndrome— meconium passage occurs in **12-22%** of women with labor.
 - 1) Incidence of passage increases as pregnancy becomes prolonged
 - 2) 10% of infants with passage will have aspiration
- 3) Oligohydramnios— AFI <5cm or GVP<2cm. Associated with poor outcomes due to umbilical cord compression, uteroplacental insufficiency and meconium aspiration

Diagnosis: key to diagnosis is accurate dating of gestation.

Factors to distinguish postdated pregnancy from misdated pregnancy:

- A. accuracy of the date of the last normal menstrual period
- B. ultrasound is most accurate for dating between 6 and 12 weeks of gestation
- C. if LMP predicts an EDD that is within 10 days of an ultrasound-determined EDD performed between 12 and 20 weeks gestation, that gestational age is considered fairly accurate

Management:

1. Antepartum: Two options once gestational age is firmly established and the patient approaches 41 weeks gestation.
 - A. Antepartum fetal surveillance
 - i. Can consider induction of labor if cervix is favorable (see Bishop Scale below). If cervix is not favorable, fetal well-being is monitored intermittently until labor occurs or cervix ripens.
 - ii. Common monitoring practices include amniotic fluid volume, non-stress tests and biophysical profiles once or twice a week
 - iii. Daily fetal movement counting can be used by mom as an indication for immediate fetal well-being
 - B. Induction of labor
 - i. Most physicians believe delivery should occur before 42 completed weeks
 - ii. Routine induction at 41 weeks, using cervical ripening agents, is associated with lower C/S rates, lower perinatal mortality, decreased length of hospital stay, decreased hospital cost and higher patient satisfaction
 - iii. C/S should be considered for EFW >5000g in women without diabetes and >4500 in women with diabetes

Bishop's Scale for Cervical Ripening^a

Factor	Points			
	0	1	2	3
Dilation	Closed	1-2 cm	3-4 cm	5+ cm
Effacement	0-30%	40-50%	60-70%	80+%
Station	-3	-2, -1	0	+1, +2
Consistency	Firm	Medium	Soft	
Position	Posterior	Mid	Anterior	

^a A score of 0 to 4 points is associated with the highest likelihood of failed induction; a score of 9 to 13 points is associated with the highest likelihood of successful induction.

27. Postpartum Hemorrhage: L&D nurse calls you to see a 20 year-old Becky, G3 now P3, one hour post vaginal delivery because of excessive bleeding.

Definition:

Excessive bleeding (blood loss > 500cc for vaginal delivery, >1000cc for C-Section) in the minutes to hours following delivery. Considered Early PPH if < or =24Hr, or late if >24 Hr to 6wks PP. Can be sudden and profuse or prolonged and persistent.

Pathophysiology/DDx

More likely causes--

1. Uterine Atony is #1 cause.
 - This is failure of the uterus to undergo normal involution postpartum.
 - The primary physiological mechanism to stop bleeding postpartum is the clamping down of the uterus, causing constriction of the spiral arteries to prevent bleeding from the placental implantation site.
2. Lacerations of vulva, vagina, or cervix

3. Retained placenta or placental fragments.
 - a. placenta accreta – placenta adheres and is inseparable from the uterine wall
 - b. placenta increta - placenta invades into myometrium (uterine muscle)
 - c. placenta percreta - complete invasion of placenta through entire myometrium and serosa, and sometimes through adjacent organs

Less Likely causes--

4. Hematomas - caused by shearing forces of baby or forceps during delivery
5. Coagulopathies
 - a. DIC-from abruptio placenta
 - amniotic fluid embolism
 - severe preeclampsia
 - b. any congenital or acquired coagulopathy
6. Subinvolution of the uterus
7. Uterine rupture
8. Uterine inversion

History:

1. Uterine Atony: ask about *risk factors*--
 - Pt. experienced prolonged or precipitous labor?
 - Was pt's labor augmented with Pitocin?
 - Is pt multiparous?
 - Did pt have polyhydramnios, multiple gestation, amnionitis?
 - Was Mg Sulfate used?
 - Was fetus macrosomic?
 - Does pt have h/o uterine masses (e.g. leiomyoma)?
2. Lacerations:
 - What was route of delivery?
 - Were forceps, or vacuum assistance needed?
 - Was labor precipitous?
 - Macrosomic infant?
 - Breech delivery?
3. Retained placenta:
 - Was delivery of placenta difficult?
 - Was delivered placenta intact?
 - Does pt have h/o prior c/s, uterine curettage, or uterine leiomyoma?
4. Coagulopathy:
 - Did pt have preeclampsia or abruptio placenta with this delivery?
 - Does pt have any genetic coagulopathy?

Physical Exam:

- General: look for signs of shock (Tach, BP, and Tilt)
- Abdomen: palpate for "boggy" fundus (of atony or subinvolution).
- Pelvic: examine cervix, vagina, and external genitalia for lacerations or hematomas. Can perform bimanual exam to palpate uterus and adnexa. Pelvic mass palpated lateral to uterus is suggestive of broad ligament hematoma of uterine rupture.

Workup:

1. CBC
2. Coags
3. Examine placenta for intactness
4. Pelvic US-can detect broad ligament hematoma, retained products of conception (placenta)

Management:

1. If suspect massive blood loss
 - a. **Large Bore IV Access x 2**

- b. Type and Cross
- 2. Uterine Atony:
 - a. Prevent with routine 20 units/L of PIT after delivery of placenta
 - b. Vigorous uterine massage
 - c. If still boggy can give another 20 units of PIT up to total of 60 units/L
 - d. Methergine 0.2mg IM (contraindicated in pts with HTN/PreE)
 - e. Prostaglandin F 2alpha (aka, Hemabate) 0.25mg IM (contraindicated in patients with asthma)
 - f. Bakri balloon
 - g. Surgery (=last resort):
 - Uterine artery ligation
 - Hypogastric artery ligation (not generally a good option)
 - Selective arterial embolization (performed by IR), or hysterectomy
- 3. Lacerations:
 - a. Repair
 - b. Evacuation of expanding hematomas
 - c. Vaginal packing
 - d. Arterial angiographic embolization
- 4. Retained placenta
 - a. Manual removal
 - b. Dilation and curettage
- 5. Coagulopathy
 - a. Correct underlying cause
 - b. Transfuse with whole blood
 - c. Transfuse platelets and fresh frozen plasma
- 6. Uterine rupture: immediate laparotomy with either repair of rupture or hysterectomy
- 7. Uterine inversion:
 - a. Manual replacement of uterine fundus with fingers or palm of hand, do NOT give PIT until uterus repositioned
 - b. Consider giving tocolytic agents such as nitroglycerin, terbutaline for uterine relaxation and aid in manual replacement of uterine fundus
 - c. Last resort-emergency laparotomy with use of traction sutures to replace uterine fundus

29. Premature Rupture Of Membranes: 22 year old Dana, G1 P0, at 27 weeks gestation comes to your office stating she had a gush of fluid from the vagina 2 hours ago. Her perineum is grossly wet.

Definition: Rupture of the chorioamniotic membrane before the onset of uterine contractions. Preterm PROM (PPROM) refers to PROM before 37.0 weeks of gestation. PPRM occurs in approximately 3% of all pregnancies and associated with approximately 1/3 of preterm births.

Pathophysiology: Etiology is not clearly understood. When contractions begin or the membranes rupture, matrix metalloproteinase activity in amnion and chorion increases and levels of basement membrane collagens decrease. This triggers a cascade of events including apoptosis of fetal membranes and connective tissue changes.

Risk Factors for PROM:

- 1) Genital tract infection (vaginal, cervical, chorioamnionitis)
 - Gonorrhea, Chlamydia
 - Group B Strep
 - Gardnerella vaginalis
- 2) Multiple gestation
- 3) Polyhydramnios
- 4) Incompetent cervix/ Cervical cerclage
- 5) Previous cervical laceration or operation
- 6) Smoking
- 7) Drug use: cocaine

- 8) Prior h/o PROM
- 9) Trauma, antepartum bleeding

Differential Diagnosis:*Most likely cause--*

1. PROM
 - pt c/o gush of fluid from vagina with ongoing leakage is PROM in 90% of cases
 - Fluid passing through vagina must be assumed to be amniotic until proven otherwise

Less likely causes--

2. leakage of urine
3. excessive normal (or infectious) vaginal d/c
4. bloody show associated with labor

History:

- Ask about Risk Factors.
- Always ask about gestational age and time and date of rupture.
- The longer the time, the more increased risk for subsequent chorioamnionitis, fetal infections, and fetal deformation.

Physical Exam:

1. Check for signs of chorioamnionitis (uterine tenderness, maternal/ fetal tachycardia, maternal fever, fetal distress, purulent amniotic fluid)
2. Perform sterile speculum exam:
 - Watery d/c may be noted externally or in vaginal pool.
 - May be observed flowing from the cervical os with fundal pressure or Valsalva maneuver.
 - Cervical dilatation and effacement may be seen . Do **NOT** perform digital cervical exam on pt with preterm PROM who is not in labor.

Workup:

- 1) Nitrazine test: if fluid turns nitrazine paper blue (ph>6.0) then suspect amniotic fluid (nl vaginal ph 4.5-6.0, amniotic fluid ph 7.1-7.3).
 - Can get false + from semen, blood, infection, or alkaline antiseptics in vagina
- 2) Microscopic slide test for ferning of vaginal fluid
- 3) U/S: look for low amniotic fluid index (AFI <5cm, Greatest Vertical Pocket <2cm), determine gestational age and presentation of fetus
- 4) Tests to r/o chorioamnionitis
 - i) CBC with Diff
 - ii) amniocentesis & culture of amniotic fluid (used infrequently)
- 5) Cervical cultures to r/o STD and Group B strep, treat with appropriate Abx to decrease risk of perinatal transmission
- 6) Fetal well being by NST
- 7) Fetal lung maturity:
 - test amniotic fluid for PG and L/S ratios
 - + PG and L/S >2.0 is very reassuring (presence of blood in amniotic fluid increases L/S ratio, meconium decreases L/S ratio; neither affects PG, but PG matures one week later than L/S).
 - only PG is used for pooled vaginal fluid; PG and L/S can be done if amnio performed
- 8) US-guided instillation of indigo carmine: Typically used when prior tests are equivocal and usually leads to definitive diagnosis. Dye injected transabdominally into amniotic fluid. Tampon placed in vagina, then removed to examine for blue staining which would indicate leakage of fluid.
- 9) AmniSure: Rapid slide test that uses immunochromatography to detect trace placental alpha microglobulin-1 protein in vaginal fluid. Advantage of test is that it is not affected by semen or trace amounts of blood.

Management:

1. Preterm PROM not in labor (**this pt**):
 - Expectant management: when risks of delivery (including prematurity) outweigh risk of expectant management (infection, cord prolapse).

- i) Prophylactic Abx: Generally amox/azith, decreases infection and prolongs onset of labor by 5-12 days
 - ii) Antenatal steroids 23-34 weeks: decreases neonatal death, RDS, IVH, NEC
 - iii) Tocolysis: only to delay delivery for 48 hours to allow administration of corticosteroids. Should not be administered in patients in advanced labor (>4cm) or have any findings suggestive of chorioamnionitis, abruption, or babies at risk of cord prolapse (dilated cervix and malpresentation).
 - iv) Hospitalization recommended with daily NST (BPP if nonreassuring), q4 hr FHR check, U/S q 3-4 wks, activity limited to bathroom and sitting in bedside chair.
 - v) Monitoring: Maternal temperature/pulse QID, uterine tenderness/contractions, avoid acetaminophen
 - vi) Avoid digital cervical exams until pt in labor
 - vii) obtain vaginal pool fluid for PG when ≥ 32 wks
 - viii) Timing of delivery for expectantly managed pregnancies: magnesium sulfate administered prior to delivery for fetal neuroprotection from 24-31.6 weeks.
 - a) fetal lung maturity attained between 32-34 weeks
 - b) maternal or fetal compromise
 - c) infection
 - d) reaches 34 weeks
2. PROM with advanced labor, chorioamnionitis, or fetal distress should undergo delivery **regardless** of gestational age

34. Preterm Labor: 24 year-old Lorna G2 P1 at 28 weeks gestation by dates (but no prenatal care) presents at L&D with regular contractions every 5 minutes.

Definition: Preterm labor is contractions leading to cervical dilation from 20 – 37 wGA.

Etiology:

- ~incidence averages about 7%
- ~idiopathic - 50%
- ~multiple gestation - 10-15%
- ~medical indications for induction - 5-20%
- ~uterine anomalies - 5-15%
- ~misc (infection, polyhydramnios, incompetent cervix) - 5%

Risk Factors (to be assessed during history):

1. Low socioeconomic status (and black race -- 2x higher rate than white race)
2. Previous preterm delivery (risk increases with # of preterm deliveries)
3. Previous 2nd-trimester abortion(s)
4. Repeated spontaneous 1st-trimester AB
5. Other med/OB factors including 1st-trimester bleeding, UTIs, multiple gestation, uterine anomalies, polyhydramnios, incompetent cervix
6. Smoking more than a half a pack a day
7. DES exposure in utero
8. History of cone biopsy

Diagnosis:

- ~Unless contraindicated (placenta previa), perform vaginal exam
- ~Rule out dehydration, cystitis, pyelonephritis, ureteral stones, and bowel disorders, all of which can mimic the symptoms of preterm labor and can actually be assoc with contractions
- ~Recheck dates to confirm labor is actually preterm, US to see if size agrees with dates
- ~Pts presenting before 37 wks who are more than 3 cm dilated, having frequent contractions (more than every 10 minutes), and more than 75% effaced are likely to be in labor
- ~Regular contractions (6 in 1 hr) in the presence of ROM may also be regarded as labor

~If pt is having regular contractions, is dilated less than 3cm, has a singleton gestation, has an EGA between 22.0 and 34.6, has no vaginal bleeding, no ROM, and no intercourse in last 24hr then obtain a fetal-fibronectin – if this is negative then chance of delivery within the next 2 weeks is less than 1-2%!

Management:

- A. Obtain CBC, UA to w/u possible infection
- B. Hydration and sedation (narcotics) - will stop contractions in 20%
- C. Tocolytic therapy: These will slow or stop contractions, however if a pt is truly in pre-term labor then 99% of the time these methods will not be effective)

Contraindications to tocolysis include severe pre-eclampsia, severe bleeding from placenta previa or abruption, chorioamnionitis, IUGR, fetal anomalies incompatible with life or fetal demise. These patients should undergo augmentation of labor given the risks of prolonging pregnancy in these situations]

1. Beta agonists (Terbutaline, Ritodrine)
 - increases cAMP which decreases the availability of free calcium, therefore decreasing contractions
 - Side effects include CV (incr HR, SBP; decr DBP; CP, myocard ischemia, arrhythmias), pulmonary edema (rare), hyperglycemia, hypokalemia due to increased insulin release
 - placental transfer occurs, but fetal effects are delayed
 - not indicated after 34 weeks of gestation
2. MgSO₄
 - drug of choice in pts with DM or heart disease
 - competes with Ca for entry into the cell at depolarization causing a decr in intracellular Ca, resulting in myometrial relaxation
 - side effects include feeling of warmth and flushing on first administration, respiratory depression at levels of 12-15mg/dl, and cardiac conduction defects and arrest at higher levels
 - low calcium in fetus may occur with loss of muscle tone and drowsiness in neonate (resulting in lower Apgar score)
 - controversial as to its effectiveness
3. PG Inhibitors (indomethacin)
 - PGs induce contractions
 - side effects include oligohydramnios, premature closure of fetal ductus which may lead to neonatal pulmonary hypertension and cardiac failure, platelet dysfunction, increased bleeding during delivery and postpartum
 - contraindicated after 32 weeks
 - also can only be given for a short course given r/o oligohydramnios
4. Ca Channel Blockers (nifedipine)
 - relaxes myometrial tissue
 - side effects relate to CV effects and include tachycardia and hypotn in mother and neonate (hypoxia and fetal acidemia leading to fetal death have also been reported)
- D. Glucocorticoids
 1. enhance fetal lung maturity to decrease respiratory distress syndrome (RDS)
 2. effective at less than 34 wks, females benefit more than males, black infants benefit more than white infants
 3. New data suggests offering as early as 22.5 wk (controversial to offer before 24wk but currently the practice at UAB)
- E. Delivery - vaginal if vertex and in no distress; C/S if breech or NRFHTs

37. Puerperal Infection: 29 year-old Babette, G3 now P3, is 36 hours post low mid-forceps delivery of a 3950 g male neonate following a 4 hour second stage of labor. The maternity unit nurse notifies you Babette has a temperature of 103.4 °F.

Definition: a puerperal fever is a temperature of 100.4 °F (38.0 °C) or higher on any 2 occasions of the first 10 days postpartum, *excluding* the first 24 hours. An *infection* is presumed when other causes are not apparent. [Practically speaking, treatment is often instituted for significant elevations of temperature *within* the 1st 24 hours, especially when accompanied by other evidence of infection]

Differential Diagnosis:

1. **Metritis:** Post-delivery infection of the uterine lining that often extends into the myometrium. Usually presents day 2-5 post-delivery, and is diagnosed when a postpartum fever is accompanied by uterine tenderness (i.e. fundal tenderness). The most important risk factor is route of delivery: the incidence is 25-50% following a C-section, and only 1-6% after spontaneous vaginal delivery. Infections are polymicrobial, and single-drug (e.g., Cefotan or Ancef) or multiple-drug (e.g., Clindamycin-gentamicin) regimens may be used.
2. **Urinary tract infections:** Usually present on the 2nd day postpartum and more common if a foley catheter was inserted (e.g., for a C-section or epidural anesthesia). Diagnosis requires a degree of suspicion: dysuria may not be present (due to decreased sensitivity of the bladder after delivery), and urinary frequency is a common postpartum finding. Costovertebral angle tenderness may suggest pyelonephritis.
3. **Mastitis:** Often characterized by a significant fever (103 °F or more) but usually presents late in the puerperium. Other symptoms include breast tenderness and erythema, malaise, and general body aching. Approximately 15% of women who do not breast feed develop postpartum fever from breast engorgement. Staph. aureus (esp. MRSA) is most commonly isolated organism.
4. **Wound infection:** In spite of bacterial contamination, infections of an episiotomy site are very uncommon (< 0.25%). Episiotomy infections are becoming less common because the procedure is performed much less frequently now than in the past. Infection of the incision site following C-section is also relatively uncommon (<10% of cases). These infections usually present on the 3rd to 4th day postpartum. Necrotizing fasciitis is a rare but deadly infection (50% fatality rate) that may occur in the perineum or abdomen.
5. **Other infection:** Pelvic thrombophlebitis is an uncommon infection that is the sequelae of pelvic infection. It usually presents as persistent (days 4-10) fever and tachycardia following several days of antibiotic treatment. Latent pulmonary TB may be activated by lowering the diaphragm following delivery. Pelvic abscesses are also possible.
6. **Atelectasis:** Common if general anesthesia was used (e.g., w/ a C-section); usually presents 1st day post-op.
7. **Pneumonia:** Uncommon, usually seen in those with pre-delivery respiratory disease; aspiration pneumonia more likely with general anesthesia.

History:

What significant medical history does the mother have? Were there any complications during pregnancy?

Predisposing factors to postpartum infections include obesity, low socioeconomic status, anemia, immunosuppression, chronic disease (e.g., diabetes mellitus), and vaginal infection (esp. bacterial vaginosis).

What is the hx of the labor and delivery?

Rupture of fetal membranes, intraamniotic infection, prolonged labor, multiple pelvic exams during labor, internal electronic fetal monitoring, and Cesarean birth all predispose to infection.

What other significant complaints has the patient had since delivery?

Pay special attention regarding pulmonary symptoms, urinary tract disturbance, and abdominopelvic pain/tenderness.

Physical Exam:

Examination should include the lungs, the back (for costovertebral angle tenderness), palpation of the abdomen, careful inspection of the incision site, a check for the presence of bowel sounds, examination of the perineum, a pelvic examination, assessment for calf tenderness, and inspection of any intravenous site. Although a pelvic examination may not elicit any findings other than uterine

tenderness, one can confirm that lochia drainage is, in fact, occurring and baseline information can be obtained concerning adnexal masses that may be important if the fever persists and an abscess develops.

Management:

Blood cultures are not usually obtained unless the infection appears severe, sepsis is suspected, fever is especially high, or the response to limited therapy is delayed. Antibiotic therapy will depend upon the most likely etiology of the infection; possible regimens include the following: dicloxacillin for mastitis, ceftriaxone/azithromycin for pneumonia, and gent/clindamycin for metritis.

Rarely, heparin may be given for pelvic thrombophlebitis.

39. Rectovaginal Fistula: 31 yo Barbara, G1 P1, 3 weeks post vaginal delivery and 4th degree laceration comes to your office complaining of what looks and smells like stool in her vagina.

Definition: Congenital or acquired epithelial lined tract between the vagina and rectum.

- Classified according to location, size, and etiology. Most RVFs are related to obstetric events and occur in the distal third of the vagina.

History: Important questions include:

1. Does patient have history of an episiotomy or laceration?
 - 1st lac: Involves fourchette, perineal skin, and vaginal mucosa
 - 2nd lac: Above + fascia and muscles of perineal body but NOT anal sphincter
 - 3rd lac: Above + disruption of external anal sphincter
 - 4th lac: Above + disruption of internal anal sphincter, extending through the rectal mucosa
2. Has pt had infection in the episiotomy repair site?
3. Does PMH include h/o lower genital tract cancer, radiation or IBD?

Physical Exam:

- Rectovaginal exam to determine extent & location of fistula
 1. Traumatic lesions usually near vaginal opening; look for suture placed through rectal wall during repair or undetected rectal injury from delivery
 2. If fistula site cannot be determined by exam, may use barium enema and/or CT scan.

Management: Depends on underlying etiology and the defect's size and location. Usually requires surgical repair, however, some women with small RVFs following obstetric trauma may be followed conservatively in anticipation of spontaneous healing of the fistulous tract.