MENSTRUAL DISORDERS

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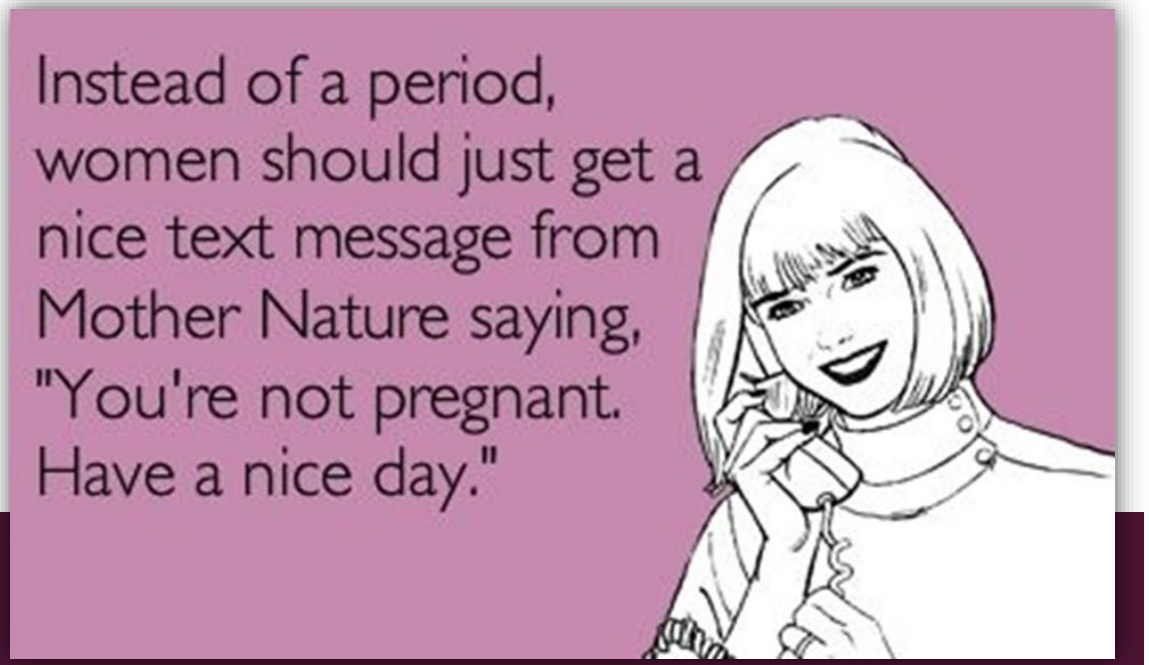
MARCH 7TH, 2019 ASAPA ANNUAL SPRING CONFERENCE



LEARNING OBJECTIVES

1. Review sexual differentiation and "normal" female pubertal development.
2. Examine the most common etiologies of primary and secondary amenorrhea.
3. Describe a logical approach to evaluate and interpret historical, physical and laboratory/diagnostic findings of a patient presenting with amenorrhea.
4. Identify potential causes of abnormal uterine bleeding (AUB) as it relates to adolescents, reproductive age non-pregnant females and post-menopausal women; discuss its general management.
5. Compare and contrast primary and secondary dysmenorrhea.
6. Discuss the management of primary and secondary dysmenorrhea based on current recommendations.
7. Evaluate which menstrual disorder(s), commonly encountered in primary care, require referral or specialist consultation.

LECTURE OUTLINE

- Normal sexual development and female puberty
- Amenorrhea
- Abnormal uterine bleeding
- Dysmenorrhea
- Referral / specialist consult

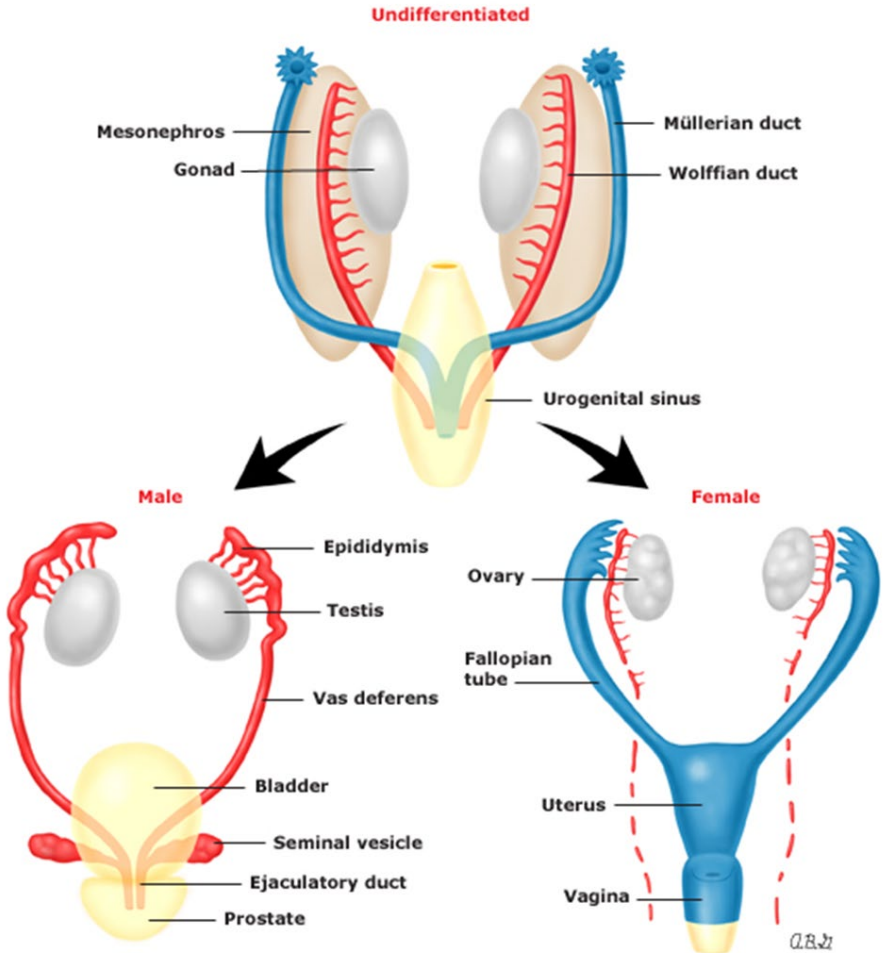
WHAT IS NORMAL?

PRENATAL SEXUAL DEVELOPMENT & NORMAL FEMALE PUBERTAL DEVELOPMENT

NORMAL SEXUAL DEVELOPMENT

Males (46, XY):

- Gonads become testes
- Wolffian ducts give rise to the epididymides, vasa deferens, seminal vesicle, and ejaculatory ducts
- *Müllerian ducts regress*



Females (46, XX):

- Gonads become ovaries
- ***Müllerian ducts give rise to the fallopian tubes, uterus, and upper vagina***
- Wolffian ducts become nonfunctional

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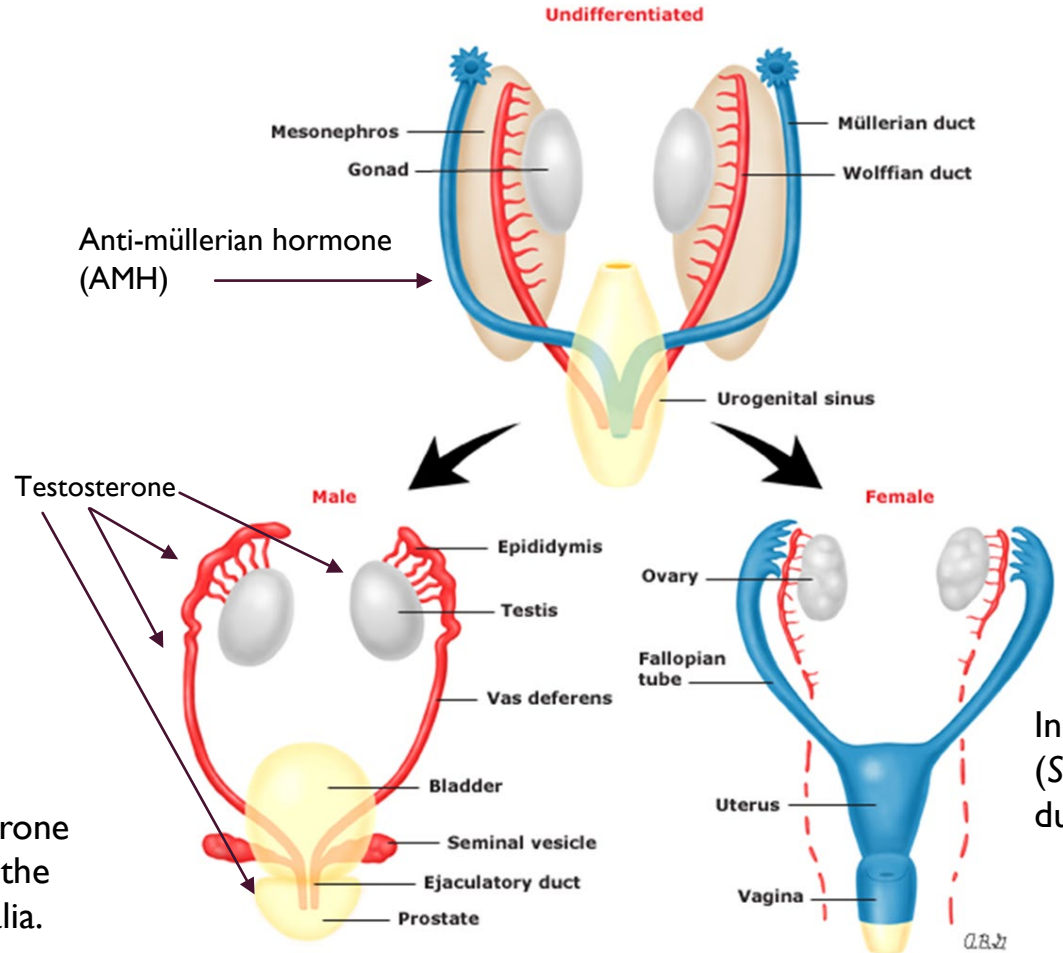

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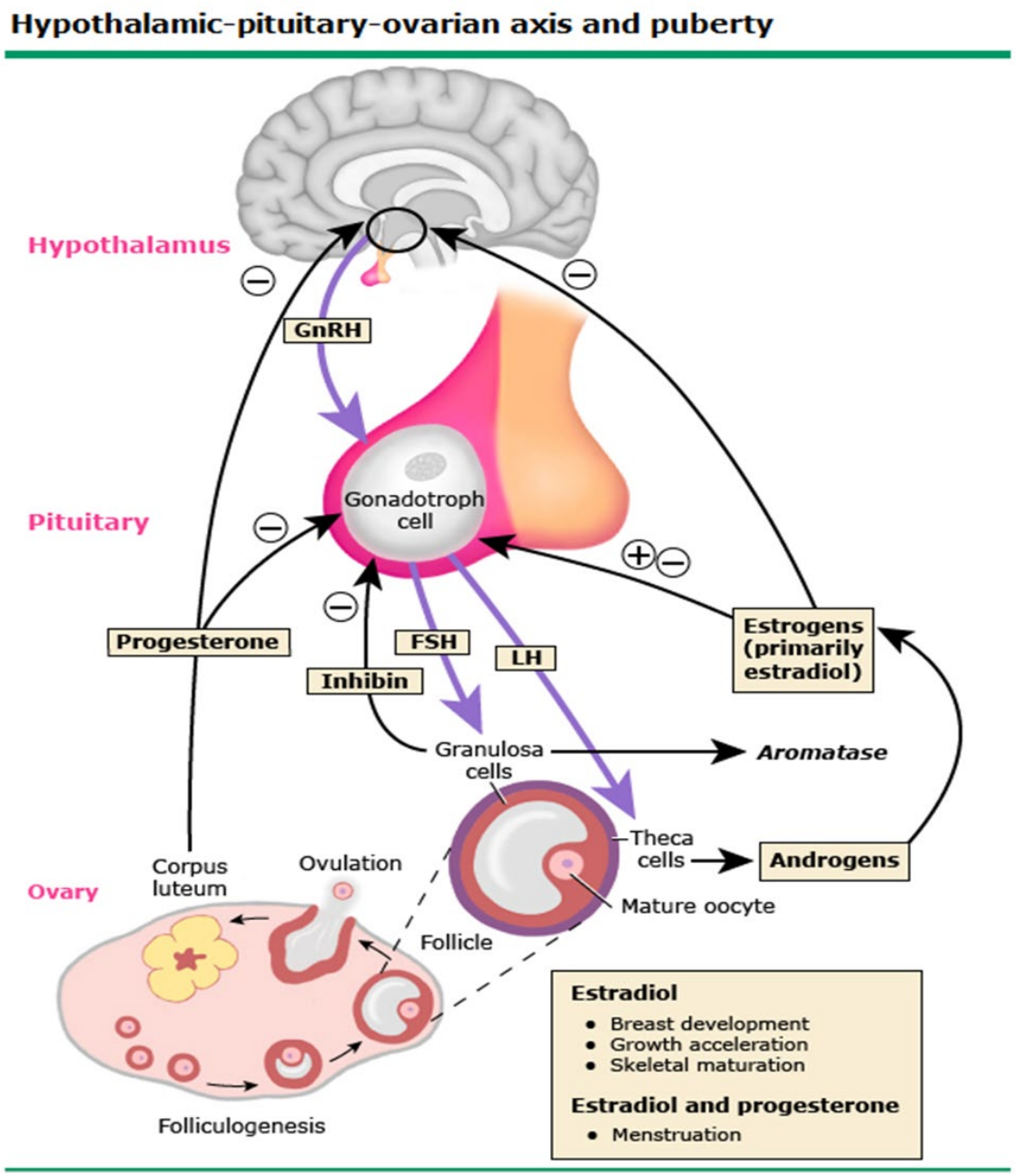
Testosterone → Dihydrotestosterone (DHT) regulates development of the prostate and male external genitalia.

In the absence of testis determining factor (*SRY* gene from Y chromosome), the Wolffian ducts degenerate.



NORMAL FEMALE PUBERTY

Early in puberty:

Hypothalamus releases pulsatile GnRH

GnRH stimulates FSH/LH from anterior pituitary

FSH/LH stimulate production of estradiol from ovaries

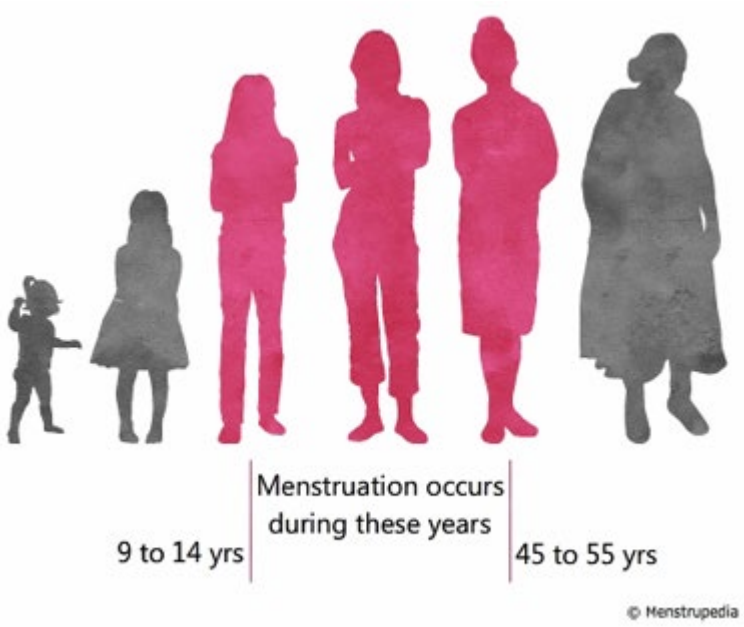
Estradiol → breast development & growth of skeleton

Later in puberty:

FSH/LH and estradiol lead to ovulation and menstrual cycles

THE NORMAL MENSTRUAL CYCLE

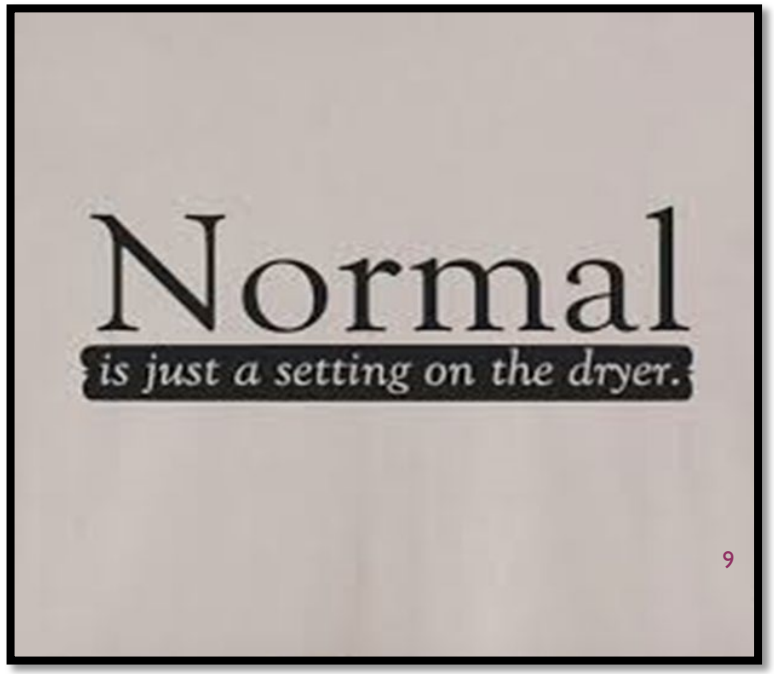
- Average age of menarche is 12 -13 years
- Average age of menopause is 51 years
- Average adult menstrual cycle last 24-38 days
  - Cycle day #1 through cycle day #1 of next cycle
- Duration of bleeding ≤ 8 days (average is 4.5 days)
- Amount of blood loss 5-80mL (30mL being the median amount)



Approach to abnormal uterine bleeding in nonpregnant reproductive-age women UpToDate
Last updated Oct. 29, 2018

THE NORMAL MENSTRUAL CYCLE

- Regular and spontaneous menstruation requires:
  - A functional hypothalamic-pituitary-ovarian (HPO) axis
  - An endometrium (uterus) competent to respond to steroid hormone stimulation
  - An intact outflow tract from internal to external genitalia



AMENORRHEA

PRIMARY AND SECONDARY AMENORRHEA

AMENORRHEA: THE ABSENCE OF MENSES

Primary Amenorrhea

- Absence of menses by age 15 in the presence of normal growth and secondary sexual characteristics

  OR

- Absence of menses by age 13 in complete absence of secondary sexual development

Secondary Amenorrhea

- Absence of menses for more than 3 cycle intervals OR 6 consecutive months in women who were previously menstruating

PRIMARY AMENORRHEA - ETIOLOGIES

- Usually the result of a genetic or anatomic abnormality
  - Gonadal dysgenesis/primary ovarian insufficiency (50%) ★
  - Hypothalamic and pituitary disease (20-25%)
  - Outflow tract disorders (20%)
  - Receptor abnormality or enzyme deficiency (5%)

PRIMARY AMENORRHEA – GONADAL DYSGENESIS

https://www.orthobullets.com/pediatrics/4106/turners-syndrome

- Dysgenesis = abnormal organ development
- **Turner Syndrome:** ovaries are unable to respond to gonadotropins (one of most common causes of premature ovarian failure) and results in "hypergonadotropic hypogonadism" (high FSH)
- **Swyer Syndrome:** "vanishing testes"; fibrous streak gonad cannot secrete anti-Mullerian hormone or testosterone

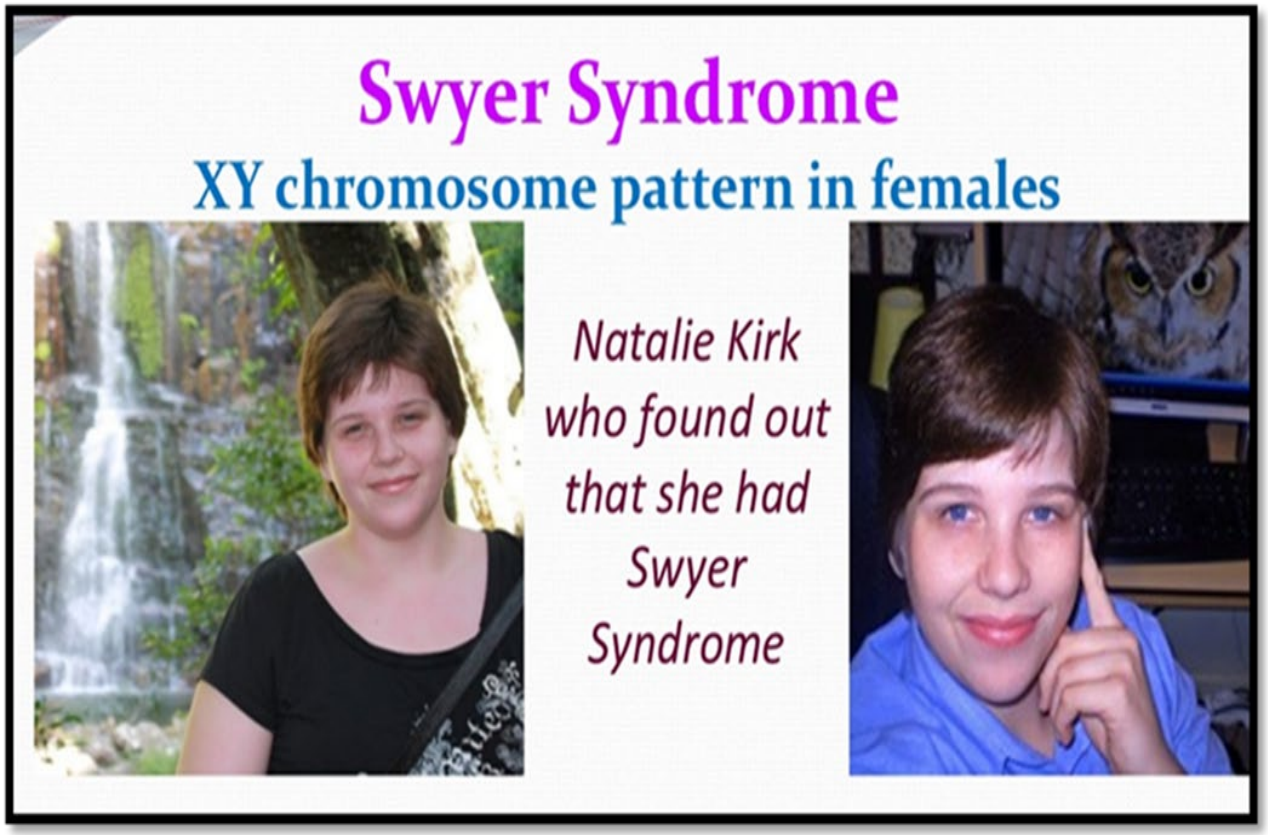
PRIMARY AMENORRHEA – GONADAL DYSGENESIS

- Turner Syndrome (45, XO gonadal dysgenesis)
  - Results in premature depletion of oocytes and follicles
  - Short stature, "shield chest" with widely spaced nipples, webbed neck
  - "Streak ovaries" and sexual infantilism

https://www.researchgate.net/figure/A-12-year-old-girl-with-severe-pterygium-colli-associated-with-Turner-syndrome_fig16_266623250

PRIMARY AMENORRHEA – GONADAL DYSGENESIS

- Swyer Syndrome (46, XY gonadal dysgenesis)
  - Mutations of SRY gene account for many cases
  - Indifferent gonads fail to differentiate into testes
  - Lack of testosterone or DHT results in normal external female genitalia
  - Secondary sex characteristics do not develop

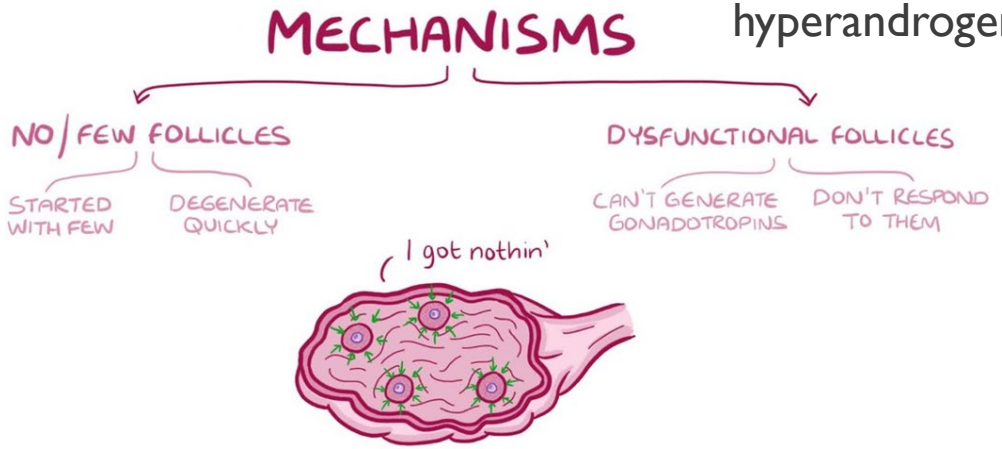


https://www.slideshare.net/iLRish/gender-presentation-15173285

PRIMARY AMENORRHEA – PRIMARY OVARIAN INSUFFICIENCY & PCOS

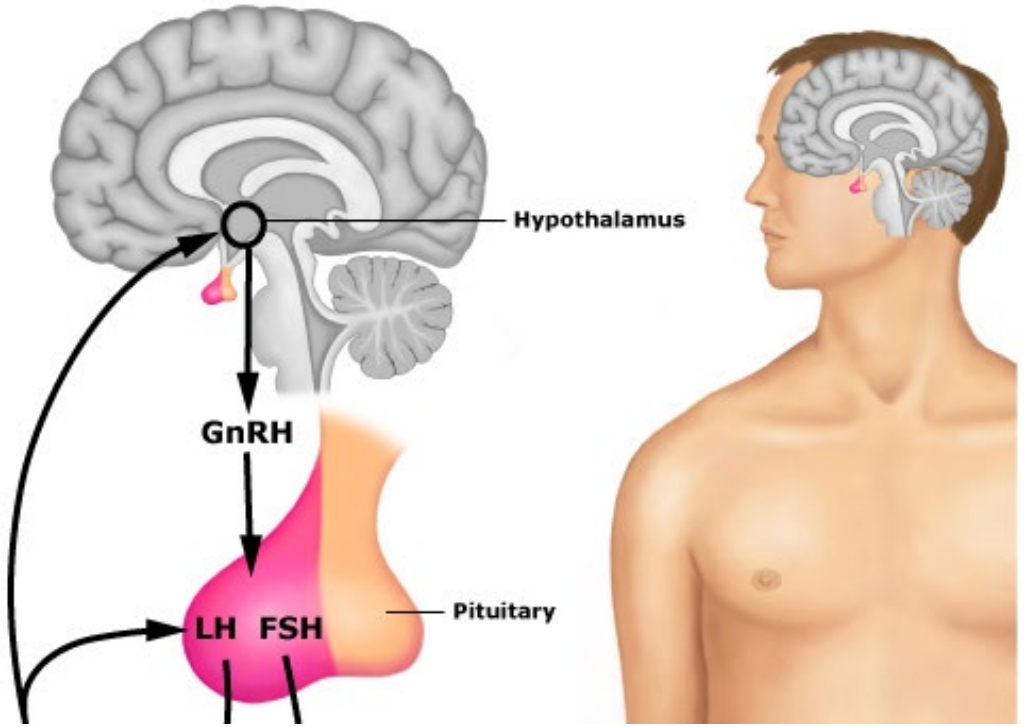
- Primary Ovarian Insufficiency (POI)
  - 46, XX with clinical menopause before age 40
  - Usually presents as secondary amenorrhea, but some present with primary amenorrhea
    - Causes include: chemotherapy, radiation, autoimmune oophoritis, Fragile X syndrome (*FMR1 gene* premutation)

- Polycystic Ovarian Syndrome (PCOS)
  - Rarely a cause of primary amenorrhea
  - Ovulatory dysfunction
  - Clinical and biochemical evidence of hyperandrogenism in the presence of advanced pubertal development and in absence of other disorders causing amenorrhea and hyperandrogenism



PRIMARY AMENORRHEA – HYPOTHALAMIC & PITUITARY CAUSES

- "Hypogonadotropic hypogonadism" (low FSH) due to:
  - Abnormal hypothalamic GnRH secretion
    - Leading to decreased gonadotropin pulse discharge
  - Congenital absence of GnRH



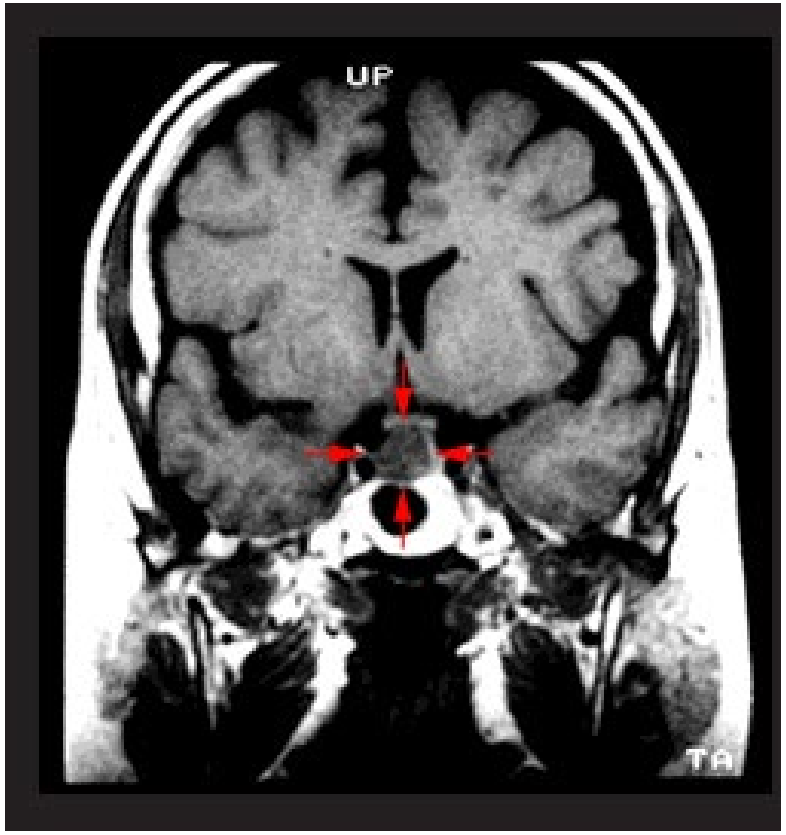
PRIMARY AMENORRHEA – HYPOTHALAMIC CAUSES

- "Functional" or "hypothalamic amenorrhea" (abnormal GnRH secretion in the absence of pathologic processes)
  - Decreased gonadotropin (FSH/LH) pulsations, low or normal LH, absent LH surge
    - Absent follicular development and ovulation; low estradiol secretion
  - FSH levels often in the normal range
  - Causes include stressors such as: eating disorders, physical or psychological stress, weight loss, excessive exercise (e.g. female athlete triad)
- "Idiopathic hypogonadotropic hypogonadism" or congenital GnRH deficiency
  - Called Kallmann's syndrome if associated with anosmia

PRIMARY AMENORRHEA – PITUITARY CAUSES

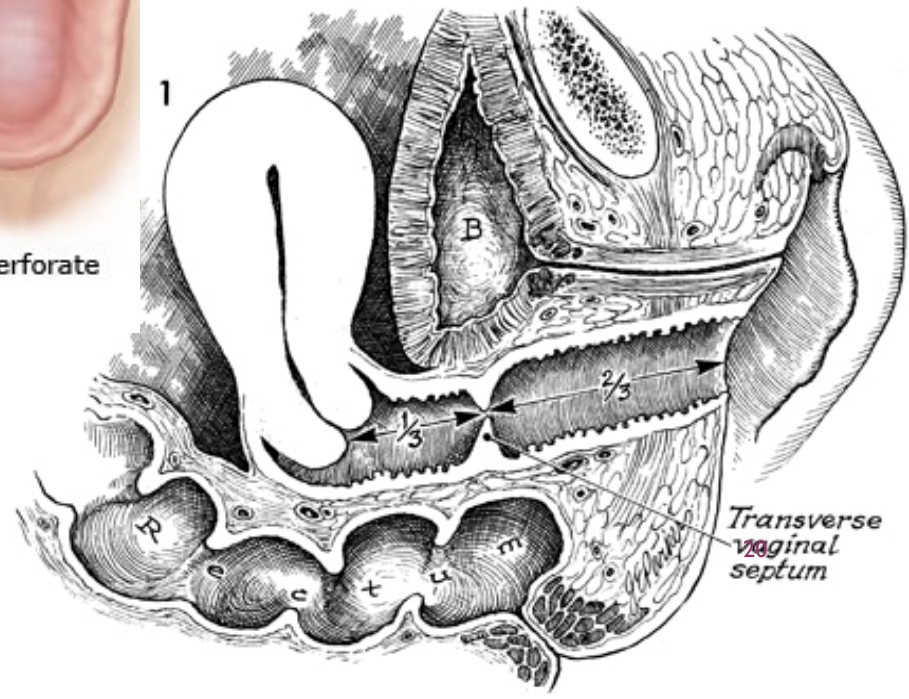
- Micro and macroadenomas (Cushing's disease, prolactinomas, thryotropinomas, etc.)
- Isolated hyperprolactinemia (though more commonly causes secondary amenorrhea)
  - Galactorrhea present
  - Hypothyroidism and some medication increase prolactin levels
- Infiltrative diseases and/or cranial tumors that cause pituitary stalk compression

Thirty-seven-year-old woman with Cushing's disease caused by a 9 x 11 x 14 mm corticotroph macroadenoma.



PRIMARY AMENORRHEA – OUTFLOW TRACT DISORDERS

- Uterine – Müllerian agenesis (also called vaginal agenesis)
  - 46, XX with congenital absence of the oviducts, uterus and upper vagina
  - Normal gonadal function (estrogen = breast dev.)
- Vagina – Imperforate hymen and transverse vaginal septum
  - Cyclic pelvic pain and perirectal mass from sequestration of blood in the vagina



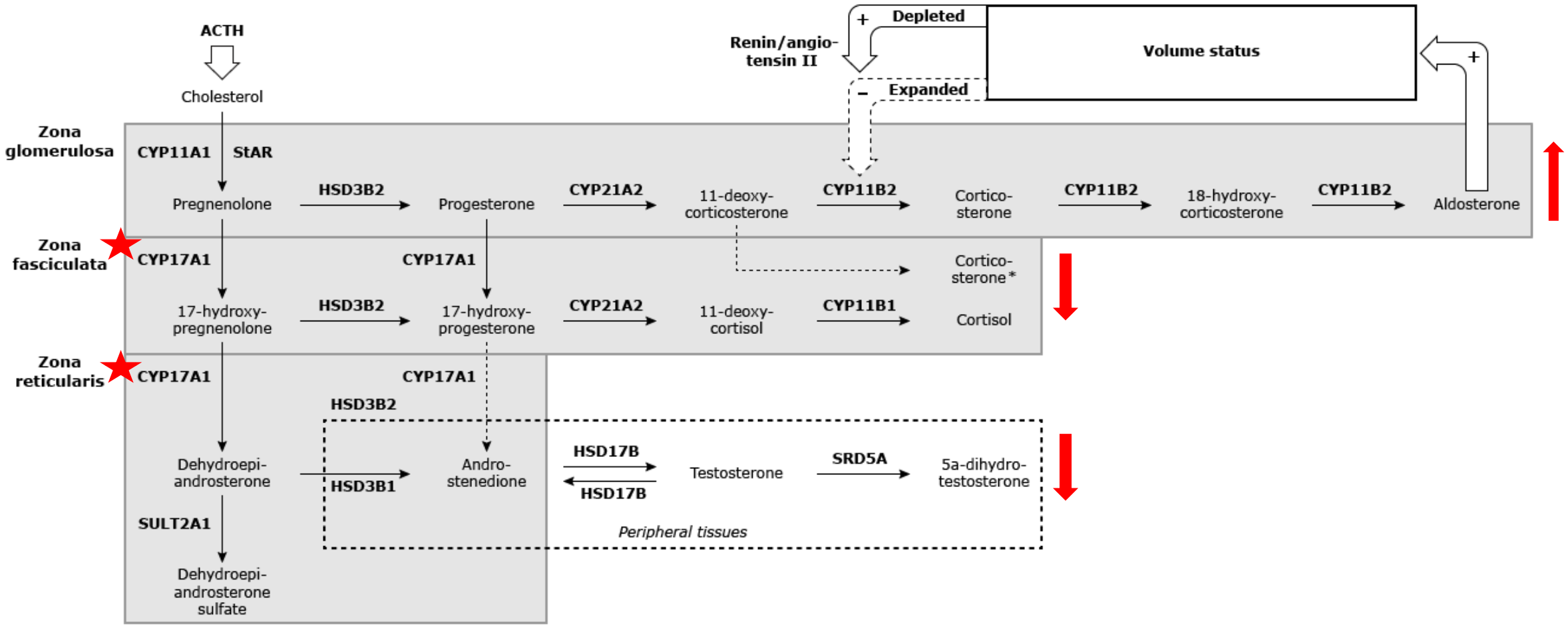
PRIMARY AMENORRHEA – RECEPTOR/ENZYME ABNORMALITIES

- Androgen Insensitivity Syndrome
  - 46, XY, with **female phenotype**
  - Abnormality of androgen receptor (either complete or partial insensitivity)
    - Testes make testosterone and AMH but body not responsive to testosterone or its active metabolite DHT
    - High serum testosterone concentrations (within normal male range)
  - Present with breast development, absence of acne and voice changes at puberty and absent (or sparse) axillary/pubic hair
  - Pelvic ultrasound:
    - Absent upper vagina, uterus and fallopian tubes on pelvic ultrasound
    - **Testes remain intra-abdominal or partially descended; should be removed due to increased risk of testicular CA**

PRIMARY AMENORRHEA – RECEPTOR/ENZYME ABNORMALITIES

- 5-alpha-reductase deficiency
  - 46, XY
  - Unable to convert testosterone to DHT → no differentiation of male genitalia during fetal development
  - **Ambiguous genitalia at birth**
  - Undergo virilization at puberty but no enlargement of external genitalia or prostate
- 17-alpha-hydroxylase deficiency *(CYP17 gene)*
  - Rare disorder, 46, XX or 46, XY
  - Decreased cortisol synthesis and lack of adrenal & gonadal sex steroids; overproduction of mineralocorticoids (high ACTH)
  - Present as phenotypic females with HTN and lack of pubertal development, or 46, XY with incompletely developed external genitalia

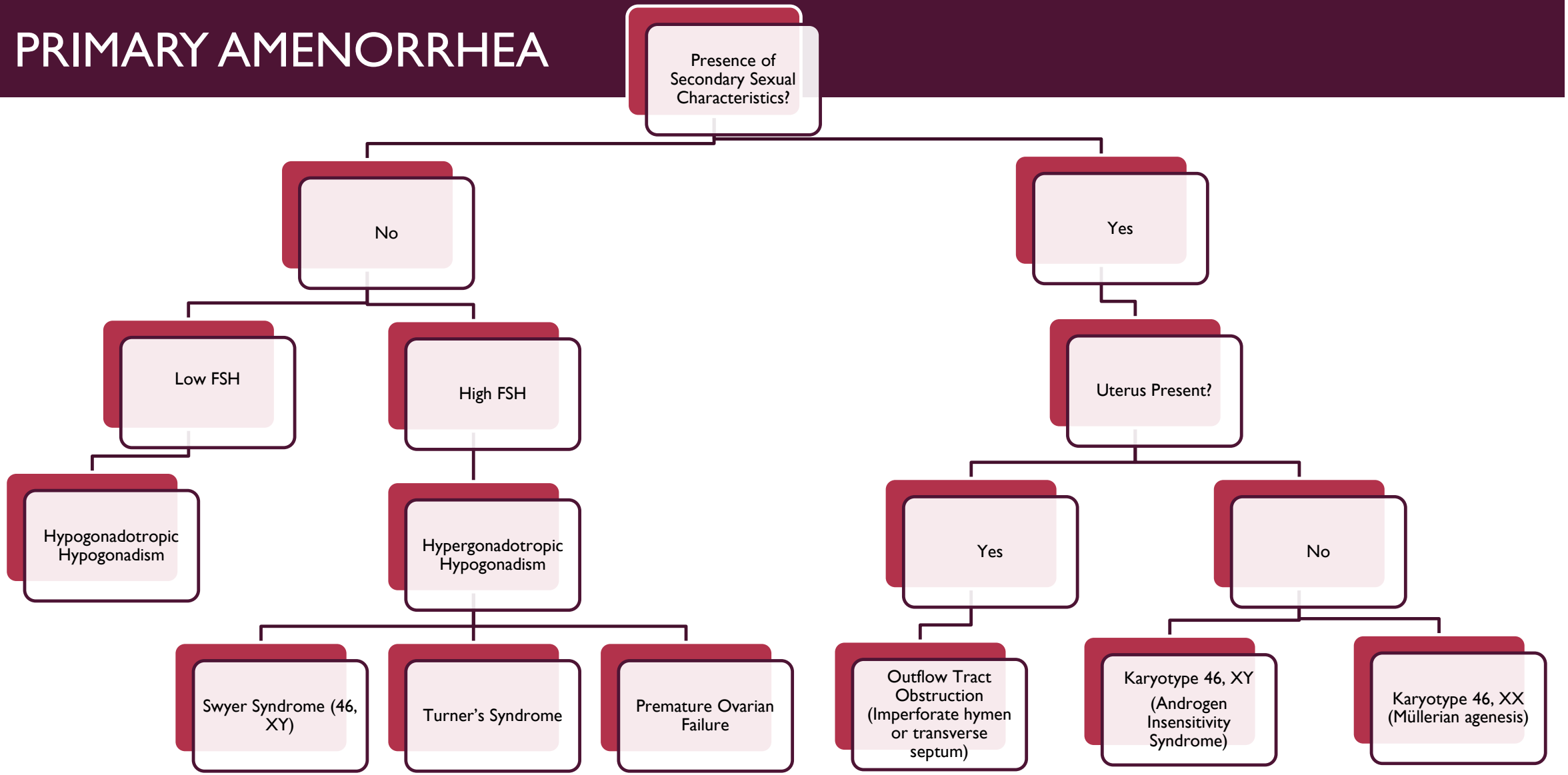
Normal adrenal steroidogenesis



ACTH: corticotropin.

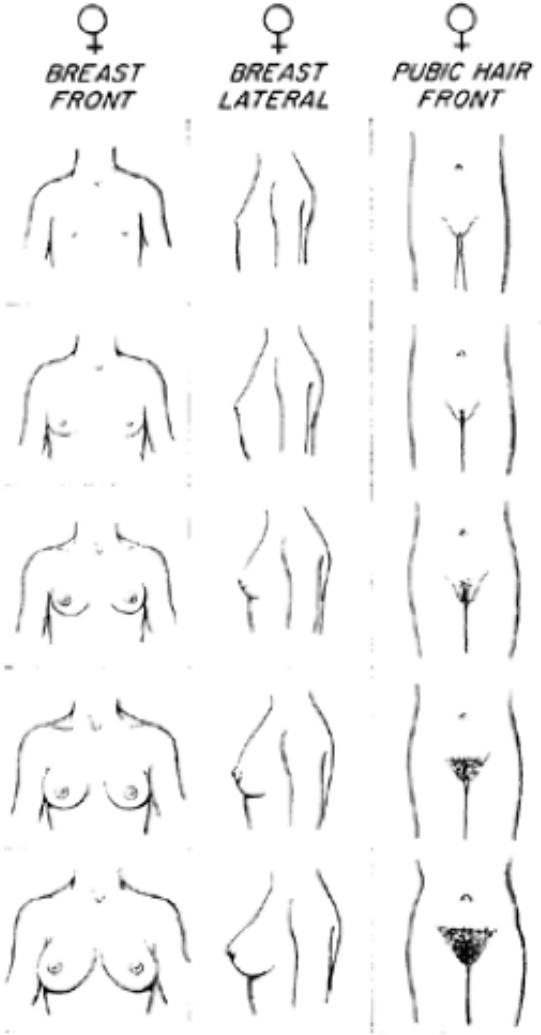
* The CYP11B1 enzyme also converts 11-deoxycorticosterone to corticosterone in the zona fasciculata, but this is ordinarily a minor pathway compared with cortisol formation, except in 17-hydroxylase deficiency when corticosterone becomes the dominant glucocorticoid.

PRIMARY AMENORRHEA



PRIMARY AMENORRHEA – WHEN TO INITIATE AN EVALUATION

- Age 15 if no uterine bleeding has occurred
- Age 13 if no menses and no evidence of thelarche
- If no menarche within 3 years of thelarche
  - The general order of female sexual development is thelarche (breasts), pubarche (pubic/axillary hair), growth spurt, then menarche (menses).



PRIMARY AMENORRHEA – HISTORY QUESTIONS

- Timeline of other stages of puberty
- Time of menarche in patient's mother/sister(s)
- Neonatal and childhood health
- Patient's height relative to other family members
- History of head trauma
- Sexual activity
- Stress, change in weight, diet, exercise habits, or illness
- Anosmia (Kallman Syndrome)
- Symptoms of virilization
- Galactorrhea
- Headaches, visual field defects

PRIMARY AMENORRHEA – PHYSICAL EXAM

- Assess vitals: weight, height, BMI
- Examine:
  - Skin: acne, virilization, hirsutism
  - Thyroid: goiter, abnormal DTRs
  - Features of Turner syndrome: webbed neck, low hair line, widely spaced nipples, short stature
  - Breast development and axillary hair growth
  - Genital exam: external genitalia, pubic hair growth, presence/absence of uterus

PRIMARY AMENORRHEA – INITIAL WORK-UP

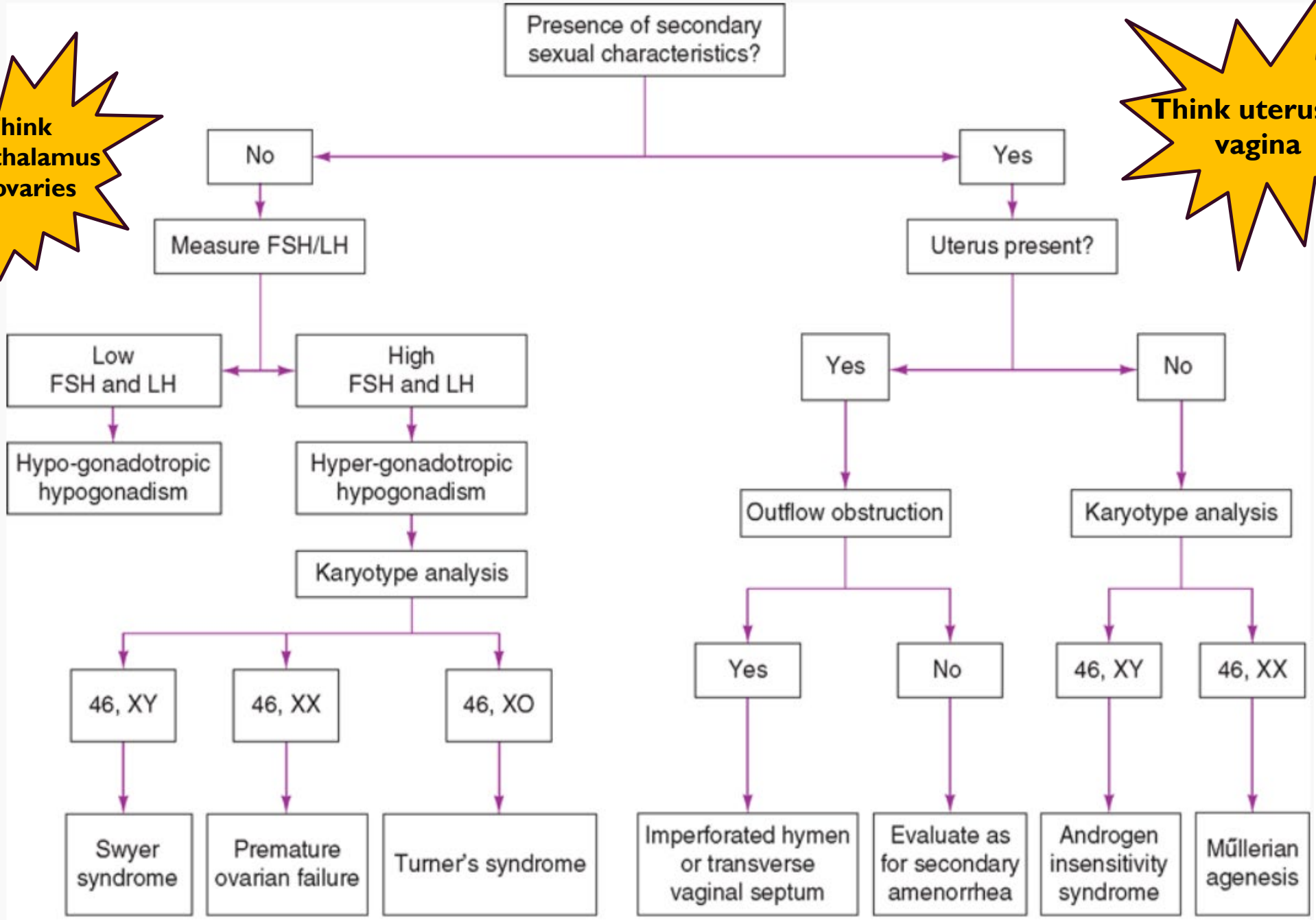
- Laboratory tests and diagnostic studies
  - Urine or serum HCG
  - Serum FSH
  - Prolactin
  - TSH
  - Pelvic ultrasound

PRIMARY AMENORRHEA – ADDITIONAL STUDIES

- Consider additional studies based on physical exam findings and results of initial work-up
  - If absent uterus: Karyotype and total testosterone (46, XX = Müllerian agenesis, or 46, XY = AIS)
  - If FSH elevated: Karyotype (45, XO = Turner syndrome or 46, XY = Swyer syndrome)
  - If FSH low/normal and…
    - Positive breast development – consider outflow tract disorder or endocrine disorder (PCOS, hyperprolactinemia, thyroid disease)
    - Negative breast development – recheck FSH, LH and consider pituitary MRI
      - If repeat FSH/LH very low, consider congenital GnRH deficiency or constitutional delay of puberty

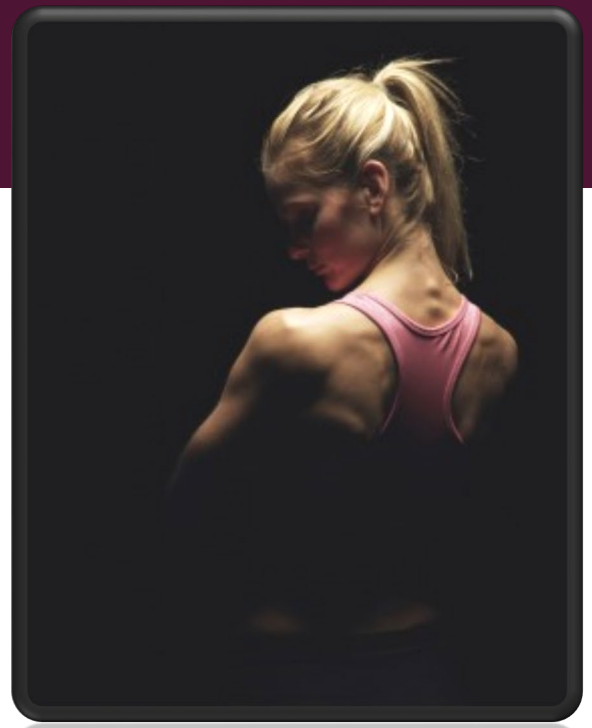
Think hypothalamus or ovaries

Think uterus or vagina



Source: DeCherney AH, Nathan L, Laufer N, Roman AS: *CURRENT Diagnosis & Treatment: Obstetrics & Gynecology*, 11th Edition: www.accessmedicine.com

PRIMARY AMENORRHEA - TREATMENT



- Treatment is based on underlying etiology
- Goals:
  - Treat underlying cause (if possible)
  - Restore ovulatory cycles and preserve fertility
  - Prevent complications (treat hypoestrogenemia / hyperandrogenism)
- Psychological counseling
- Referral to endocrinologist and/or gynecologist
- Surgical referral is necessary for correction of outlet obstruction or for gonadectomy

SECONDARY AMENORRHEA - ETIOLOGIES

- PREGNANCY!!!
- Other causes:
  - Ovarian dysfunction (40%)
  - Hypothalamic dysfunction (35%)
  - Pituitary dysfunction (17%)
  - Uterine dysfunction (7%)

"We've never had an accident – aside from three of our five kids."

SECONDARY AMENORRHEA – OVARIAN DYSFUNCTION

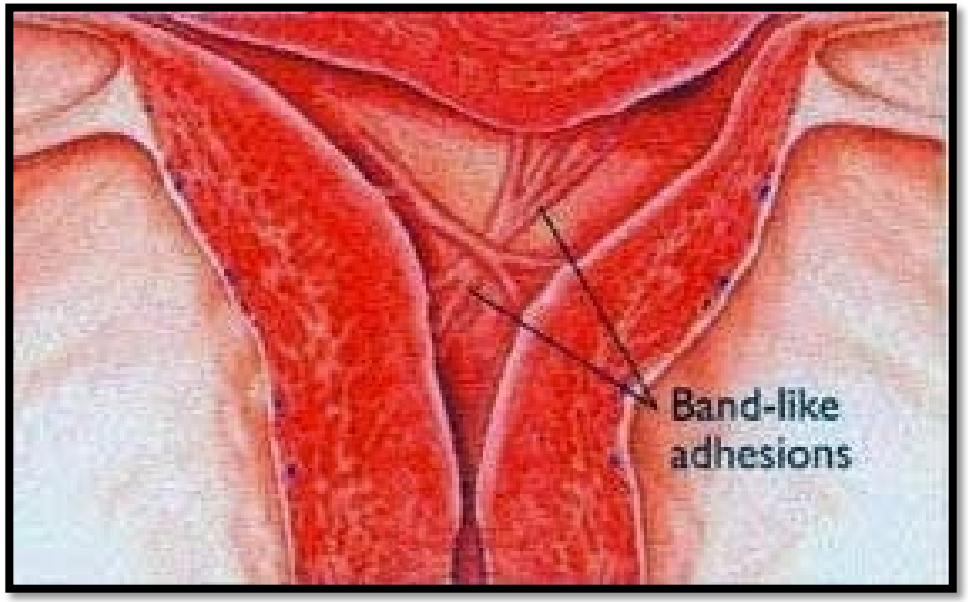
- Polycystic Ovarian Syndrome
  - Androgen excess (acne, hirsutism, elevated total testosterone)
  - Ovulatory dysfunction (amenorrhea or oligomenorrhea)
  - Polycystic ovaries
- Primary Ovarian Insufficiency (formerly "Failure")
  - Depletion of oocytes before age 40
  - Etiologies: Turner syndrome, Fragile X premutation, autoimmune ovarian destruction, or unknown cause
  - Can result from radiation or chemotherapy
- Hyperandrogenism
  - Adrenal or ovarian tumors that secrete androgens; pronounced virilization

SECONDARY AMENORRHEA – HYPOTHALAMIC & PITUITARY CAUSES

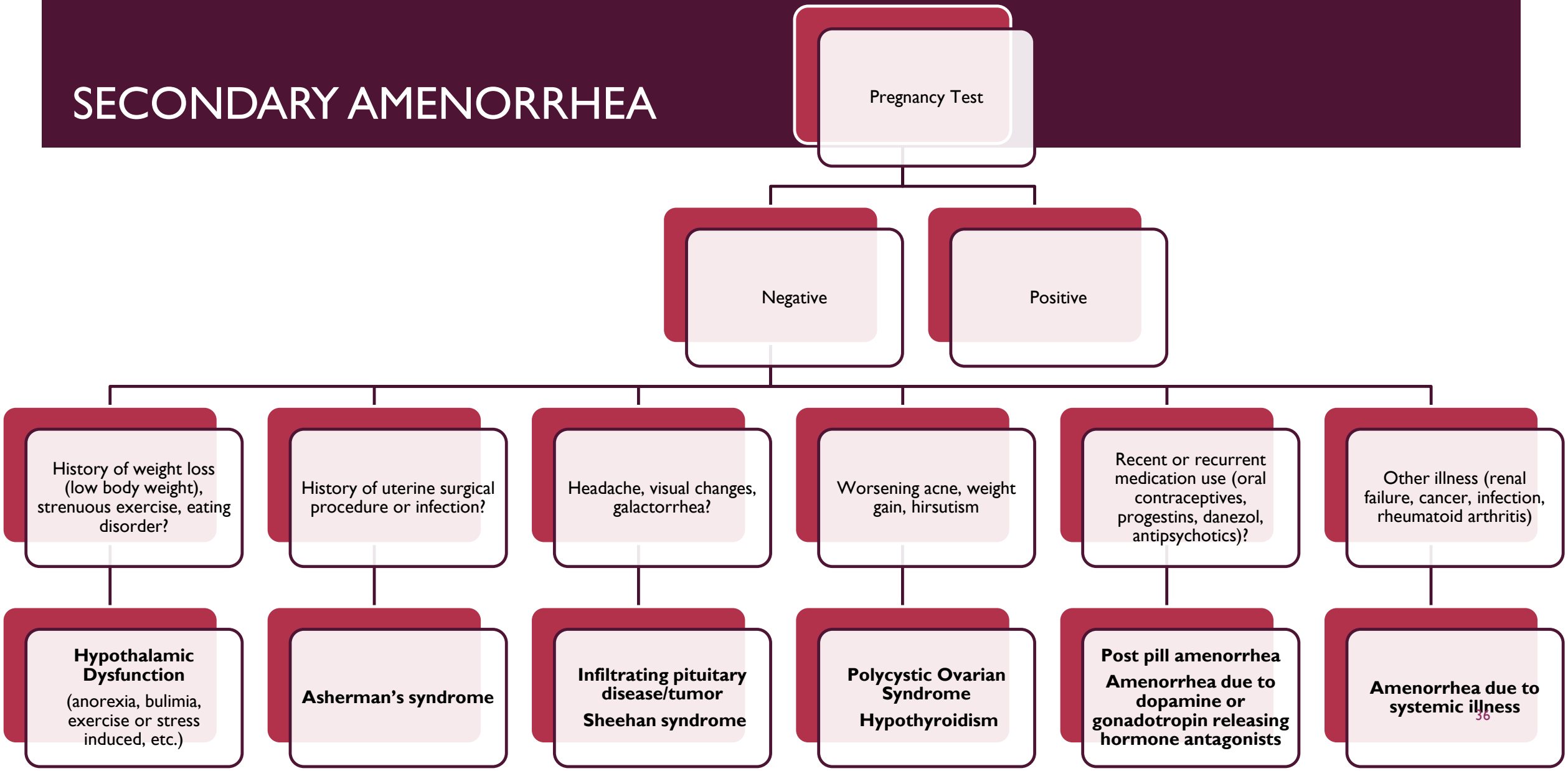
- Functional Hypothalamic Amenorrhea
  - Causes include: weight loss, exercise, nutritional deficiencies, stress, infiltrative lesions, celiac disease, head trauma
- Pituitary Disease
  - Hyperprolactinemia – prolactinoma or medication induced (e.g. antipsychotics)
  - Sheehan's syndrome
    - Postpartum amenorrhea resulting from postpartum pituitary necrosis secondary to severe hemorrhage and hypotension
  - Iron deposition (hemosiderosis)
  - Primary hypothyroidism
    - Due to thyrotroph and/or lactotroph hyperplasia

SECONDARY AMENORRHEA – UTERINE DYSFUNCTION

- Asherman's Syndrome
  - Acquired scarring of the endometrial lining, usually secondary to postpartum hemorrhage or endometrial infection followed by instrumentation such as dilatation and curettage.



SECONDARY AMENORRHEA



SECONDARY AMENORRHEA – HISTORY QUESTIONS

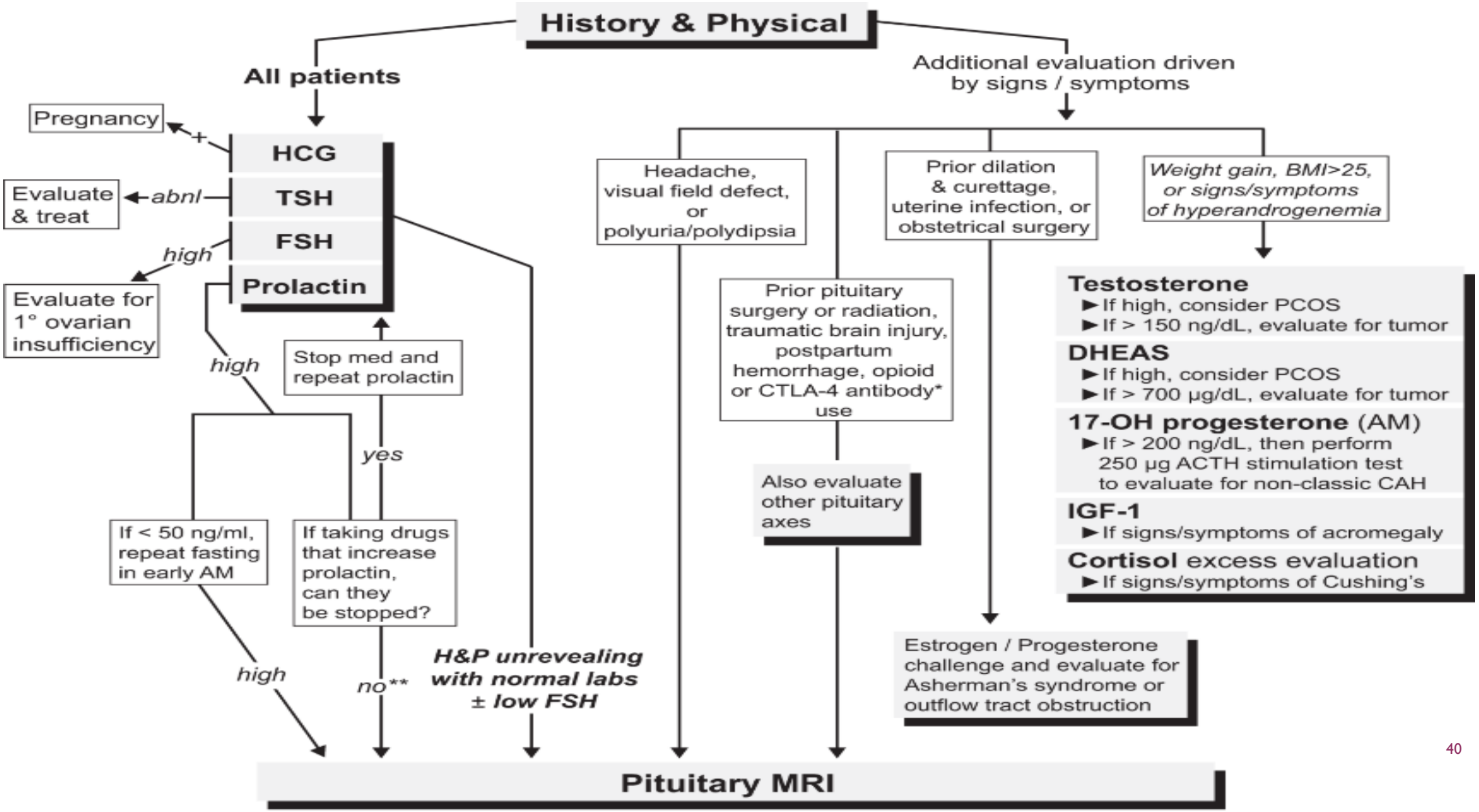
- Previous menstrual history
- Potential for pregnancy, currently breastfeeding?
- PMH (recent illnesses, stress)
- Medications
- Exercise habits
- Weight change
- History suggestive of Asherman syndrome
- Skin (hirsutism, acne, hair loss)
- Galactorrhea
- Symptoms of estrogen deficiency (vaginal dryness, hot flashes, poor sleep, decreased libido)
- Headaches, visual field defects, fatigue

SECONDARY AMENORRHEA – PHYSICAL EXAM

- Assess vital signs: height, weight, BMI
- Examine:
  - Skin: oily skin, acne, hirsutism, acanthosis nigricans, vitiligo, bruising
  - Thyroid: exophthalmos, goiter, abnormal DTRs
  - Breast exam: galactorrhea
  - Pelvic exam: vulvovaginal exam for signs of estrogen deficiency or clitoromegaly

SECONDARY AMENORRHEA – INITIAL WORK-UP

- Laboratory studies:
  - Urine or serum HCG ← **ALWAYS!!!!!!**
  - FSH
  - Prolactin
  - TSH
  - Total Testosterone (if evidence of hyperandrogenism)

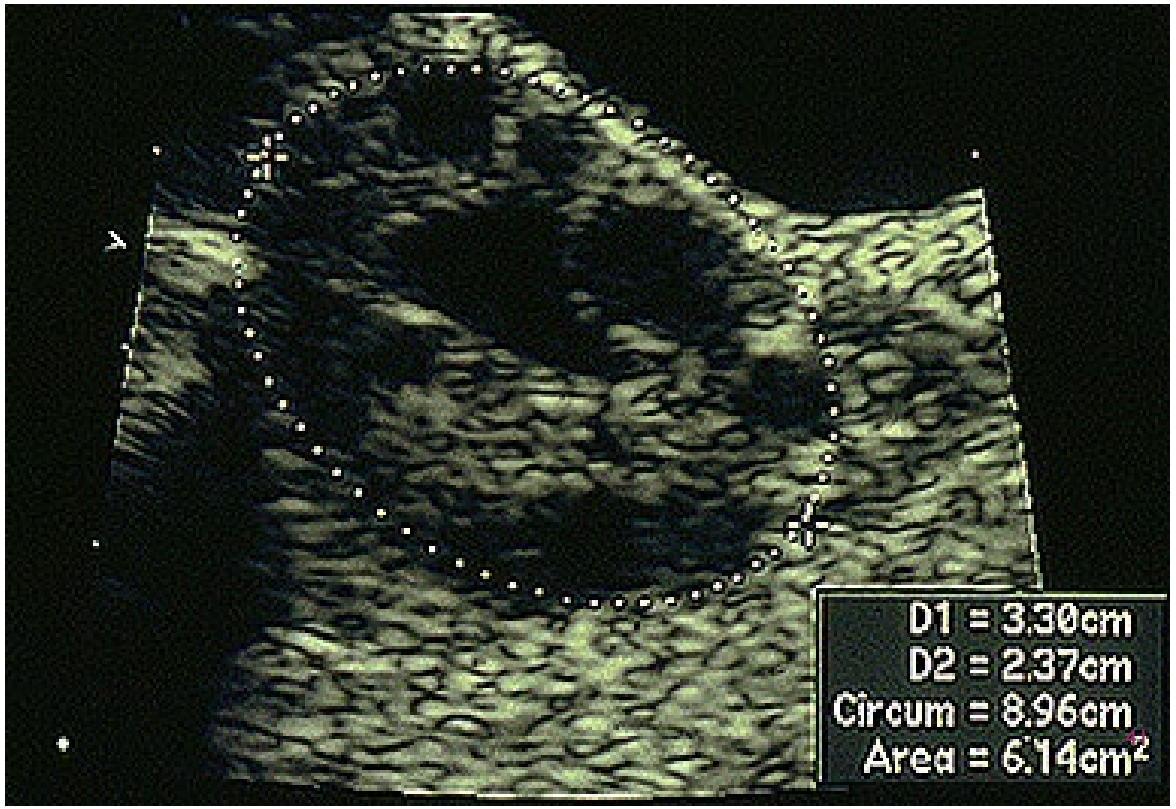


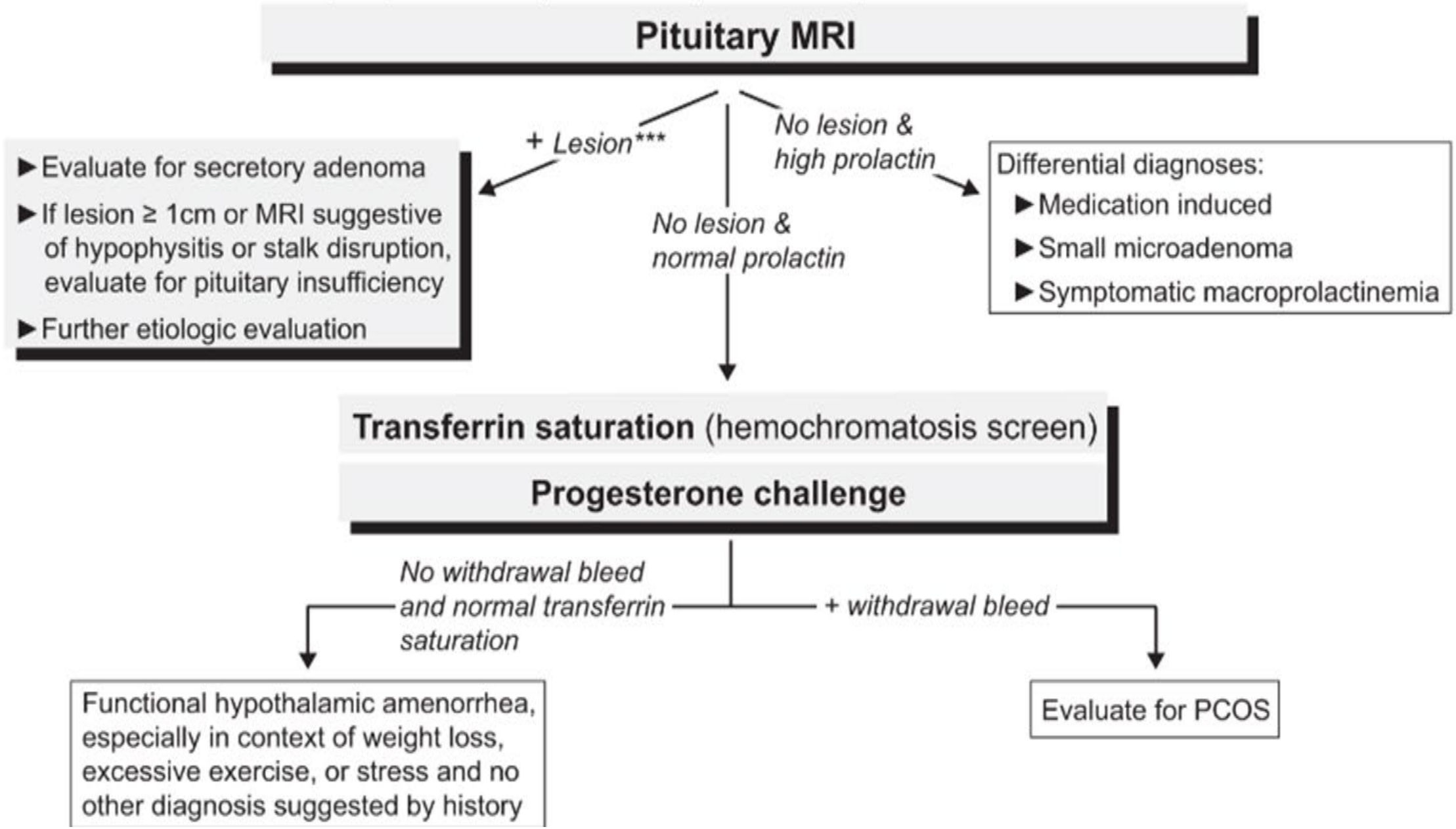
J Clin Endocrinol Metab. 2015;100(3):812-824. doi:10.1210/jc.2014-3344

SECONDARY AMENORRHEA – ADDITIONAL WORK-UP (CONT.)

- Imaging studies:
  - Pelvic Ultrasound
  - Pituitary MRI – if suspected pituitary pathology
  - Adrenal CT – if significant virilization and elevated testosterone

Ultrasonographic appearance of a polycystic ovary in a 15-year-old with PCOS





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SECONDARY AMENORRHEA - TREATMENT

- Treatment is based on underlying etiology
- Goals:
  - Treat underlying cause if possible (lifestyle, d/c offending medications)
  - Restore ovulatory cycles and preserve fertility
  - Reduce risk of complications (hypoestrogenemia / hyperandrogenism)
- Psychological counselling:
  - If hypothalamic failure due to anorexia, excessive exercise, abuse or stress
- Consider referral to endocrinologist, gynecologist and/or reproductive endocrinologist

CASE #1

- An 18-year-old nulliparous adolescent woman complains of primary amenorrhea. She denies weight loss or excessive exercise. Each of her sisters achieved menarche by age 13. She is 5'6" tall and weighs 140lbs, BP 110/60. Thyroid gland is normal. She has Tanner stage IV breast development, external genitalia, axillary and pubic hair. There are no skin lesions.
- Pelvic ultrasound – reveals an absent uterus
- What is the most likely diagnosis?

- **Müllerian agenesis**
  - Primary amenorrhea
  - + Breast development → presence of estrogen
  - + axillary/pubic hair → presence of androgens
  - Absent uterus on pelvic u/s
- How would you confirm the diagnosis?
  - Karyotype
  - Serum testosterone

https://obgyn.mhmedical.com/CaseContent.aspx?gbosID=395933&gbosContainerID=184&viewByNumber=false#17648225l

CASE #2

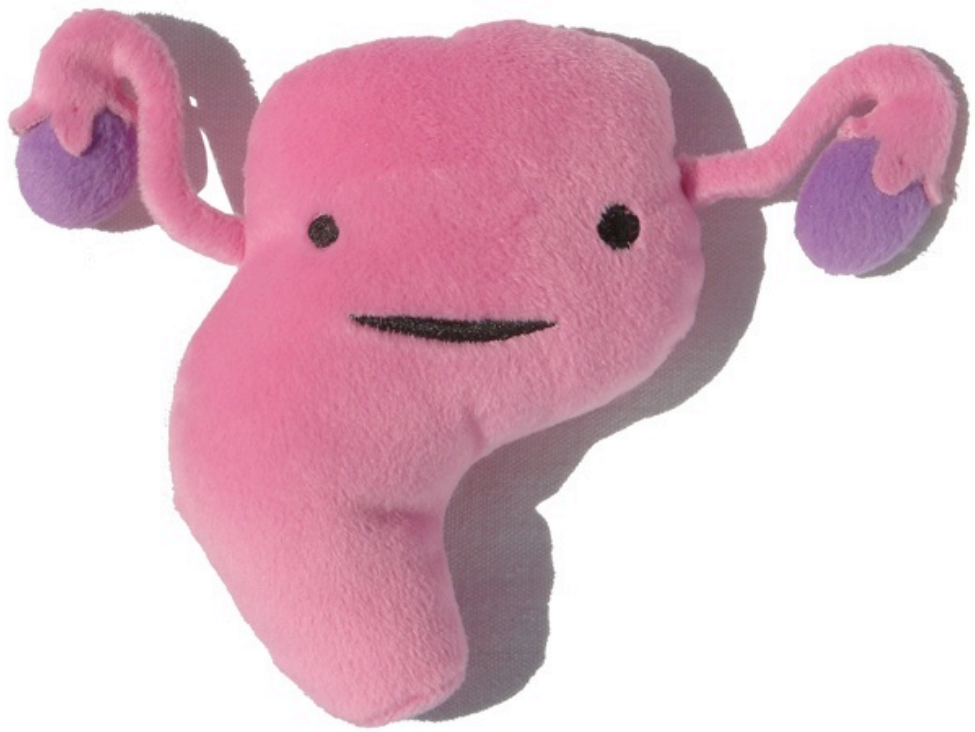
- 30-year-old parous woman presents with secondary amenorrhea and watery breast discharge x 6 months. She has hx of Graves disease (s/p radioactive iodine tx) and is currently not taking any medications. BP 120/80, HR 80 bpm. Breast are symmetric w/o masses or retraction. A white d/c can be expressed from both breasts.
- Urine pregnancy test – negative
- What is the most likely diagnosis?

- **Hyperprolactinemia, secondary to hypothyroidism**
  - Secondary amenorrhea
  - Galactorrhea due to hypothyroidism; increase in TRH level acts as a prolactin-releasing hormone
  - Increased dopamine interrupts GnRH pulsatile release
- What is the next step in evaluation of this patient?
  - Check TSH and prolactin levels
- If TSH elevated, treat with levothyroxine
- If TSH normal and elevated prolactin, order pituitary MRI

https://obgyn.mhmedical.com/CaseContent.aspx?gbosID=395928&gbosContainerID=184&viewByNumber=false#176481770

ABNORMAL UTERINE BLEEDING

FORMERLY KNOWN AS DYSFUNCTIONAL UTERINE BLEEDING



ABNORMAL UTERINE BLEEDING (AUB)

- Definition: menstrual bleeding of abnormal quantity, duration or schedule (cycle <24 or >38 days*, bleeding >8 days, blood loss >80mL, or intermenstrual bleeding)
  - New terminology AUB/HMB and AUB/IMB
- AUB accounts for 1/3 of outpatient gynecologic visits
- The most common etiologies are **anovulation**, structural uterine pathology, disorders of hemostasis, and neoplasia
  - PALM-COEIN is the current etiology classification system for AUB (2011 International Federation of Gynecology and Obstetrics Etiology Classification)

PALM-COEIN CLASSIFICATION

Abnormal Uterine Bleeding:
Heavy Menstrual Bleeding (AUB/HMB)
Intermenstrual Bleeding (AUB/IMB)

Structural Causes

- **P**olyp
- **A**denomyosis
- **L**eiomyoma
- **M**alignancy and endometrial hyperplasia

Nonstructural Causes

- **C**oagulopathy
- **O**vulatory dysfunction
- **E**ndometrial
- **I**atrogenic (anticoagulants, hormonal contraceptives)
- **N**ot otherwise classified

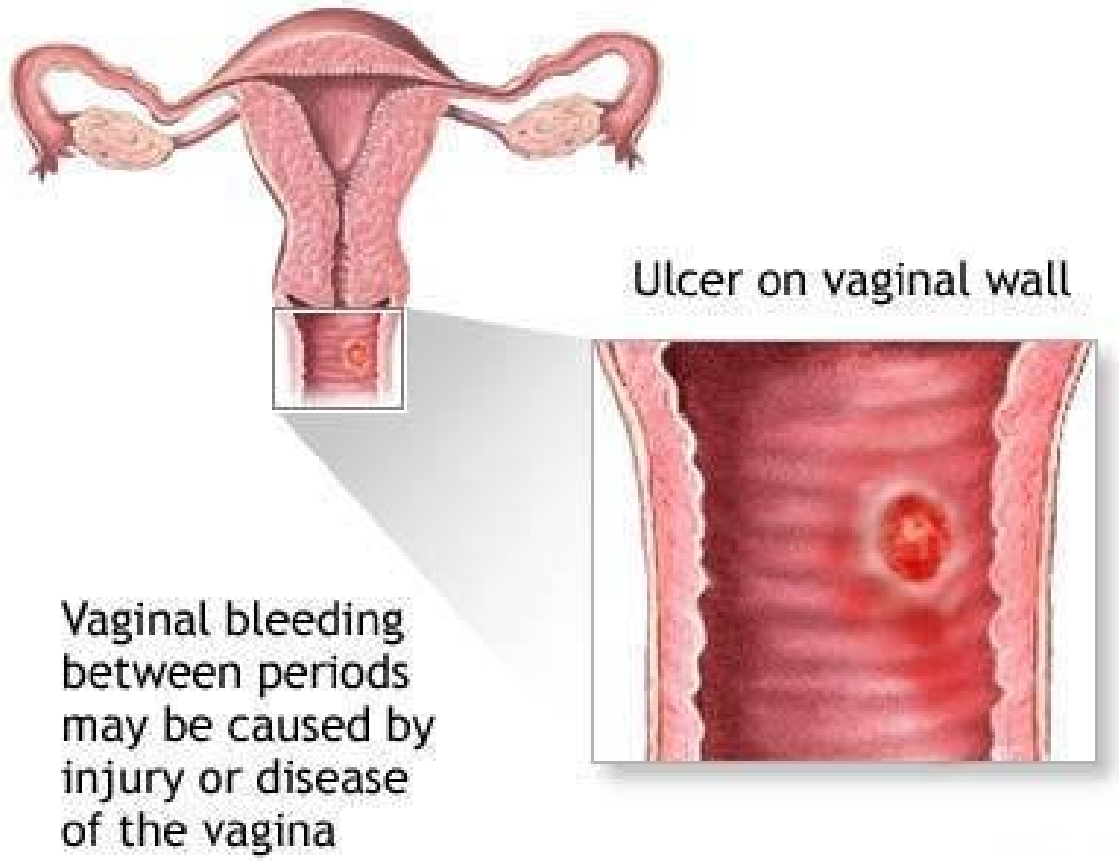
AUB – COMMON DIFFERENTIALS BY AGE

13-18 years	19-39 years	40-Menopause
Anovulation OCP Pelvic Infection Coagulopathy Tumor *Most common cause among adolescents is persistent anovulation due to immature H-P-O axis	Pregnancy Structural lesions (leiomyoma, polyp) Anovulatory cycles (PCOS) OCP Endometrial hyperplasia Endometrial cancer (less common)	Anovulatory bleeding Endometrial hyperplasia and carcinomas Endometrial atrophy Leiomyoma

https://www.slideshare.net/KemiDDeleIjagbulu/abnormal-uterine-bleeding-by-dr-kemi-dele

AUB – INITIAL EVALUATION

- Confirm the uterus is the source of bleeding
- Determine if the patient is premenarche or postmenopausal
- Exclude pregnancy



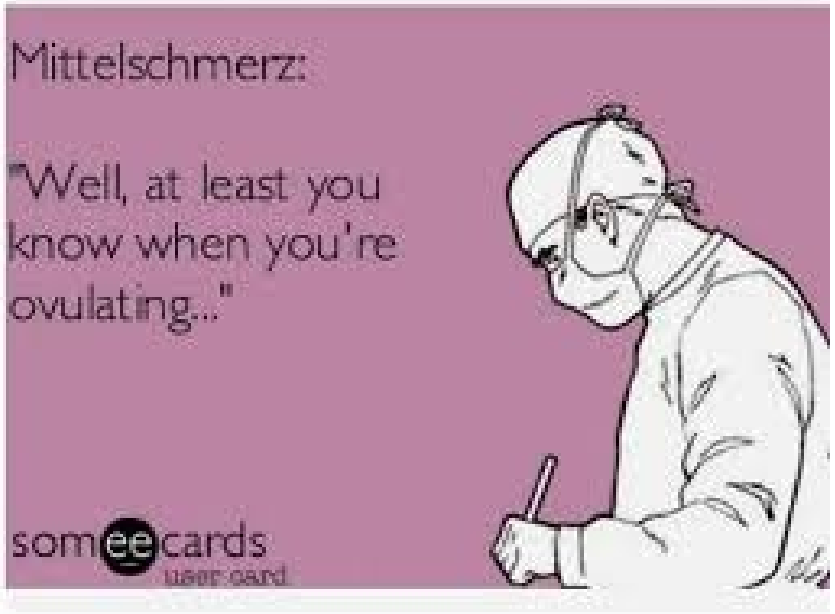
AUB – FURTHER EVALUATION

- Determine pattern, severity and etiology of AUB
  - What is the bleeding pattern?
  - Is bleeding related to a contraceptive method or medication?
  - Consider the need to obtain a CBC, coagulation profile, or endometrial sampling
  - Consider concurrent factors (e.g. a women with both a uterine fibroid and von Willebrand disease)

AUB – ADOLESCENT PRESENTATION

- Most common adolescent presentations:
  - Anovulation – due to an immature HPO axis
  - Menorrhagia – due to anovulation or a bleeding disorder
  - Amenorrhea – due to pregnancy, chromosomal abnormality (Turner's syndrome), hypothalamic hypogonadism, congenital absence of the uterus, cervix and vagina, or structural abnormalities (transverse vaginal septum or imperforate hymen)

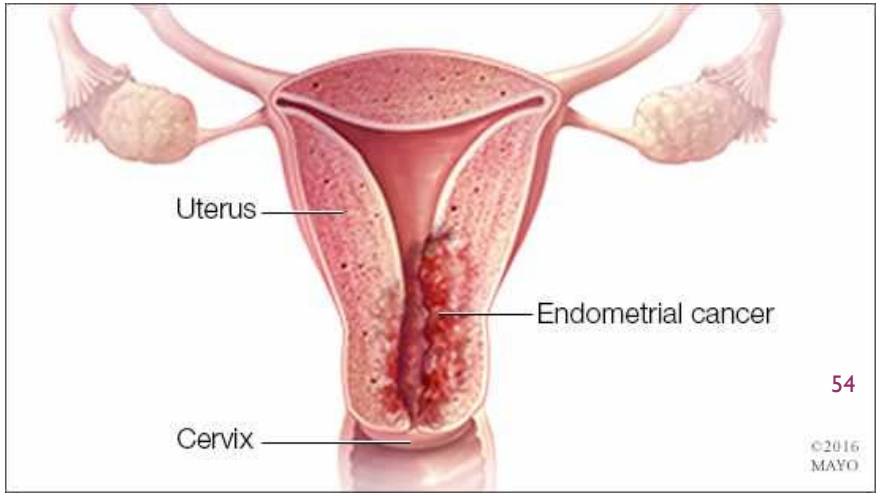
AUB – REPRODUCTIVE AGE NON-PREGNANT WOMEN



- Most common (non-pregnant) presentations:
  - Anovulatory AUB: **unpredictable**; varying bleeding amounts and intervals
    - Related to hypothalamic abnormalities or PCOS
  - Ovulatory AUB: **regular cycle length**, Mittelschmerz, presence of PMS symptoms, changes in cervical mucus
    - Menorrhagia (heavy or prolonged bleeding) – associated with structural lesions (leiomyomas, endometrial polyps or hyperplasia), coagulation disorder, liver failure or chronic renal failure
    - Polymenorrhea (bleeding at short intervals) – due to luteal-phase disorder or short follicular phase
    - Oligomenorrhea (infrequent bleeding) – due to prolonged follicular phase
    - Intermenstrual bleeding – due to cervical pathology (dysplasia or infection) or an IUD

AUB – PERIMENOPAUSAL & MENOPAUSAL PRESENTATION

- Perimenopause (occurs on average at age 47 years)
  - Abnormal bleeding in the 5-10 years prior to menopause (age 51) is very common
  - Most common pathology is **anovulation** due to declining numbers of ovarian follicles
    - Causes lengthening of intermenstrual intervals, skipped cycles and episodes of amenorrhea
  - Bleeding that is frequent, heavy or prolonged should be evaluated with endometrial biopsy (EMB) to exclude endometrial hyperplasia or cancer.
- Postmenopausal bleeding = ABNORMAL
  - Concerning for endometrial carcinoma
  - Assess with pelvic ultrasound and/or endometrial biopsy (EMB)



AUB – HISTORY QUESTIONS

- Age of menarche and menstrual history
- Detailed description of menstrual bleeding/bleeding pattern
  - Heavy, intermenstrual or irregular bleeding (the latter suggests ovulatory dysfunction)
- Molimina symptoms – breast tenderness, ovulatory pain, bloating?
- Current birth control method (CBM)
- Medications
- Personal or FH of bleeding disorders
- Weight changes
- Symptoms of anemia

AUB – PHYSICAL EXAM

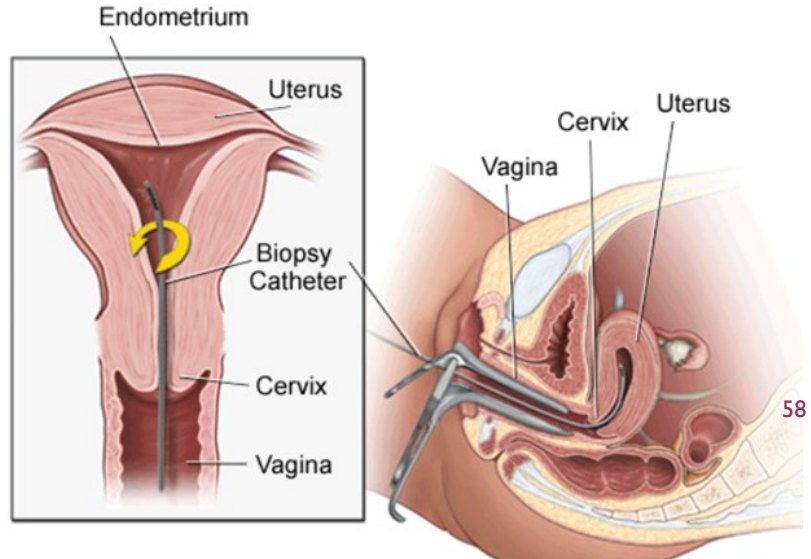
- Assess vital signs
- Evaluate for:
  - Signs of systemic illness (fever)
  - Signs of bleeding disorder (petechiae, pallor, ecchymosis)
  - Enlarged thyroid
  - Evidence of hyperandrogenism (hirsutism, acne, male pattern balding)
- Perform pelvic exam:
  - Verify source of bleeding is uterus
  - If has IUD, check for IUD strings
  - Assess uterine size/contour

AUB – LABORATORY & DIAGNOSTIC STUDIES

- **Pregnancy test first!**
- If suspect **anovulatory** bleeding -
  - Check CBC; consider TSH, prolactin, and fasting glucose with fasting insulin level
  - *Screen for eating disorder, stress, and female-athlete triad via history
- If suspect **ovulatory** bleeding -
  - Menorrhagia
    - Check CBC; consider LFTs, BUN/creat and coagulation profile
    - Order pelvic U/S (to exclude uterine fibroids)
    - Consider EMB to exclude endometrial hyperplasia
  - Intermenstrual bleeding
    - Obtain pap smear and cervical cultures

AUB – ENDOMETRIAL BIOPSY

- Who should undergo endometrial biopsy sampling?
  - **Postmenopausal women with ANY uterine bleeding!**
  - Age 45 years – menopause with AUB: if ovulatory OR if bleeding is frequent, heavy or prolonged (>5 days)
  - Age < 45 years old with AUB *AND*:
    - Risk factors for unopposed estrogen exposure (e.g. obesity, chronic anovulation, PCOS, etc.)
    - Persistent bleeding
    - Failed medical management for AUB



American College of Obstetricians and Gynecologists (ACOG)

ACUTE AUB – MANAGEMENT OF ACUTE BLEEDING EPISODES

Inpatient Management

- Admit to hospital if heavy bleeding with signs and symptoms or hemodynamic instability
  - Treat with IV estrogen or possible D&C

Outpatient Management

- Hormonal treatments
  - Combined oral contraceptives (COCs)
    - Monophasic pill with 35mcg ethinyl estradiol (3 pills qd x 7 days)
  - Medroxyprogesterone (Provera) orally
  - High dose estrogen (oral) with an antiemetic
- Tranexamic acid (Lysteda) IV or oral
  - An option for women who do not desire or should not take hormonal treatment.

CHRONIC AUB - MANAGEMENT

Medical Treatment

- Hormone therapy:
  - Levonorgestrel (Mirena) IUD
  - Depot medroxyprogesterone (Depo-Provera)
  - Estrogen/progestin OCP
- Tranexamic acid (Lysteda) – antifibrinolytic, given 3x daily for up to 5 days during menstruation
- NSAIDs – start 1st day of bleeding and continue until menstruation ceases

Surgical Treatment

- Endometrial ablation
  - Amenorrhea rate of ~50% and relief of excessive bleeding in most of the remaining patients
- Hysterectomy
  - Reserved for extreme cases
- *Endometrial artery embolization or myomectomy for leiomyomas*

"Well... I think we should run
a pregnancy test. Just to make sure!"

CASE #3

- A 40-year-old G5P5 woman complains of heavy vaginal bleeding with clots x 2 yrs. She denies bleeding or spotting between periods. A previous doctor told her she had an enlarged uterus. D&C 1 year ago showed benign pathology. She denies fatigue, cold intolerance, or galactorrhea. She takes Ibuprofen w/o relief of bleeding. BP 135/80, HR 80 bpm, 140lbs, T 98°F. Pelvic exam reveals irregular midline mass (~18 wks size) that moves in conjunction with the cervix. No adnexal masses.
- Urine pregnancy test – negative
- CBC – low HGB 9.0 g/dL, otherwise normal.
- What is the most likely diagnosis?

- **Symptomatic uterine fibroid (leiomyoma)**
  - Abnormal Uterine Bleeding
    - Heavy menstrual bleeding
  - Anemia despite use of Ibuprofen
- What management might you consider?
  - Hysterectomy
  - Hormone therapy (progestins, GnRH analog)*
  - Uterine artery embolization**

*Used to shrink size or correct anemia prior to operative treatment.
**Large fibroids may not respond as well.

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CASE #4

- A 60-year-old nulliparous woman who underwent menopause at 55 yo, presents with a 4-week history of vaginal bleeding. She denies the use of ERT. PMH is significant for DM Type 2. BP 150/90, T 99°F, 5'3", 190lbs.
- Physical exam –
  - Heart and lungs normal
  - Abdomen is obese, no masses palpated
  - External genitalia appear normal
  - Uterus normal size without adnexal masses
- What is the most likely diagnosis?

- **Postmenopausal Bleeding**
  - Abnormal uterine bleeding
- What is the next step in the evaluation of this patient?
  - Pelvic ultrasound and endometrial biopsy to assess for endometrial carcinoma

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DYSMENORRHEA

PRIMARY AND SECONDARY DYSMENORRHEA

DYSMENORRHEA – DEFINITIONS

Primary dysmenorrhea

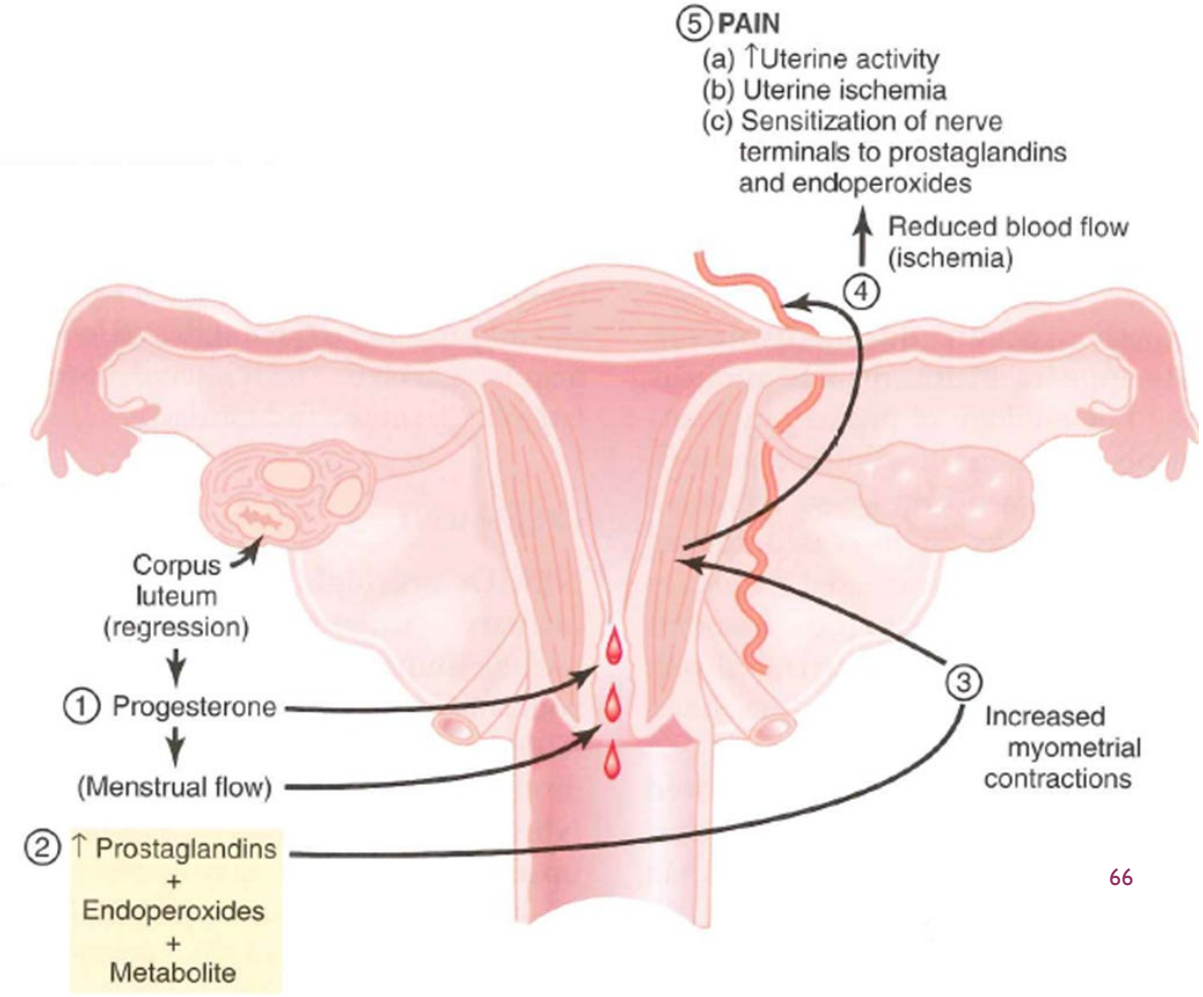
- Painful menstruation with no readily identifiable cause
- Occurs during ovulatory cycles
- Age 17-22 years is typical age

Secondary dysmenorrhea

- Painful menstruation due to organic pelvic disease (e.g. endometriosis, adenomyosis, or uterine fibroids)
- More common as a woman ages

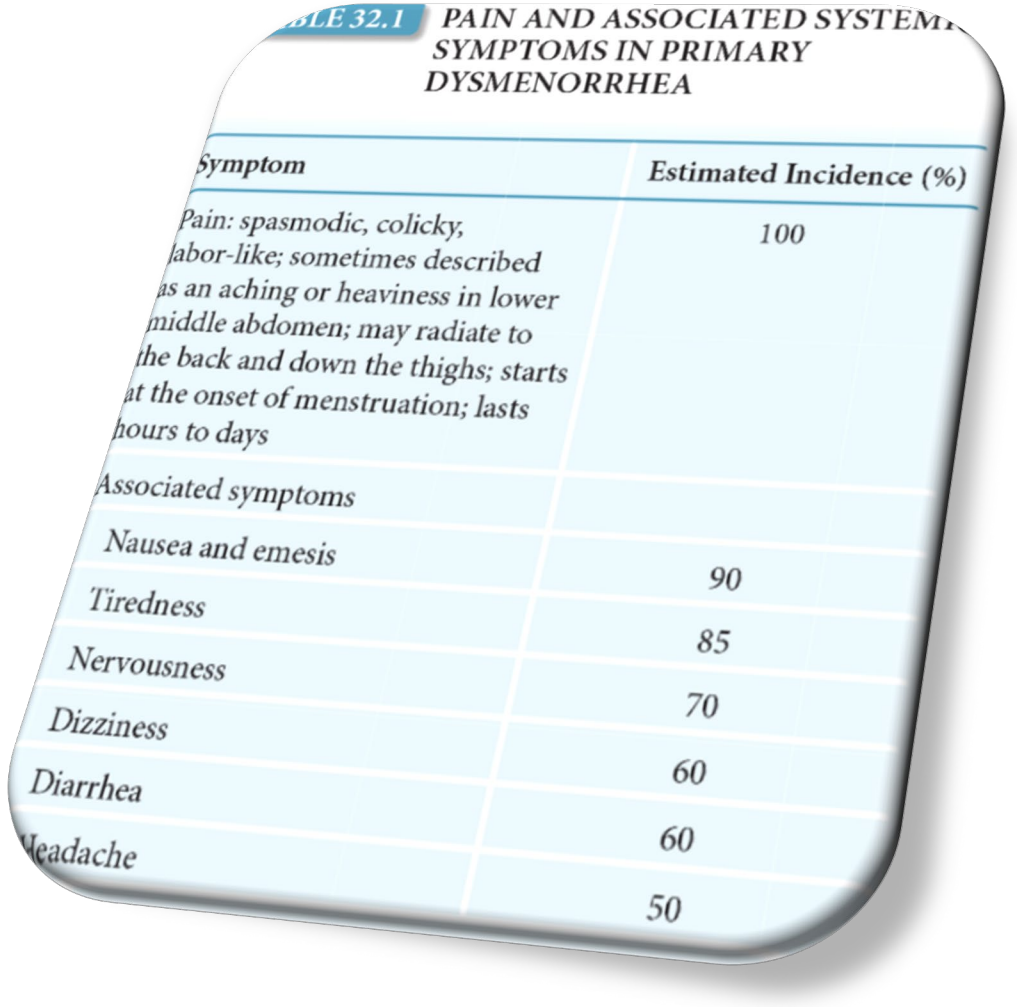
PRIMARY DYSMENORRHEA - BACKGROUND

- Corpus luteum (from dominant follicle) causes peak in progesterone
  - This in turn increases prostaglandin (PGF_2 and PGE_2) production in the uterus
- If ovum not fertilized, menstruation occurs
- Prostaglandins are released from the endometrium during cell lysis
  - Causes uterine contractions and ischemia → pain



PRIMARY DYSMENORRHEA – PRESENTATION

- Symptoms begin a few hours before or just after onset of menstruation; lasts 12-72 hours
- Pain described as cramp-like and intermittent
- Pain most intense in the lower abdomen
- May radiate to lower back and/or upper thighs
- Associated symptoms include: N, V, D, headache, LBP and fatigue
- Pelvic exam usually normal



BLE 32.1 PAIN AND ASSOCIATED SYSTEM
SYMPTOMS IN PRIMARY
DYSMENORRHEA

Symptom	Estimated Incidence (%)
Pain: spasmodic, colicky, labor-like; sometimes described as an aching or heaviness in lower middle abdomen; may radiate to the back and down the thighs; starts at the onset of menstruation; lasts hours to days	100
Associated symptoms	
Nausea and emesis	90
Tiredness	85
Nervousness	70
Dizziness	60
Diarrhea	60
Headache	50

PRIMARY DYSMENORRHEA – LABORATORY TESTS & DIAGNOSTICS

- HCG
- Consider pap smear and vaginal cultures
- If history and physical consistent with primary dysmenorrhea, other labs studies or imaging not typically indicated

Clinical Diagnosis

PRIMARY DYSMENORRHEA - TREATMENT

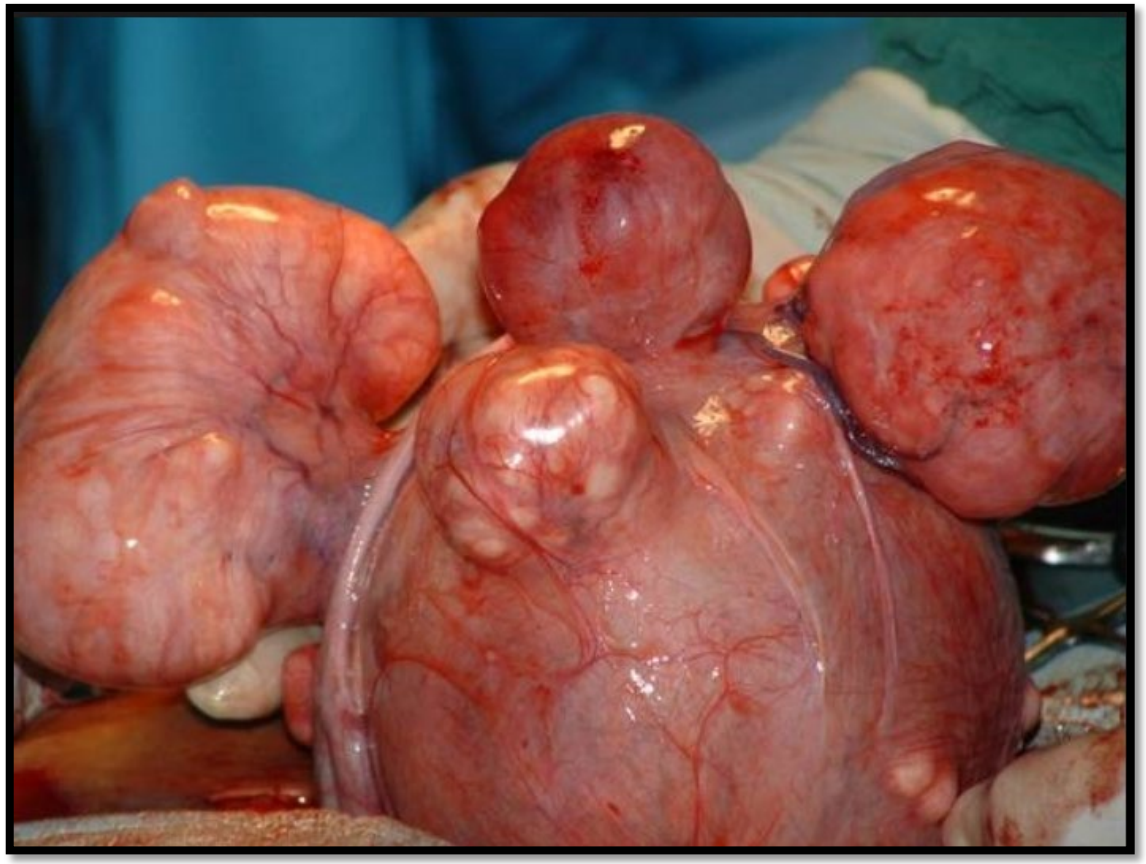
- Self Care:
  - Apply heat
  - Gently massage lower abdomen
  - Exercise/yoga
  - Nutritional supplements – increase dairy consumption, B complex vitamin
  - Smoking cessation
- NSAIDs (first line therapy)
  - Ibuprofen 400mg, 1 PO q4-6 hours x 3-4 days
- Hormonal contraceptives (to reduce menstrual flow and inhibit ovulation)
  - COC, progestin-only pill, Depo-Provera, Mirena IUD

PRIMARY DYSMENORRHEA – TREATMENT (CONT.)

- Resistant cases – consider laparoscopy and/or possible GnRH analogue

- Follow up and/or **referral** is needed if:
  - Pain worsening with each menses
  - Pain lasts longer than first 2 days of menses
  - Medication is no longer controlling the pain
  - Menstrual bleeding becomes increasingly heavy
  - Pain accompanied by fever
  - Abnormal discharge or bleeding occur
  - Pain occurs at times unrelated to menses

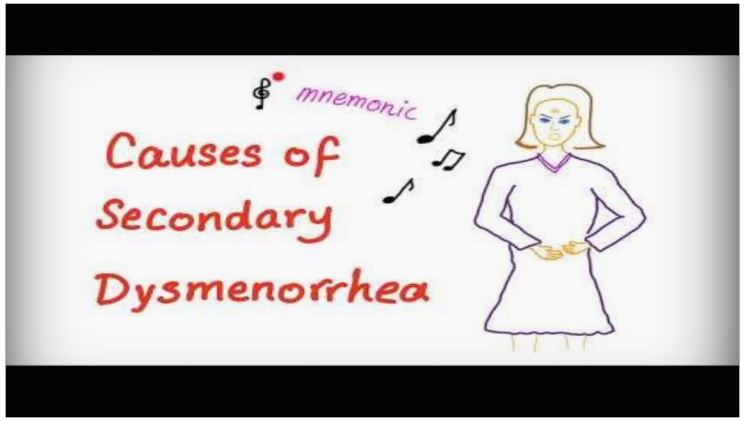
SECONDARY DYSMENORRHEA - BACKGROUND



- Pain is **secondary** to an underlying cause
- Less related to first day of menses
- Pain is not limited to menses, but may worsen at this time
- Usually associated with other symptoms
  - Dyspareunia, infertility or AUB
- Usually develops in women aged 30-40 years

SECONDARY DYSMENORRHEA BACKGROUND

- Common causes:
  - Endometriosis (presence of endometrial glands outside of the uterus)
  - Adenomyosis (ectopic endometrial tissue within the myometrium)
  - Adhesions
  - Pelvic inflammatory disease (PID)
  - Leiomyomas (uterine fibroids)



Extrauterine Causes
Endometriosis
Tumors (benign and malignant)
Inflammation
Adhesions
Psychogenic (rare)
Nongynecologic causes

Intramural Causes
Adenomyosis
Leiomyomata

Intrauterine Causes
Leiomyomata
Polyps
Intrauterine contraceptive devices
Infection
Cervical stenosis and cervical lesions

SECONDARY DYSMENORRHEA - TREATMENT

- Treat the underlying cause
- Hormone therapy with COCs
  - If not an estrogen candidate (e.g. hx of VTE, breast CA, etc.) try progestins and/or NSAIDs
- Complicated cases may require pelvic surgery
  - Diagnostic laparoscopy
  - Hysterectomy
  - Oophrectomy
  - Myomectomy

CASE #5

- A 32-year-old G0P0 woman complains of dysmenorrhea during the last year as well as pelvic nonmenstrual pain and dyspareunia of recent onset. Menarche was at age 13 (painless and regular until recently). Denies vaginal discharge or prior STIs. Stopped using OCP since being married. BP 110/70, HR 85 bpm, T 97°F. Heart and lungs normal. On pelvic exam, retroverted and displaced uterus with palpable cystic mass right adnexa.
- Urine pregnancy test – negative
- CBC – slightly low HGB 11g/dL, otherwise normal
- Pelvic u/s – 9cm cystic mass of right ovary attached to posterior surface of the uterus with fluid in pouch of Douglas.
- What is the most likely diagnosis?

- **Endometriosis with ovarian endometrioma**
  - Secondary dysmenorrhea
  - Painful menses later in life, gradually accompanied by nonmenstrual pain and dyspareunia
- What is the next step in the management of this patient?
  - Referral to an OBGYN for diagnostic laparoscopy

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CONSIDERATIONS FOR REFERRAL TO SPECIALIST(S)

- Primary amenorrhea – if suspected chromosomal abnormality, outlet obstruction or psychological disorder
- Secondary amenorrhea – if suspected pituitary pathology, Asherman's syndrome or psychological disorder
- Abnormal uterine bleeding – for acute bleeding episode requiring hospitalization, for surgical treatment (based on previous medication tried, age and desire for future fertility)
- Primary dysmenorrhea – if pharmacologic measures ineffective
- Secondary dysmenorrhea – for identification of etiology and potential surgical treatment

QUESTIONS???

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