From Menstrual Disorders to Menopause

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WOMEN'S HEALTH COLLECTIVE

Menstrual Disorders

Puberty

Amenorrhea

Abnormal Uterine Bleeding

Premenstrual Syndrome

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Puberty

- Adrenarche
  - Contributes to development of pubic hair (pubarche) and sebaceous glands
  - Production of weak androgens by zona reticularis of adrenal cortex
  - Begins with a change in response to ACTH (vs a change in secretion of ACTH)
    - Results in increases in DHEAS
  - Begins around 6 yrs old in both males and females
  - Triggers unknown – may be pituitary in origin, related to increases in BMI, or in utero and neonatal factors

Puberty

- Thelarche
  - Appearance of breast tissue
  - Precedes menarche
  - Precedes appearance of pubic and axillary hair ~60% of the time
  - Earliest detectable secondary sexual characteristic on PE in most girls
    - Pubic hair is the initial manifestation about 15% of the time
  - Primarily due to action of estradiol from the ovaries
  - Begins between ages 8-13 yrs (average onset is 10.3 yrs)
  - Estimated mean time for full breast development is 4.2 years

Puberty

- Menarche
  - 1st menstrual bleed
  - Not often associated with ovulation
    - Typically caused solely by the effects of estradiol on endometrial lining
  - Occurs relatively late in the series of developmental milestones
  - Gradual decline in age of menarche over past century
  - Possible relationship between earlier age and adipose tissue
  - Occurs on average 2 -2.5 years after puberty
  - Average age 12.5 years in US
  - Girls who reach menarche later (>13 yrs old) – only 50% will ovulate regularly within 4.5 years

Menstrual Disorders

Abnormal Uterine Bleeding

Premenstrual Syndrome

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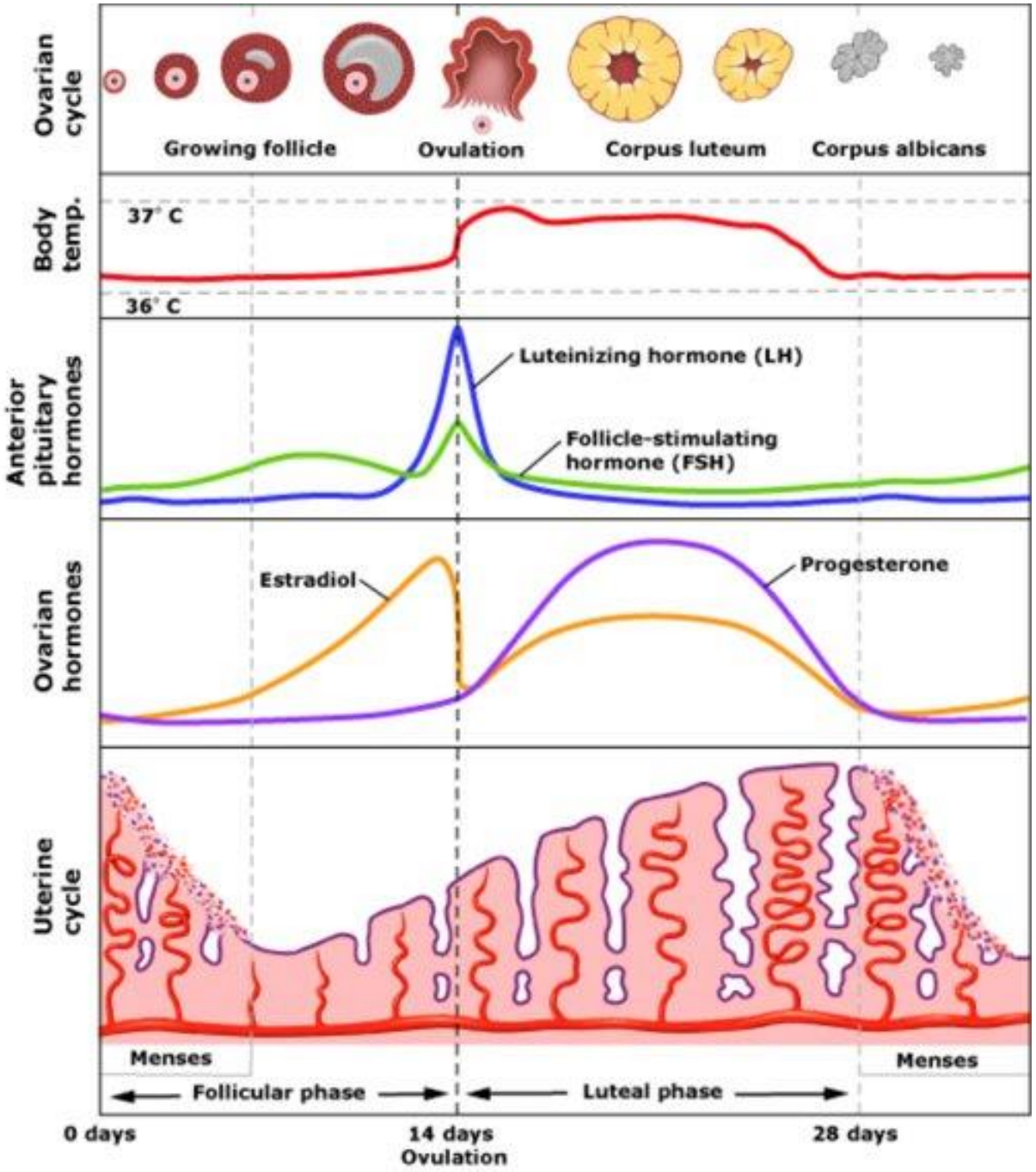
Typical Cycle

- Day 1 of cycle is 1st day of menstrual bleeding
- Menstrual bleeding should become regular within 2-4 years of menarche
- Normal 28 day cycle – normal range 24-35 days
- Cycle to cycle variability in individual woman is typically +/- 2 days
- Luteal phase length relatively consistent at 12-14 days in normal cycle
- Variability in cycle length mostly due to variations in follicular phase
- Menstrual bleeding duration ~ 4-6 days (shortening gradually > 35yrs)
- Typically ovulatory if cycles do not vary > 4 days
- Mittleschmerz: ovulatory pelvic pain thought to be due to rapid expansion of dominant follicle



Menstrual cycle

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Amenorrhea

- Primary Amenorrhea
  - Absence of menses by age 15 in the presence of normal growth and secondary sex characteristics
  - Requires thorough eval to determine cause
  - Start eval earlier if no menses and absence of secondary sex characteristics by 13
  - Start eval earlier if positive secondary sexual characteristics but no menses prior to 15 with cyclic pelvic pain – r/o outflow tract obstruction
  - Transient, intermittent, or permanent
  - Dysfunction of hypothalamus, pituitary, ovaries, uterus, or vagina

Primary Amenorrhea Causes

- Gonadal dysgenesis (incl. Turner Syndrome)
  - 43%
- Congenital abnormalities (incl. Mullerian agenesis)
  - 15-20%
- Physiologic delay of puberty (chronic systemic disease, acute illness)
  - 14%
- Polycystic ovary syndrome (PCOS)
  - 7%
- Isolated GnRH deficiency
  - <5%
- Transverse vaginal septum
  - 3%
- Weight loss/eating disorder
  - 2%
- Hypopituitarism
  - 2%
- Imperforate hymen, Complete androgen insensitivity syndrome (CAIS), hyperprolactinemia/prolactinoma, other pituitary tumors, CAH, hypothyroidism, CNS defects, craniopharyngioma, and Cushing's dz
  - <1%

Amenorrhea

- Secondary Amenorrhea
  - Absence of menses for:
    - > 3 months in girls/women who previously had regular menstrual cycles
    - > 6 months in those who had irregular menses
  - Oligomenorrhea
    - <9 menstrual cycles/yr or cycle length > 35 days
  - All causes of secondary amenorrhea can also present as primary amenorrhea
  - Logical approach to workup: consider the disorder based upon the level of control of the menstrual cycle
    - Hypothalamus and pituitary
    - Ovary
    - Uterus and vagina

Secondary Amenorrhea Causes

- Pregnancy
  - Most common cause of secondary amenorrhea
  - Pregnancy cannot be excluded by presence of apparent menstrual bleeding
- Ovary
  - 40% (30% PCOS, 10% POI)
- Hypothalamus (eating disorders, celiac disease, emotional stress, illness or MI)
  - 35%
- Pituitary
  - 17% (mainly hyperprolactinemia)
- Uterus
  - 7% (all due to intrauterine adhesions)
- Other
  - 1% (CAH, ovarian and adrenal tumors, hypothyroidism)

Female Hypogonadism

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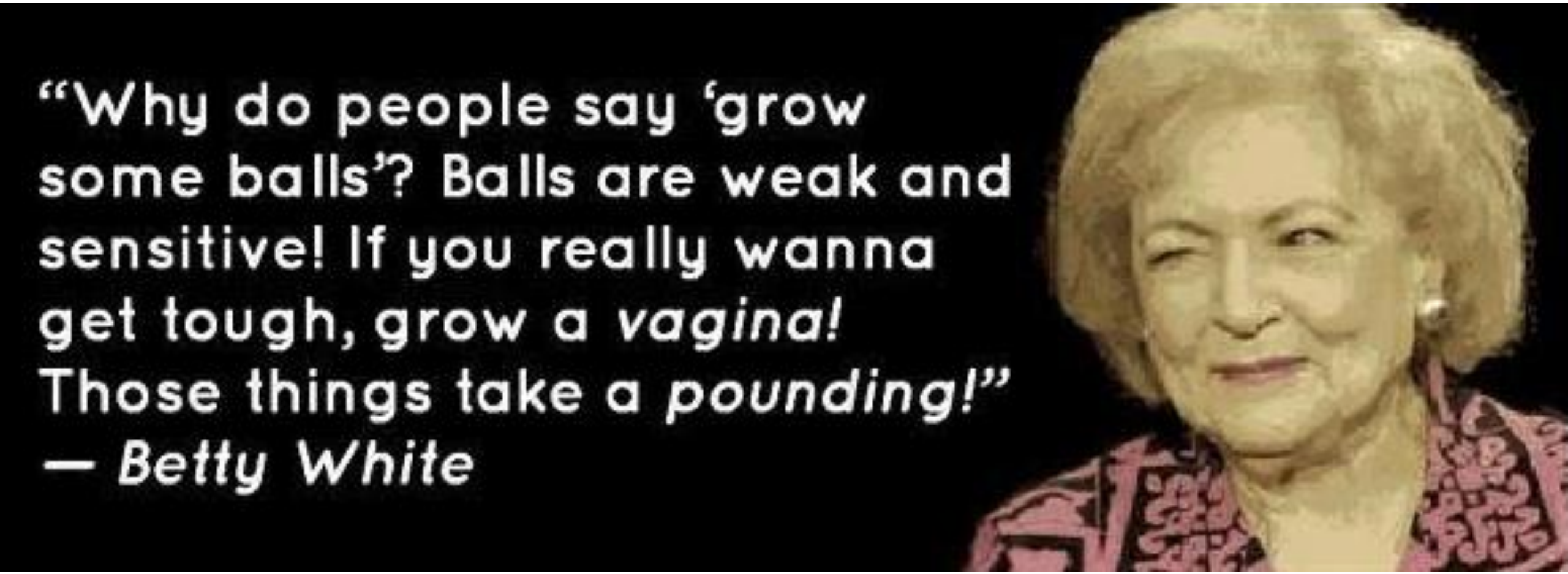

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Female Hypogonadism

- Primary hypogonadism in females is defined as ovarian failure accompanied by high serum FSH
- Primary ovarian insufficiency (POI) (previously referred to as premature ovarian failure or premature menopause)
  - Defined as depletion or dysfunction of ovarian follicles with cessation of menses in women < 40 yrs (nml is 51-52 yrs)
  - > 50% of women will intermittently and spontaneously produce estrogen and ovulate rendering the term premature ovarian *failure* inaccurate
  - 5-10% of women conceive after dx
- Etiology unknown in 75-90% of cases
- 1:250 by age 35
- 1:100 by age 40

Evaluation

- Presence of amenorrhea is NOT required to make diagnosis of POI
- Definitive diagnosis in women < 40 with irregular menses and FSH in postmeno range
- Hot flushes/night sweats suggestive of POI, but lack of does not rule out possibility of POI
- In addition to FSH and estradiol:
  - Pregnancy test
  - PRL
- DXA scan at time of diagnosis
- Annual TSH as women with spontaneous POI are at increased risk for developing autoimmune hypothyroidism

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Treatment

- Most common terms used by women after receiving a diagnosis of POI
  - “Devastated”
  - “Shocked”
  - “Confused”
- Inform women that 50-75% with 45,XX spontaneous POI experience intermittent ovarian function and that 5-10% are able to become pregnant
  - Combined oral contraceptives are a reasonable option
- Systemic HT at least until age 50-51 in all women with POI without CIs
  - Manage estrogen deficiency
  - Prevent long term health risks (OP, CAD, mortality, cognitive decline, dementia)
  - Typically start with 100mcg estradiol patch, need a cyclic progestogen if uterus is present

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Prognosis/Complications

- Bone loss/osteoporosis
  - Higher risk with younger age at POI
- Cardiovascular morbidity and mortality
  - Possibly related to endothelial dysfunction
- Diminished sexual well-being
- Impaired cognition
- Emotional health decline
  - Due to sequelae as well as early loss of fertility
- Primary adrenal insufficiency
  - In women with autoimmune oophoritis
  - ~3% of women with spontaneous POI develop adrenal insufficiency

Normal menstruation parameters

Frequency

- 24-35 days

Regularity

- Variation < 7-9 days

Duration

- <= 8 days

Volume

- <= 80ml per cycle
- Realistically – subjective and defined as volume that does not interfere with physical, social, emotional, and/or material QOL

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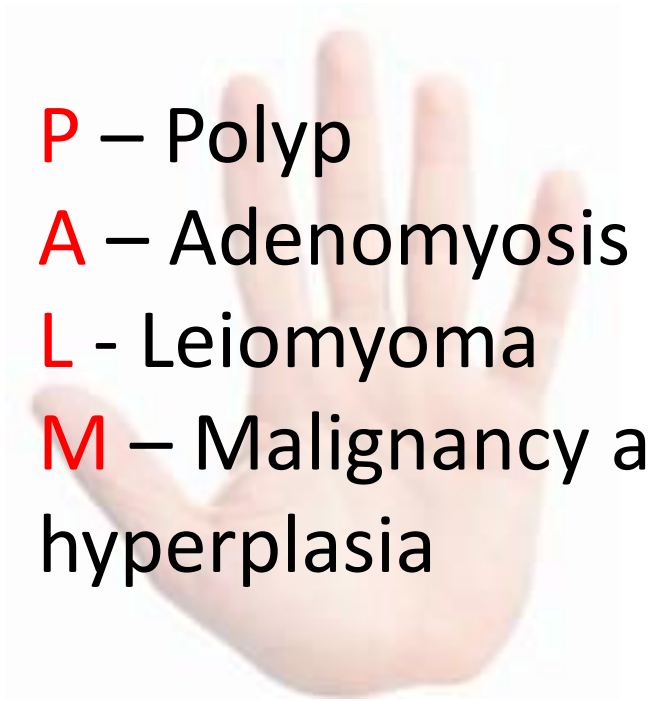
Abnormal uterine bleeding

- Review >= 6 months of bleeding
- Acute
  - Episode of bleeding in a woman of reproductive age that is abn in frequency, regularity, duration, and/or volume
- Chronic
  - As above, occurring for the majority of the past 6 months

PALM-COEIN

Structural



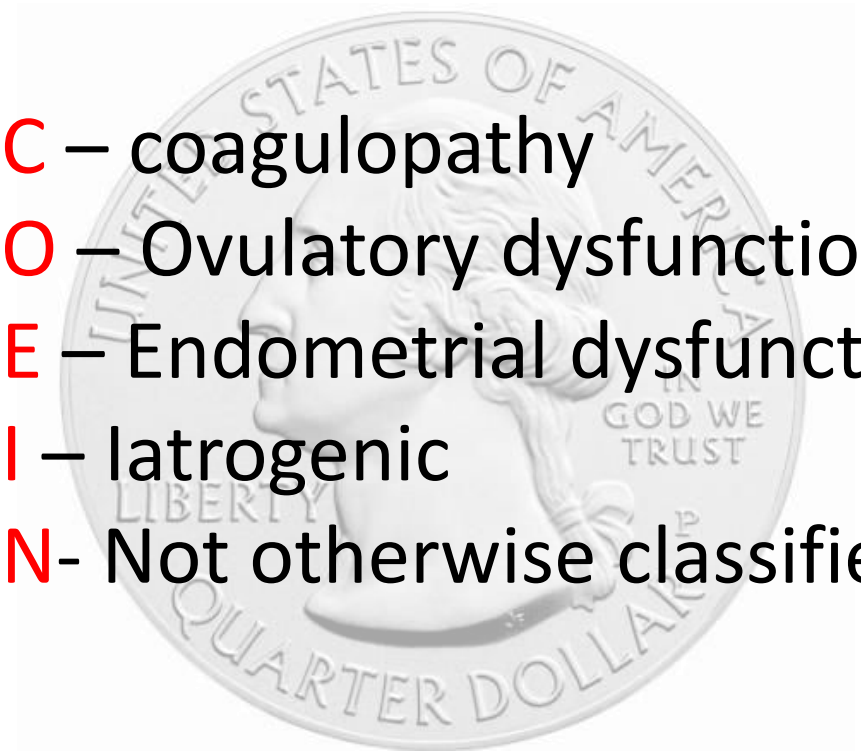
P – Polyp

A – Adenomyosis

L - Leiomyoma

M – Malignancy and hyperplasia

Non-structural



C – coagulopathy

O – Ovulatory dysfunction

E – Endometrial dysfunction

I – Iatrogenic

N- Not otherwise classified

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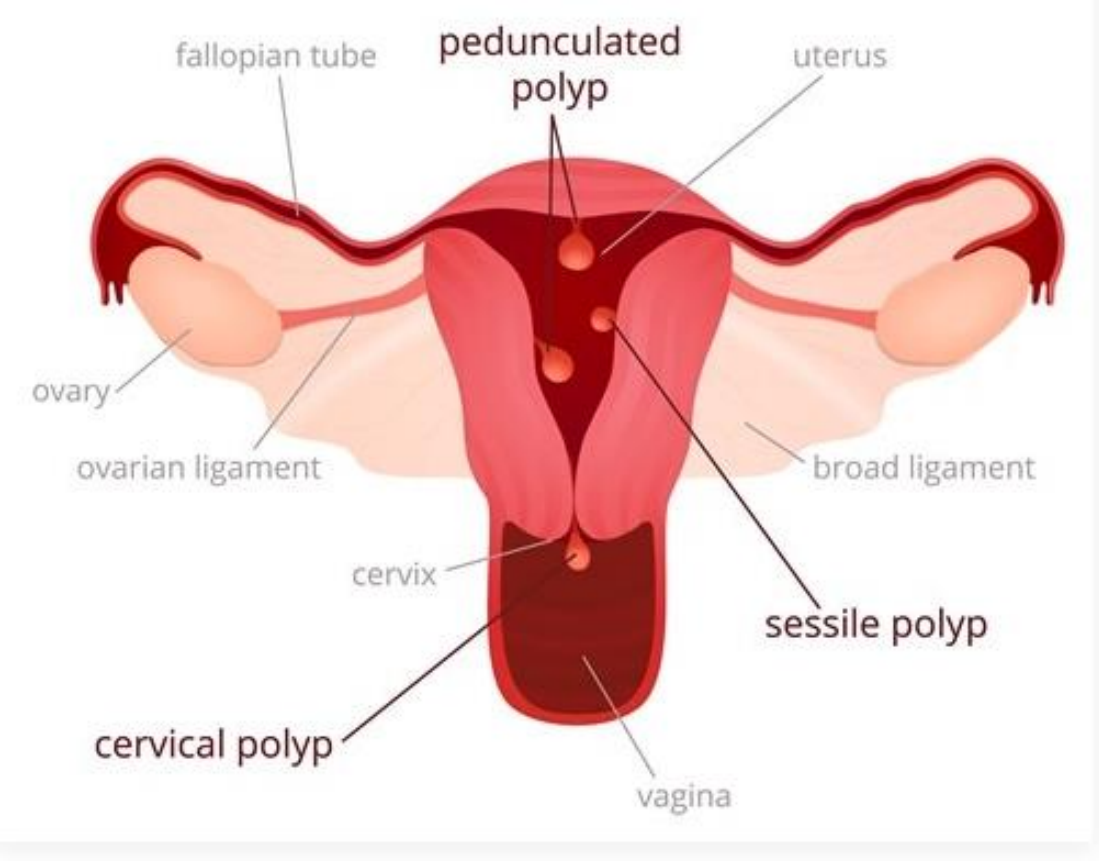
Polyps

- Localized epithelial tumors
- Endometrial cavity or cervical canal

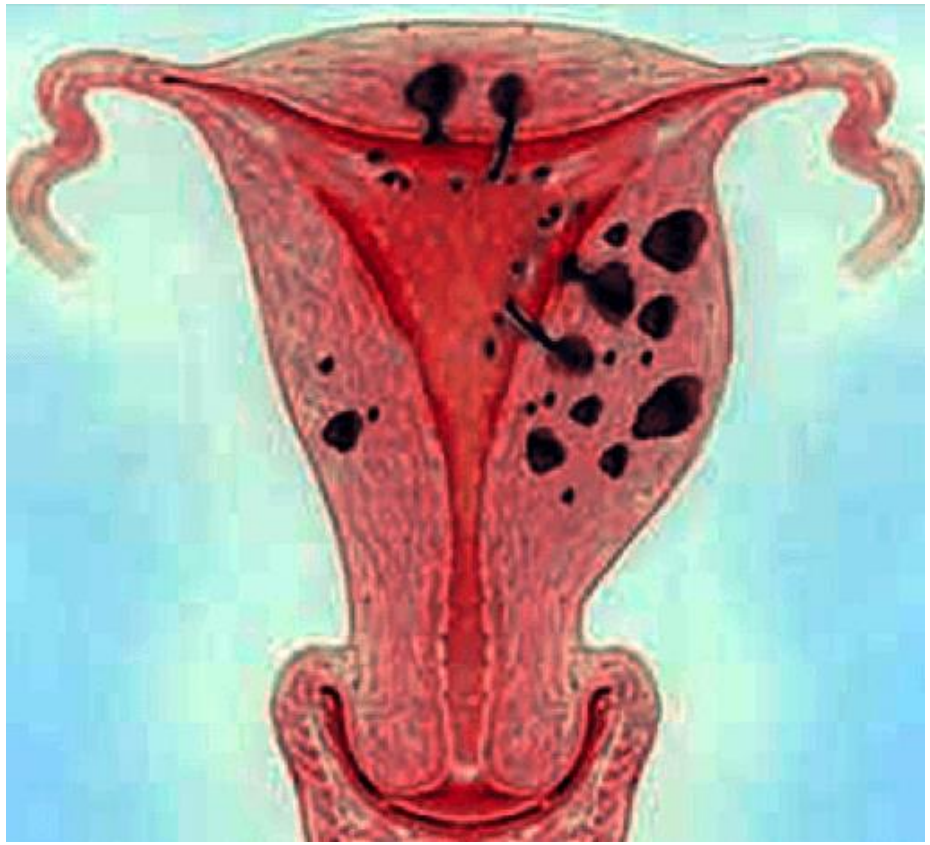


Adenomyosis

- Presence of endometrial-type glands and stroma within the myometrium
- Can now be

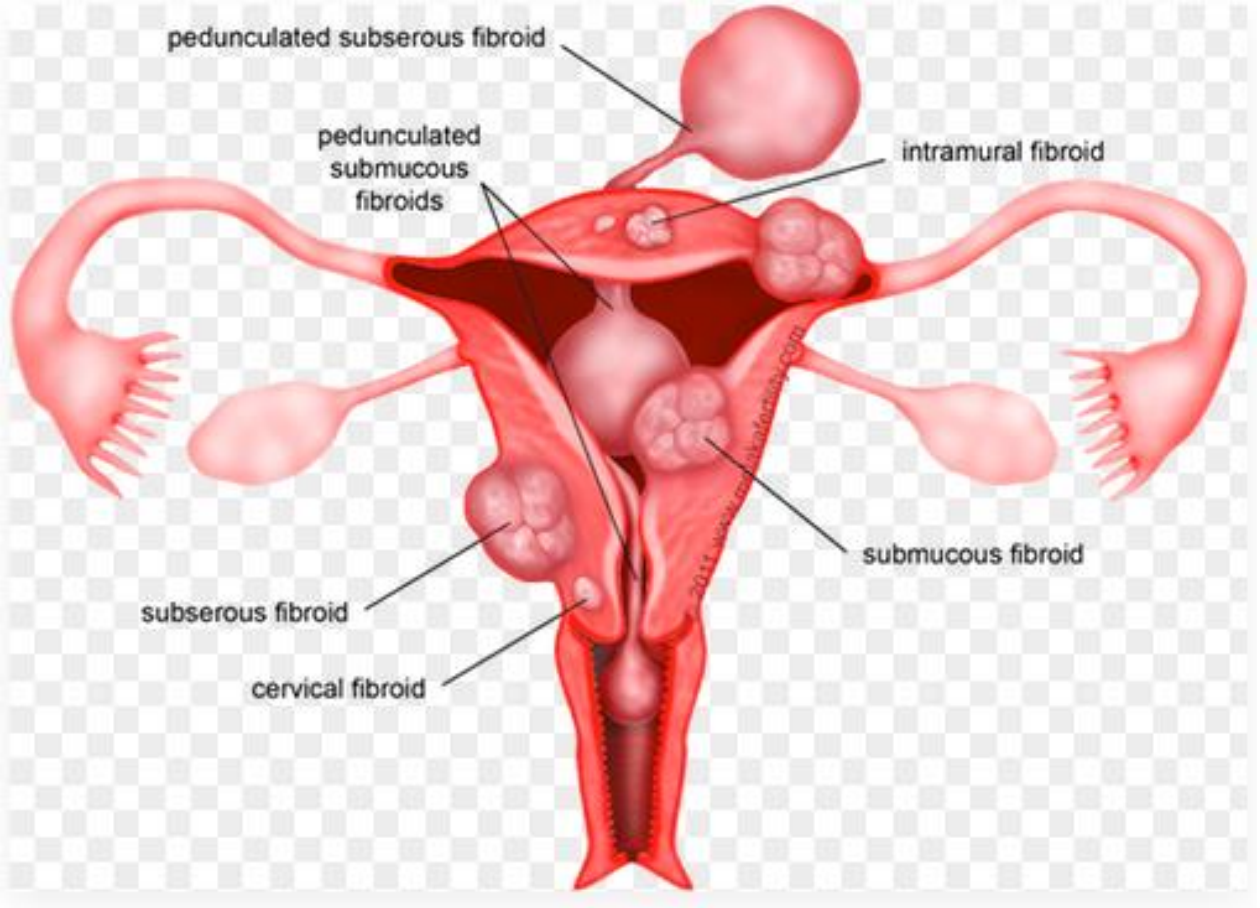
diagnosed with TV

ultrasound or MRI



Leiomyomas

- AKA Myoma or uterine fibroid
- Benign smooth muscle neoplasm



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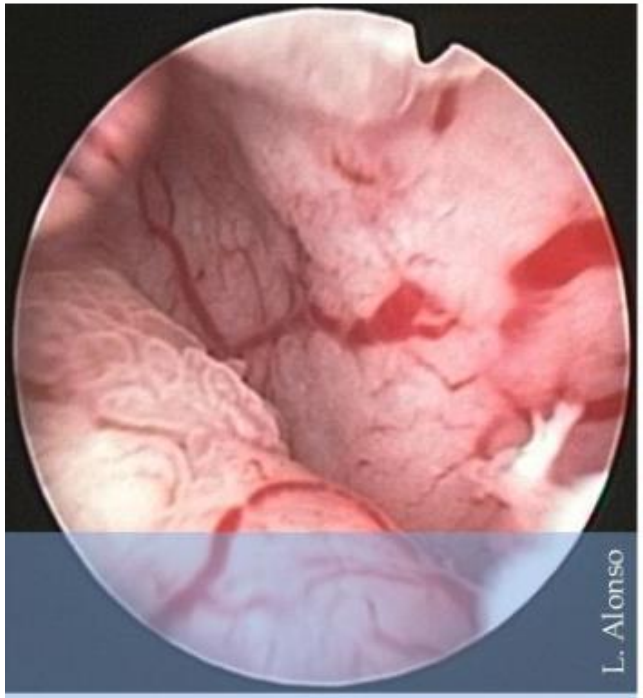
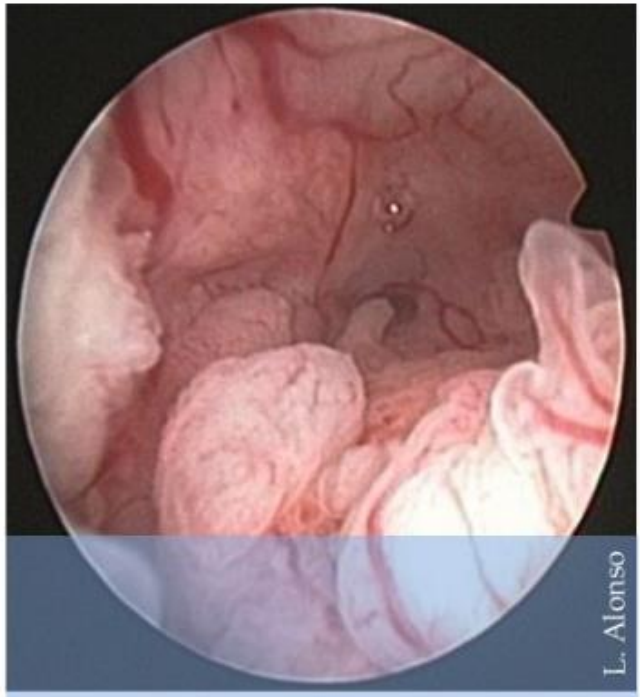
Malignancy and hyperplasia

- Epithelial neoplasms
- Endometrial hyperplasia with cytological atypia and carcinoma
- Inclusive of endometrial stromal sarcomas



Pattern of complex hyperplasia with atypical cells in the lining of the glands



23% of the complex hyperplasia with atypia would, if untreated, progress to endometrial cancer

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Coagulopathy

- Numerous disorders of hemostasis
- Identifiable in up to 24% of women with heavy menstrual bleeding
- Most common is mild vonWillebrand disease

Ovulatory dysfunction

- Encompasses anovulation, infrequent ovulation, or luteal out-of-phase events.
- Cycle length in the previous 12 months needs to have varied by > 7days
- Psychologic stress (weight loss or gain), excessive exercise, medications, endocrinopathy (hyperprolactinemia, thyroid disease, PCOS)
- Women may have normal cycle length (24-35 days) and yet be anovulatory

Endometrial causes

- Diagnosis of exclusion
- Cause of bleeding is a primary disorder of the endometrium
- May be present even in the presence of other findings such as adenomyosis or leiomyomas
- May also be caused by something else
  - Ex: endometritis caused by *Chlamydia trachomatis*

Iatrogenic causes

- AUB due to medications or medical devices
  - IUDs
  - Gonadal steroids
  - GnRH analogues, AIs, SERMs
- Anticoagulants
- Meds that interfere with dopamine metabolism or cause hyperprolactinemia

Not otherwise classified

- Numerous other entities that can contribute to AUB
- Known and to be discovered
- Rare entities
  - AVM
  - Uterine isthmocele

Premenstrual Syndrome (PMS)

- Most common symptoms are bloating and extreme sense of fatigue
  - Next is breast tenderness and headaches
- Emotional symptoms leading to greatest impairment
  - Irritability and mood swings
- Also increased appetite, food cravings, diminished interest in activities, sensitivity to rejection, hot flushes, dizziness.
- Repetitive physical and behavioral symptoms
- Clinically significant PMS occurs in 3-8% of women
- More severe variant is termed premenstrual dysphoric disorder (PMDD)
- Begins in the 2nd half of cycle (luteal phase) and often into the first few days of bleeding
- PMDD affects ~ 2% of women

PMS and PMDD

- Risk factors:
  - Caucasian
  - Lower education level
  - Cigarette smoking
  - h/o trauma
  - Anxiety d/o
- Most likely neurotransmitter involved is serotonin
- Genetic and environmental factors

Diagnosis of PMS/PMDD

- PMS – per ACOG, at least one symptom (but < 5) associated with economic or social dysfunction that occurs during the 5 days before the onset of menses and is present in at least 3 consecutive menstrual cycles
- PMDD requires presence of at least 5 symptoms – one must be an affective symptom
- Labs should be limited – consider TSH
- Confirm cycle length and timing of symptoms – be sure symptoms are cyclic vs continuous
- Have patient record symptoms and timing for at least 2 months
- Symptoms must cause functional impairment

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Treatment of PMS/PMDD

- Treatments with demonstrated efficacy
  - SSRI (1st line if contraception is not a priority) (continuous vs luteal phase dosing)
  - OCs containing drospirenone (higher risk VTE) (4 day pill free interval)
  - COCs (containing any progestin)
  - GnRH agonists
- Treatments with possible efficacy
  - Cyclic OCs (not containing drosperinone)
  - Exercise
  - Acupuncture
- Ineffective treatments for mod/severe symptoms
  - Progesterone
  - Vitamin supplements
  - Dietary restrictions
  - Alprazolam (not recommended)

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Polycystic Ovarian Syndrome

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Polycystic Ovarian Syndrome (PCOS)

Most common cause of anovulatory symptoms and hyperandrogenism in women

Typically manifests in adolescence

6-10% prevalence

Interaction of complex genetic and environmental factors

Most common postnatal environmental contributor is obesity

Notable risks:

- Infertility
- Metabolic syndrome
- Insulin resistance (50-70% above and beyond that determined by their body weight)
- CVD
- Endometrial carcinoma
- Obstructive sleep apnea
- Fertility

Actual range of practice for screening varies considerably

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PCOS “2 hit” hypothesis

- Congenital predisposing “hit”
  - Heritable traits and gene variants affecting ovarian function
  - Heritable traits and gene variants predisposing to insulin resistance, obesity, and type 2 diabetes mellitus
  - Congenital virilization
  - Disturbed fetal nutrition
- Postnatal provocative “hit”
  - Insulin resistant hyperinsulinemia
    - Metabolic syndrome
    - Postnatal obesity
  - Puberty

Diagnosis of PCOS

- Consider in any adolescent female with CC of:
  - Abnormal degree of hirsutism or inflammatory acne vulgaris that is poorly responsive to topical therapies (occurs in ~75% of PCOS cases)
  - Menstrual abnormality
  - Obesity or focal hirsutism accompanied by menstrual abnormality
- Be sure to screen for medication that could mask or cause symptoms of PCOS
- ¼ to ½ of normal adolescents meet adult criteria for polycystic ovarian morphology (PCOM)
  - Therefore PCOM is not included in 2015 consensus diagnostic criteria for PCOS in adolescents

2003 Rotterdam Criteria

- 2 of the following 3 factors necessary to diagnose PCOS
  - Oligo- and/or anovulation
  - Clinical (hirsutism) and/or biochemical (hyperandrogenemia) signs of hyperandrogenism
  - Polycystic ovaries by ultrasound (not required in adolescents – but can r/o other causes of hyperandrogenism)
- Not all experts agree that women with oligomenorrhea and polycystic ovaries, but not hyperandrogenism, should be diagnosed with PCOS
- Summary report from 2012 NIH Workshop suggest that Rotterdam criteria continue to be used
- 2013 Endocrine Society Clinical Practice Guidelines for the Diagnosis and Treatment of PCOS also suggest using Rotterdam

Diagnosis of PCOS

- Diagnosis only confirmed when other conditions that mimic PCOS are excluded
  - Disorders that cause oligo/anovulation and/or hyperandrogenism
    - Thyroid disease
    - NCCAH
    - Hyperprolactinemia
    - Androgen secreting tumors
- Hyperandrogenism may be diagnosed using either clinical or biochemical criteria
  - Patient with oligomenorrhea and clinical evidence of hyperandrogenism, but nml serum androgen levels, is still considered to have PCOS
  - Lack of hyperandrogenism in adolescents effectively rules out PCOS. However, ovarian hyperandrogenism may not become notable until a few years after menarche.

Laboratory evaluation

- All lab testing best done without current use of hormonal contraception
- Serum testosterone (total vs free)
- DHEAS if concerns about a possible androgen-secreting tumor causing the hyperandrogenism
  - So if onset of hirsutism at a late age with rapid progression, signs of virilization such as deepening of the voice or clitoromegaly
- TV ultrasound in women who meet only 1 of the 2 criteria (oligoovulation and hyperandrogenism)
- If presenting symptom is oligomenorrhea
  - Serum hCG
  - PRL
  - TSH
  - FSH

Additional screening tests based on presenting symptoms

- If obese, can consider serum cortisol
- If acromegaloid features consider an IGF-1
- 17-OHP – 8am
  - NCCAH is the most common condition mimicking PCOS
  - Consider serum progesterone level also to r/o possibility of unexpected ovulation (> 400 ng/dl or > 12.7 nmol/L indicative of ovulation)
- DHEAS > 700mcg/dL suggests adrenal virilizing tumor or a rare form of NCCAH

Treatment of PCOS in adults

- Goals
  - Reduction of hyperandrogenic features (hirsutism, acne, scalp hair loss)
  - Management of underlying metabolic abnormalities and reduction of risk factors for type 2 diabetes and CVD
  - Prevention of endometrial hyperplasia and carcinoma due to chronic anovulation
  - Contraception if pregnancy is not desired
  - Ovulation induction for those pursuing pregnancy

Treatment of PCOS

- First line for obese women with PCOS is diet and exercise
  - Followed by pharmacotherapy (consider liraglutide) then, if necessary, bariatric surgery
  - Improves insulin resistance risk and hyperandrogenism
  - Also appears to have reproductive benefits with 5-10% wt loss
- Always r/o pregnancy prior to initiation of pharmacologic therapy
- COCs are mainstay of pharmacologic therapy
  - VTE risk, particularly if BMI > 30kg/m^2 and in women > 40 yrs
  - Alternatives include cyclic progestin therapy, continuous progestin therapy, and LNG IUD

Treatment of PCOS

- Hirsutism – COC is 1st line
  - Antiandrogen can be added after 6 months if needed
  - Spironolactone sometimes associated with menstrual irregularities (not to be used during pregnancy/breastfeeding)
  - Effect of hormone tx are maximal after 9-12 months of therapy
  - Weight loss results in decrease in serum androgens, can improve hirsutism
  - Topical agent (Eflornithine/Vaniqa)
  - Laser/IPL, electrolysis
- Irregular menses and endometrial protection – COC is 1st line
  - Intermittent progestin therapy 2nd line
- COC
  - Typically start with 20mcg ethinyl estradiol (EE) combined with lower androgenic as well as lower VTE risk progestin (norethindrone)
  - Sometimes higher doses of EE are necessary for suppression of ovarian androgens and mgmt of hyperandrogenism
- Spironolactone
  - 50-100mg BID

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Treatment of PCOS

- Metformin
  - Restores ovulatory menses in ~ 30-50% of women with PCOS (safe to use in pregnancy if desired)
  - potential alternative to restore menstrual cycle regularity
  - Can reduce insulin levels
  - May also reduce ovarian androgen production and restore nml menstrual cycles
  - Role in treating infertility is limited
  - Ability to provide endometrial protection is not well established
  - Current guidelines recommend against use of metformin in obese women with PCOS, except in women with glucose intol who have failed lifestyle interventions
- Ovulation induction
  - Clomiphene citrate
  - Letrozole (higher live birth rates in women with BMI >30 kg/m^2 vs clomiphene citrate)
    - Ovulation induction is off-label use

Menopause

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Menopause

- Defined as 12 months after a final menstrual period (FMP)
- Represent permanent cessation of menses due to loss of ovarian follicular function
- Average age of natural menopause – 51.4 yrs
- Diagnosed by noting 12 months of amenorrhea without any other pathological or physiological cause and may have an elevated FSH level (you would only know **if** you checked it!)
- Perimenopause – occurs after reproductive years, but before menopause, characterized by irregular menstrual cycles, endocrine changes, and symptoms such as hot flushes
  - Average 4 years
  - Range 2-12 years

Clinical Presentation

- Hot flushes – affects up to 80%, only 20-30% seek medical treatment
  - 2-4 minutes often w/ profuse sweating and occasionally palpitations, sometimes followed by chills and shivering and feeling of anxiety
  - Untreated typically resolve spontaneously within 4-5 years (9% report>70yrs)
- Sleep disturbances – even in the absence of night sweats
  - ~32-46% affected starting in early transition
  - >50% have sleep apnea, RLS, or both
- Mood swings – significant increased risk of new-onset depression during menopausal transition
- Cognitive changes – substantial evidence points to importance of estrogen to cognitive function
- Joint pain – 50-60% - many note relief with estrogen and/or progestin therapy

Clinical Presentation

- Vaginal dryness – as opposed to vasomotor symptoms (VMS), genitourinary syndrome of menopause (GSM) symptoms are progressive and worsen
  - Labial pallor, vestibular pallor or erythema, lack of nml rugae, scarce pubic hair, diminished elasticity and turgor of vulvar skin, introital narrowing, decreased moisture, fusion or resorption of labia minora
- Sexual function – partially due to GSM, shortening or narrowing of the vaginal vault and introitus. Systemic hormonal influences as well as body image, fatigue
- Breast pain – common in early transition but diminish in late transition. Likely due to estradiol fluctuations
- Menstrual migraines – may worsen in frequency and intensity

Long term consequences of estrogen deficiency

- CVD – risk increases after menopause
  - Lipid profile begins to change during perimenopause
- Bone loss – begins during menopausal transition, greatest during 1 yr before FMP through 2 yrs after
- Dementia – role of estrogen here is yet unclear
- Osteoarthritis – estrogen deficiency may contribute, but data limited
- Body composition – gain fat mass and lose lean mass
- Skin changes – estrogen deficiency decreases collagen content in skin and bones
- Balance – impaired balance may be a central effect of decreased estrogen

Late reproductive years

- FSH slight increase
- Estradiol levels steady
- Luteal phase progesterone levels decrease as fertility potential declines
- ***Ovulatory cycles, but follicular phase shortens***

Diagnosis of menopause

- Currently – no single test of ovarian function that will predict or confirm menopause
- Usually confirmed based on symptoms and medical/menstrual history
- Non-ovarian hormone tests sometimes necessary to r/o other causes for symptoms (ex: TSH)
- Patients often ask for baseline and/or intermittent hormone testing based on insistence from some compounding pharmacists, clinicians, partners
  - No scientific basis for baseline hormone levels or intermittent checks
  - Recommended practice is to titrate med doses based on patient's report of symptom relief and AEs

Reasons to order hormone testing in clinical practice

- Estradiol
  - To assess absorption in those with persistent vasomotor symptoms on HT
- PRL
  - To differentiate causes of oligomenorrhea or galactorrhea
- TSH
  - To differentiate causes of oligomenorrhea, atypical hot flushes, sleep disorders, fatigue, and weight changes

Here's why we don't use FSH to diagnose menopause

- Generally accepted that a person has reached menopause if they have **consistently** elevated levels of FSH > 30 mIU/mL
- FSH levels in the postmeno range can return to premeno ranges a few days, weeks, or months later
- FSH levels in perimeno patients are often normal, or can be elevated, while estradiol levels paradoxicaly remain in a premeno range
- Elevated early follicular FSH is enough only to put someone in the late reproductive stage
- LH elevation occurs much later than FSH elevation in the menopausal transition

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- So patients > 45 yrs who present with irregular menses with menopausal symptoms (hot flushes, mood swings, sleep disturbances) need no further diagnostic evaluation

40-45 yrs

- Those who present with irregular menstrual cycles, with or without menopausal symptoms
  - Perform same endocrine eval as for anyone with oligo-/amenorrhea
    - Serum hCG – r/o pregnancy
    - Serum PRL – r/o hyperprolactinemia
    - Serum TSH – r/o thyroid d/o
    - Serum FSH

Perimenopausal birth control users

- COCs are considered safe in non-smokers up to the age of menopause
  - To determine menopause for these patients, d/c COC and measure serum FSH 2-4 weeks later
  - FSH >= 25 IU/L indicates likely in menopausal transition
  - No FSH value that would provide absolute reassurance that patient is postmeno
  - Often, these patients will experience hot flushes when estrogen is stopped abruptly. Consider tapering (ex: taper by 1 pill per week)

Menopausal therapy

- Goal
  - Relieve menopausal symptoms/vasomotor symptoms
  - Emotional lability/depression, GSM, dyspareunia, insomnia, joint pains have all been shown to also respond to estrogen therapy (ET)
- Treat vasomotor symptoms with systemic estrogen (if HT is chosen)
- Treat GSM with low-dose topical therapy or ospemifene (Osphena)
- Alternative therapies are available if hormones are not desired or CI, however none are as effective as estrogen

Side effects

- Breast tenderness
- Mood symptoms and bloating possible with progestin therapy
- Vaginal bleeding common in early months of continuous estrogen-progestin regimen
  - Occurred almost always with previously used cyclic regimens

Contraindications to hormone therapy

- h/o breast ca
- CHD
- h/o VTE or stroke/TIA
- Active liver disease
- Unexplained vaginal bleeding
- High risk endometrial cancer

- Should be avoided in:
  - Hypertriglyceridemia
  - Active gallbladder disease
  - Known thrombophilias (ex: FVL)

- *Transdermal estrogen is preferred for those with migraines with aura*

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Things to consider

- All routes of estrogen appear to be equally effective for symptom relief (and bone density), but their metabolic effects differ
  - VTE/stroke risk lower with transdermal vs oral
  - Oral estrogens increase SHBG
- Select initial treatment agent based upon main concern
  - Depression is main concern with mild hot flushes – choose SSRI
    - Some SSRIs help vasomotor symptoms in low doses as well
  - Hot flushes are main concern with mild mood swings – choose HT

Things to consider

- HT is considered safe to initiate for healthy, symptomatic people within 10 yrs of menopause or younger than 60 yrs of age without CIs
- Vaginal estrogen is not associated with an increased risk of CV events or breast ca
  - Still has class effect black box warning!
- Younger patients s/p BSO often require higher doses for the 1st 1-3 yrs after surgery
- Newly menopausal or perimenopausal patients can expect breakthrough bleeding (BTB) due to occasional ovarian “surge” of endogenous hormone

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Progestin therapy

- Oral micronized progesterone is 1st line
  - Necessary if intact uterus only
  - Natural progesterone may be safer for CV system (no adverse lipid effects) and possibly the breast
  - WHI studied MPA
    - Showed increased risk CHD and breast ca when given with conjugated estrogen
  - May use LNG IUD for uterine protection
- May cause mood SEs and bloating if taken orally
- Perimenopausal patients will often have less BTB with cyclic progesterone due to endogenous hormone activity

SERMs

- We have 2 we will typically use for the postmenopausal/perimenopausal patient
- Conjugated estrogen/bazedoxifene (Duavee)
  - SERM prevents estrogen induced endometrial hyperplasia, so progestin is unnecessary
  - Indicated for mod/severe VMS and post meno osteoporosis prevention
  - Risk of VTE is increased with bazedoxifene and other SERMs
- Ospemifene (Osphena)
  - Estrogen agonist in vaginal epithelium and endometrium
  - Indicated for mod/severe dyspareunia

Duration of therapy

- Short term use is suggested
  - Generally not more than 5 years or not beyond age 60
- Hot flushes persist average 7.4 years
- Many continue to have them for more than 10 years
- Those with persistent symptoms may choose longer term therapy

WOMEN'S HEALTH COLLECTIVE

WHI

- Risk of breast cancer with combined EPT did not increase until the 4th year
- Breast cancer risk
  - 3 additional cases per 1000 women per 5 years of hormone use with combined estrogen-progestin therapy
  - 2.5 fewer cases per 1000 women per 5 years of hormone used with estrogen alone therapy
- Average age of women enrolled ~ 63 yrs

Discontinuation

- Taper Taper Taper!!
- Per WHI, ~55% of women will have recurrent VMS if HT is stopped abruptly
- For transdermal, gradual dose reduction over 3-6 months
- For oral, decrease by 1 pill per week every 2-4 weeks
- ACOG and NAMS agree that HT use should be individualized and not d/c'd based solely on age
- Use > 60-65 yrs may be reasonable when clinician and patient agree that benefits of symptom relief outweigh risks

Bioidentical hormones

- I start by asking my patient what they mean by and expect from “bioidentical hormones”
  - This means something different to each person
  - Often they mean compounded hormones
  - Asking reasoning will help you educate
  - “What is it about bioidentical hormones that is appealing to you”
  - Often reply is “It’s more natural” “It’s safer” “There is less risk”
  - NAMS, ACOG, Endocrine Society have all issued scientific statements advising against the use of custom-compounded hormones
  - They are not required by law to include PI, however this does not render them without risk

WOMEN'S HEALTH COLLECTIVE

GSM

- Normal pH of vagina 3.5-4.5
  - With loss of estrogen and lactobacilli, becomes more alkaline
  - Increase in parabasal cells, decrease in superficial cells
- Topical estradiol or DHEA as well as oral ospemifene
- Minimal systemic absorption with topical therapy (stays within expected postmenopausal levels)
  - However, no data to tell us it is safe in breast ca survivors
- Vulvar and vaginal tissue is both estrogen receptor dependent as well as testosterone receptor dependent
- Lubricants, moisturizers, vibe therapy
- Laser/CO2 therapy

Questions???

WOMEN'S HEALTH COLLECTIVE