UVM Project ECHO
Women's Health:
Improving Care and Reducing Disparities

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Didactic presentation is recorded. Registered participants will receive the link.

The University of Vermont
LARNER COLLEGE OF MEDICINE
OFFICE OF PRIMARY CARE & AHEC PROGRAM

Project ECHO
University of Vermont

Session Agenda

- Welcome Participants and Presenters
- Objectives
- Didactic Presentation (35-40 min)
  - Q&A
- Case presentation(s)
  - Clarifying questions
  - Discussion
  - Recommendations
- Closing Announcements
  - Submission of new cases
  - Completion of evaluations

ECHO Model: All Teach, All Learn

Cohort-based learning on ZOOM

- Have your camera on as much as possible, especially when joining the meeting and during discussions
- Questions and comments are welcome – use the “raise hand” feature or put them in the chat
- This is not a webinar! Participation is key

Case-based learning

- 1-2 participant cases each session using provided template
- Contact Mark Pasanen to present a case

Series Objectives

Learning objectives for this ECHO series include the ability to:

- Assess, diagnose and manage a range of gynecological conditions
- Describe current screening guidelines and approaches to cancer detection
- Identify strategies to promote well-being during life stages, preconception to post menopause
- Implement practices to reduce disparities in women's health care delivery.

CMIE Disclosures

- University of Vermont (UVM) Office of Continuing Medical and Interprofessional Education (CMIE) is approved as a provider of Continuing Medical Education (CME) by the ACCME. UVM designates this internet live activity for a maximum of 1.25 ***AMA Category 1 credit***™.
- UVM CMIE is accredited by the American Nurses Credentialing Center (ANCC) to provide CE for the healthcare team. This program has been reviewed and is acceptable for up to **1.25 Nursing Contact Hours**.
- Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to: **1.25 MOC points** in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program; It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM or ABP MOC credit.

Participants should claim only the credit commensurate with the extent of their participation in the activity.

CMIE Disclosures

Interest Disclosures: As an organization accredited by the ACCME to sponsor continuing medical education activities, UVMCMIE is required to disclose any real or apparent conflicts of interest (COI) that any speakers may have related to the content of their presentations.

Meeting Disclaimer: Regarding materials and information received during this educational event, the views, statements, and recommendations expressed during this activity represent those of the authors and speakers and do not necessarily represent the views of the University of Vermont.

Menopause/Amenorrhea

Julia V. Johnson, M.D.

Professor, OB/GYN

April 19, 2023

The University of Vermont
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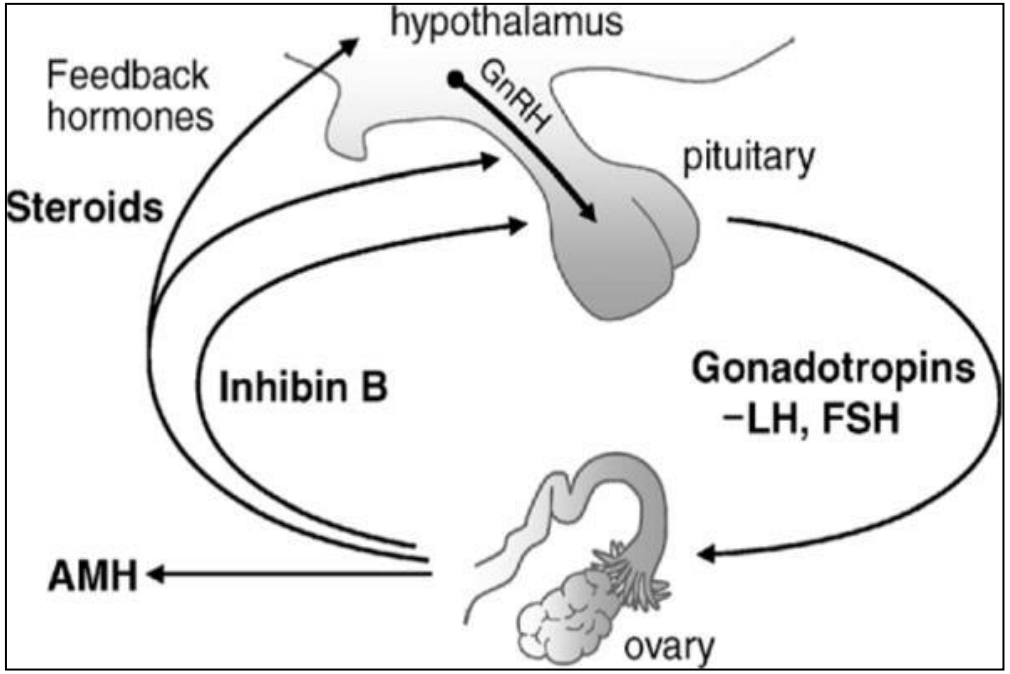
Session Objectives

- Review normal processes
  - Menstrual cycle
  - Perimenopause
  - Menopause
- Define menopause and amenorrhea
- Discuss etiologies for premature menopause and amenorrhea
- Review treatment options for amenorrhea/menopause

The Menstrual Cycle

Hypothalamic-Pituitary-Ovarian Axis

- Closed loop feedback system
  - Exception = mid-cycle gonadotropin surge
  - Pituitary Gonadotropins
    - Luteinizing Hormone (LH)
    - Follicle Stimulating Hormone (FSH)
  - Ovarian Hormones
    - Steroid Hormones
      - Estradiol
      - Progesterone
      - Testosterone



Burger HG, et al. Cycle and hormone changes during perimenopause: the key role of ovarian function. Menopause 2008;15:603

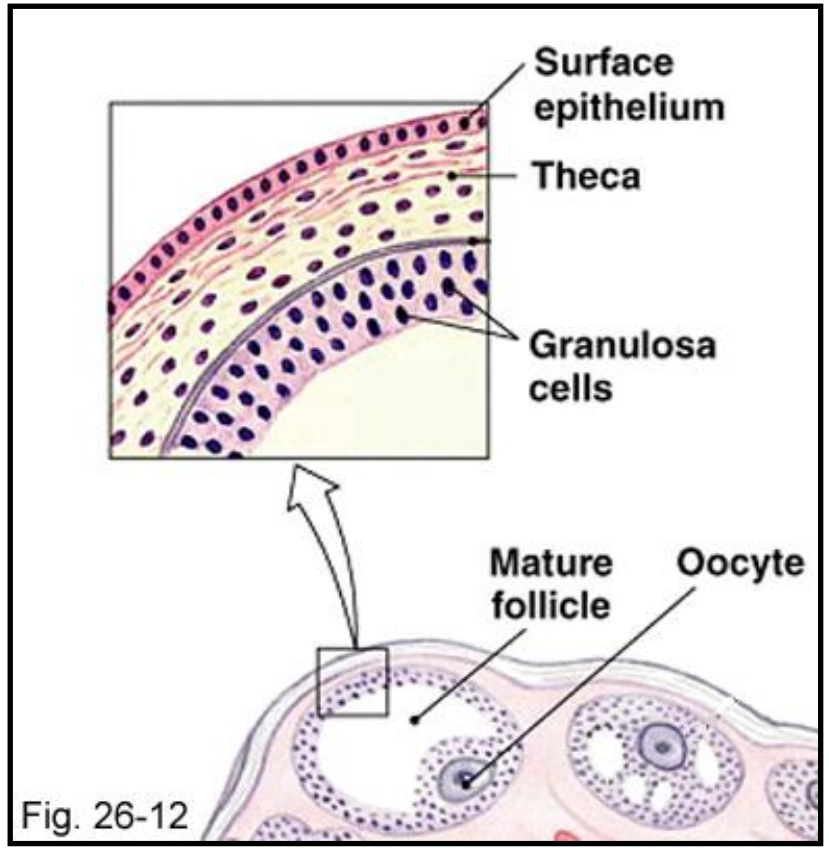
2-Cell, 2-Gonadotropin System

Theca Cell

- Regulated by LH
- Cholesterol→ Androgen
  - Androstenedione
  - Testosterone
    - Substrate for aromatization to estrogen in GC

Granulosa Cell

- Regulated by FSH
- Androgen → Estrogen
  - Estradiol
  - Estrone



The Menstrual Cycle
Early Follicular Phase

Hypothalamus

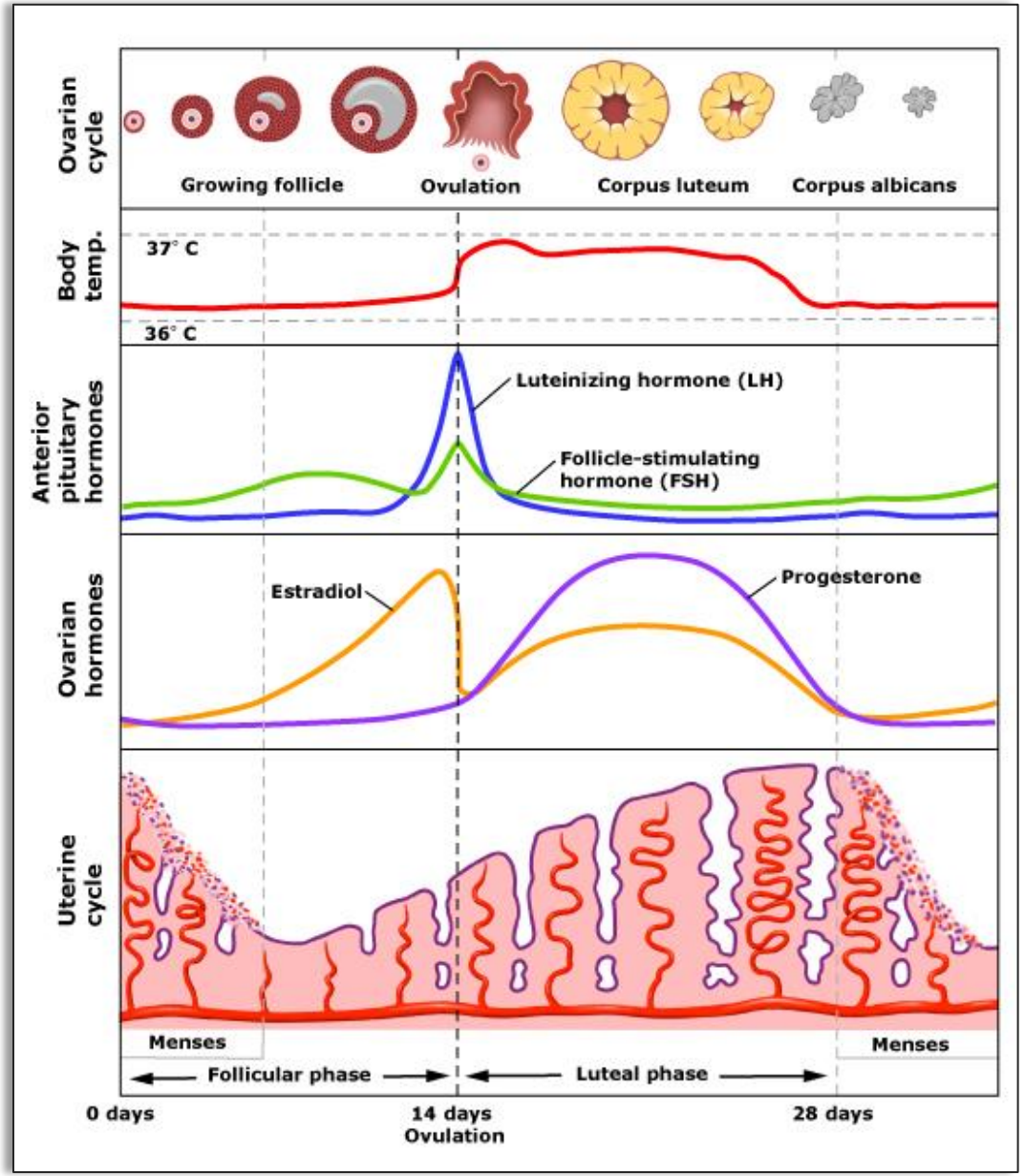
- ↑ GnRH pulse frequency

Pituitary

- ↑ FSH – 30%

Ovary

- Follicular recruitment
- Aromatization = ↑ estrogen
- ↑ FSH receptors on GC
  - Induced by FSH and estrogen



The Menstrual Cycle: Ovulation

LH Surge

- 34-36 hrs prior to follicle rupture
- Threshold [LH] maintained for 14-27 hrs
- Initiates
  - Continuation of meiosis
  - Lutenization of granulosa cells
  - Synthesis of local contributory factors

Proteolytic Enzymes

- ↑ in response to FSH, LH, P
- Proteoytic digestion of follicular apex (stigma)

The Menstrual Cycle
Luteal Phase

Luteal function

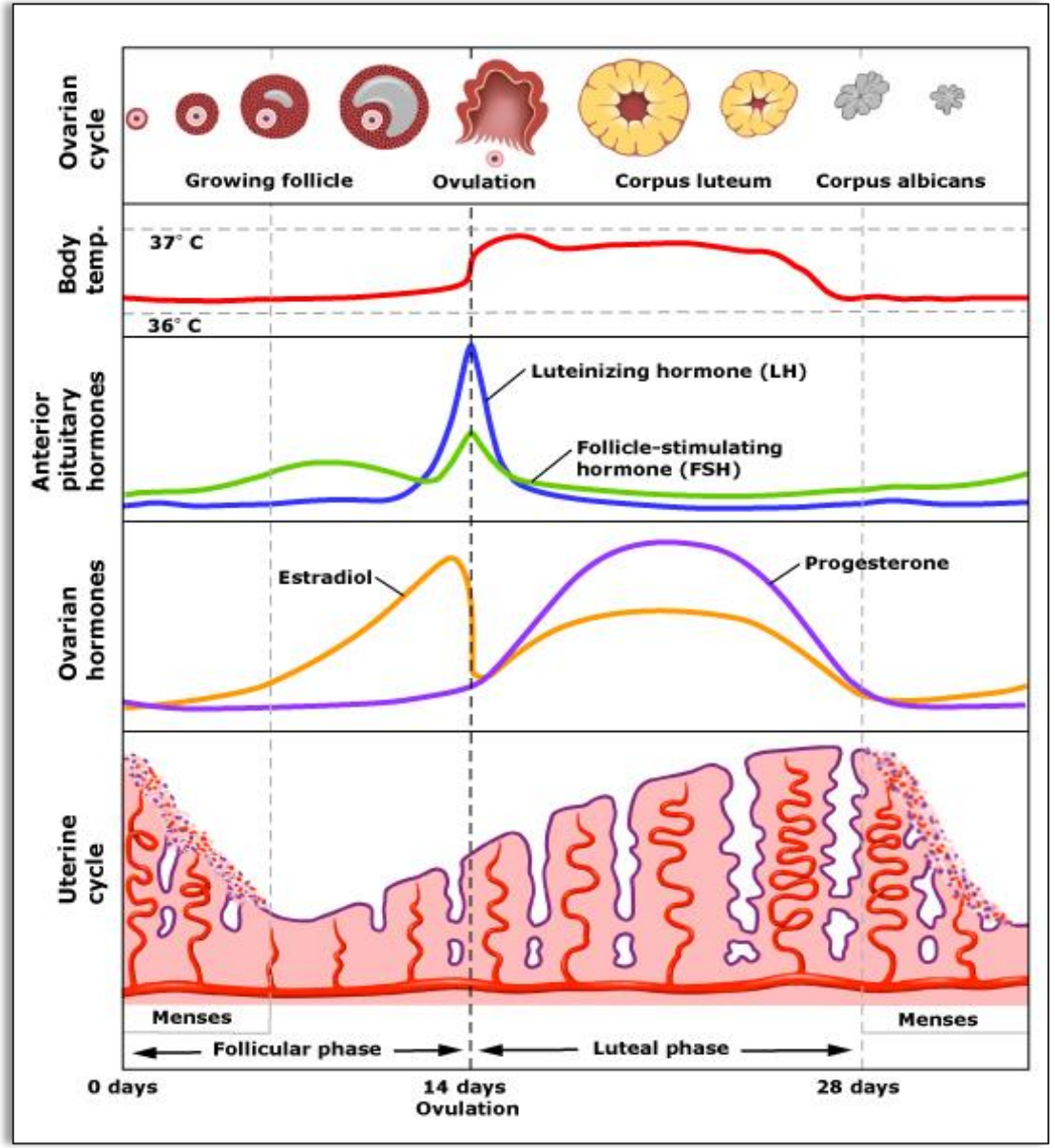
- Accumulation of LH during follicular phase
- Tonic LH secretion

Luteolysis

- 9-10 days after ovulation
- Mechanism unknown

Pregnancy

- hCG rescues CL
- Maintains function until placentation

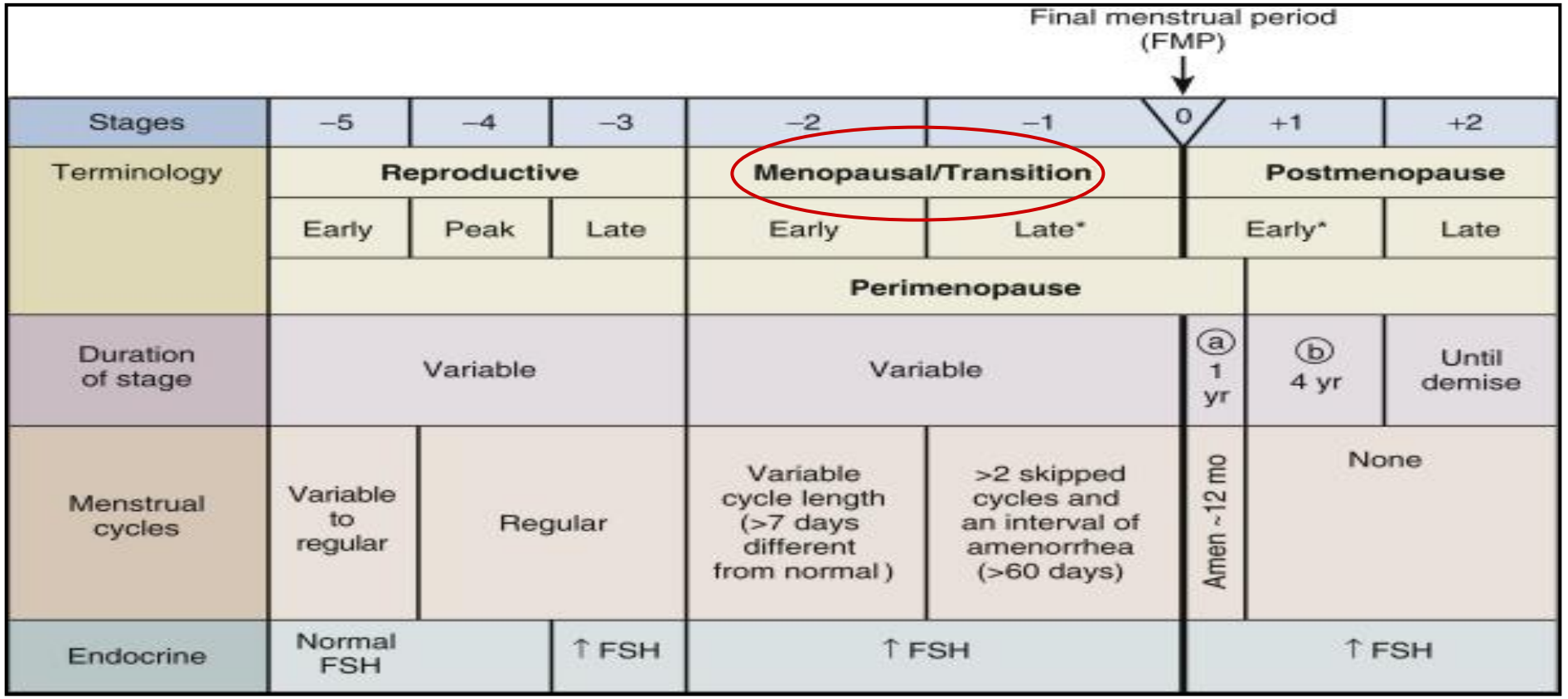


Endocrine Changes Associated With Reproductive Aging

Early Studies

- Regular cycles
  - Monotropic increase in FSH
  - Shortened follicular phase
  - Minimal change in steroid hormone concentration
- Irregular cycles
  - Increased FSH and LH
  - Unpredictable changes in estradiol, progesterone

Stages of Reproductive Aging Workshop (STRAW) Staging System



Menopause definition

Menopause is a natural event in all women's lives

Menopause is the last menstrual cycle; one year without a period and you are menopausal

- Average age is 51; occurs between age 40—58
- Many women will experience menopausal changes prior to their last period or "Perimenopause"
- 1% of women undergo premature menopause before age 40

There is no prediction of the age of menopause

- Best predictor is the age of menopause of female relatives; likely genetically determined
- Age of menopause is not affected by age of first period, pregnancy, use of birth control, use of fertility medication

Menopausal Symptoms and treatment

Related to loss of ovarian estrogen

Vasomotor symptoms

- Effects 85% of menopausal women; 25% of perimenopausal women
- Causes hot flushes, sleeplessness, potential mood changes, decreased cognitive function
- Treatment is critical to improve quality of life
  - 60% improvement with SSRI; 50% reduction with gabapentin
  - 90+% improvement with estrogen (progestin in women with uterus); not CV risk before age >60 and minimal breast cancer risk
  - New nonhormonal medication pending approval from FDA

Vaginal atrophy

- Affects all women after menopause with symptoms in 50% of women
- Treated effectively with lubricant or vaginal estradiol
- Vaginal estradiol is not systemically absorbed and safe for women of all ages

Amenorrhea definition

Amenorrhea

- Primary = absence of menarche by age 15
- Secondary = absence of menses for > 3 months with history of regular menses OR absence of menses for > 6 months for with history of irregular menses

Involves one of 4 sites

- Hypothalamus
- Pituitary
- Ovary
- Uterus

Sites for Amenorrhea

Hypothalamic

- Rare—GnRH deficiency, craniopharyngioma or other tumor, brain injury, radiation therapy
- Functional—Weight loss/eating disorder, excessive exercise, prolonged illness

Pituitary

- Hyper or hypothyroidism
- Hyperprolactinemia
- Rare—corticotrope adenoma (Cushing's) and other tumors, pituitary apoplexy

Sites for Amenorrhea

Ovarian

- Polycystic ovarian syndrome
    - ALSO consider adrenal etiologies: late onset congenital adrenal hyperplasia
- Ovarian tumor—hormone producing
- Premature ovarian insufficiency/menopause
    - Turner's syndrome
    - Fragile X
    - Chemotherapy or RXT
    - Idiopathic (?autoimmune)— at least 10% return to normal menses

Uterine

- Pregnancy
- Intrauterine adhesions due to procedure or infection (Asherman's)
- Androgen insensitivity syndrome (abnormal androgen receptor) with absence of uterus
- Congenital abnormality in Mullerian development including Mullerian agenesis
- Congenital defect in urogenital sinus including transverse septum

Evaluation for Amenorrhea

Medical history

- START WITH RULING OUT PREGNANCY
- Pubertal history
  - Delayed or incomplete development
- Menstrual history
  - Irregular or previous amenorrhea
- Sexual history
  - Any issues with attempted intercourse?
- Lifestyle changes
  - Weight changes or exercise increase
  - New onset fatigue
- Medical and surgical events
  - Chemotherapy or radiation to abdomen or brain
  - Galactorrhea
- Medications
  - Antipsychotic medication
  - Opioids
  - Any hormonal contraceptive

Evaluation for Amenorrhea

- Exam
  - Constitutional features including BMI and exam for hirsutism or virilization
  - Thyroid exam
  - Pelvic exam to evaluate for mullerian anomaly, vaginal septum
- Testing
  - If hyperandrogenic: testosterone, 17-OH progesterone, and DHEAS with ultrasound of ovaries for PCOS
    If not identified as PCOS or CAH: Rule out Cushing's (ACTH/Dex suppression test) and adrenal tumor (CT of adrenal glands)
  - Labs: hCG, FSH, TSH, prolactin, estradiol
    - If low FSH/E2 and normal TSH: MRI to rule out brain lesion
    - If elevated prolactin: evaluate pituitary prolactinoma
    - If elevated FSH before age 40: genetic testing for Fragile X as cause of premature ovarian insufficiency

Summary of Evaluation for Amenorrhea

Always consider pregnancy (even if presumed menopause!)

If not pregnant, then consider history and physical for potential causes for amenorrhea (eg. Sudden onset of fatigue and weight gain may indicate hypothyroidism; galactorrhea may indicate hyperprolactinemia).

Consider the 4 sites for amenorrhea– hypothalamic, pituitary, ovarian, and uterine. Look for something in the history that suggests one of these sites (e.g. training for the next marathon).

If the cause is not clear based on exam (e.g. Mullerian agenesis), then routine labs are prolactin, TSH, and FSH for the most common pituitary reasons for amenorrhea.

If androgen excess, check testosterone level and consider PCOS if other causes are ruled out.

If all labs normal and considering hypothalamic etiology, obtain MRI.

Treatment of Amenorrhea

Based on etiology, treatment is required

Primary amenorrhea based on genetic or medical etiology

- Treat with estradiol and progesterone to protect bone and CV health

Primary amenorrhea due to mullerian anomaly

- Possible surgical therapy

Secondary amenorrhea based on PCOS

- Regulate menses with progestin or OCPs

Secondary amenorrhea based on other medical condition or premature menopause

- Treat medical condition or start hormone therapy

Questions?

Case 1

18 yo presents with primary amenorrhea

What is your first step?

What are critical questions to ask?

What are findings at your physical that may be informative?

What labs/tests will you order based on the initial H & P?

Once you have a diagnosis, what treatment is indicated?

First Step is Always

PREGNANCY TEST

What are the critical questions?

- Have you had any breast and pubic hair development and when did it start?
- Any issues with hirsutism or acne?
- Are you on any medications? Any treatment for cancer?
- Do you have any gynecologic or breast concerns?
- Has your weight changed?
- Tell me about your exercise?

What are the critical questions?

- Have you had any breast and pubic hair development and when did it start?
  - *Yes—since I was 12 I had breast development and some pubic hair*
- Any issues with hirsutism or acne?
  - *Mild acne around age 14, but it is better now.*
- Are you on any medications? Any treatment for cancer?
  - *No. I have always been healthy.*
- Do you have any gynecologic or breast concerns?
  - *No. I have never had an exam, but no pain or discharge.*
- Has your weight changed?
  - *Some people say I am thin, but my weight is stable. I like it.*
- Tell me about your exercise?
  - *I do not really exercise, I dance as a ballerina and am going to be professional.*

What are the next steps?

- Physical examination
- Laboratory tests
- Additional testing
- Diagnosis?
- Treatment?

What are the next steps?

- Physical examination
  - *Perform breast (no galactorrhea) and GYN exam (rule out Mullerian anomaly or possible AIS).*
  - *Check BMI. If less than 18.5, this suggests functional hypothalamic amenorrhea.*
- Laboratory tests
  - *Rule out other causes*
    - *FSH—if high, then premature ovarian insufficiency. If normal, this is reassuring.*
    - *TSH—thyroid disease*
    - *Prolactin—hyperprolactinemia*
    - *No need for androgen testing.*
- Additional testing
  - *With normal exam, normal FSH, TSH, PRL, then needs MRI to rule out tumor*
- Diagnosis?
  - *Functional hypothalamic amenorrhea*
- Treatment?
  - *Must prevent bone loss with estradiol + progestin OR OCPs*
  - *Consider behavioral therapy based on BMI and level of concern for eating disorder*

Case 2

16 yo presents with no menses for 9 months

What is your first step? YOU KNOW!

What are critical questions to ask?

What are findings at your physical that may be informative?

What labs/tests will you order based on the initial H & P?

Once you have a diagnosis, what treatment is indicated?

What are the critical questions?

- Tell me about your periods prior to 9 months ago
- Have you had any breast and pubic hair development and when did it start?
- Any issues with hirsutism or acne?
- Are you on any medications? Any treatment for cancer?
- Do you have any gynecologic or breast concerns?
- Has your weight changed?

What are the critical questions?

- Tell me about your menses prior to 9 months ago
  - *They started when I was 11 and I have them every 2 to 3 months*
- Have you had any breast and pubic hair development and when did it start?
  - *Yes, although I have more hair on my abdomen than my friends*
- Any issues with hirsutism or acne?
  - *I do have a problem with acne and see a dermatologist.*
- Are you on any medications? Any treatment for cancer?
  - *My mom made me take birth control pills for a while, but I stopped them*
- Do you have any gynecologic or breast concerns?
  - *I have never had an exam, but I guess I am normal.*
- Has your weight changed?
  - *I keep gaining weight, but I eat well and exercise regularly.*

What are the next steps?

- Physical examination
- Laboratory tests
- Additional testing
- Diagnosis?
- Treatment?

What are the next steps?

- Physical examination
  - *Normal breast exam, but under her arms there are darkened areas with raised lesions*
  - *Normal GYN exam*
  - *Marked hair growth in mid-abdomen. No facial or mid-chest hair seen. Mild acne.*
- Laboratory tests
  - *Can confirm normal FSH, TSH, PRL*
  - *Testosterone level is total = 80, free = 4.5.*
- Additional testing
  - *17-OH progesterone level is normal*
  - *Cushing's or other androgen excess diseases are rare and testing is not indicated without other factors*
- Diagnosis?
  - *PCOS with possible hidradenitis suppurative*
- Treatment?
  - *Progestin withdrawal followed by regular progestin use or OCPs*
  - *Referral to Dermatology for antibiotics and possible steroid therapy*

Case 3

45 yo presents with onset of amenorrhea for the past year

What is your first step? YOU KNOW!

What are critical questions to ask?

What are findings at your physical that may be informative?

What labs/tests will you order based on the initial H & P?

Once you have a diagnosis, what treatment is indicated?

What are the critical questions?

- Tell me about your periods prior to 12 months ago
- Have you had any health changes in the past year?
- Do you have any changes in your body that are concerning?
- Do you have any gynecologic or breast concerns?
- Has your weight changed?

What are the critical questions?

- Tell me about your periods prior to 12 months ago
  - *It is odd because I always had regular periods until a year ago when they suddenly stopped*
- Have you had any health changes in the past year?
  - *Not really. I have regular mammograms.*
- Do you have any changes in your body that are concerning?
  - *I developed some facial hair and lost some hair on my head, but my friends tell me that happens near menopause*
- Do you have any gynecologic or breast concerns?
  - *My breast seem a little smaller, but that is normal with aging—right?*
- Has your weight changed?
  - *I have always been thin, but it is unchanged.*

What are the next steps?

- Physical examination
- Laboratory tests
- Additional testing
- Diagnosis?
- Treatment?

What are the next steps?

- Physical examination
  - *She has normal breast exam and pelvic exam. She does have facial hair that is diffuse despite frequent plucking. Her hair on her head is somewhat thin. She has mid-abdominal and back hair.*
- Laboratory tests
  - *Normal FSH, TSH, PRL.*
  - *Elevated testosterone total = 720*
- Additional testing
  - *Pelvic ultrasound showed normal inactive ovaries.*
  - *Adrenal MRI was normal.*
  - *Ovarian venous sampling (by IR) demonstrated high testosterone level from right ovary; some from IR about process*
- Diagnosis?
  - *Benign ovarian Leydig cell tumor*
- Treatment?
  - *Removed both ovaries at laparoscopy to assure that there was not second tumor in left ovary*
  - *Started on hormone therapy to prevent bone loss and maintain CV health (to age 50)*
  - *Followed testosterone level for several years which is within normal range*

Case 4

30 yo G2P1 presents with amenorrhea for 6 months; desires fertility

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What is your first step? YOU KNOW!

What are critical questions to ask?

What are findings at your physical that may be informative?

What labs/tests will you order based on the initial H & P?

Once you have a diagnosis, what treatment is indicated?

What are the critical questions?

- Tell me about your periods prior to 6 months ago
- How long ago where you pregnant?
- Have you had any health changes in the past year?
- Do you have any changes in your body that are concerning?
- Do you have any gynecologic or breast concerns?

What are the critical questions?

- Tell me about your periods prior to 6 months ago
  - *My periods were regular and then a few years ago they starting coming every other month, but this is the first time of 6 months without a period*
- How long ago where you pregnant?
  - *My son is 9. I had a miscarriage 3 1/2 years ago with a new partner.*
- Have you had any health changes in the past year?
  - *No. I am healthy. No new medications.*
- Do you have any changes in your body that are concerning?
  - *No. I do not have any changes in my weight and my hair and skin are normal.*
- Do you have any gynecologic or breast concerns?
  - *No. My last pap was fine and I was told to try to get pregnant again before it was 'too late'.*

What are the next steps?

- Physical examination
- Laboratory tests
- Additional testing
- Diagnosis?
- Treatment?

What are the next steps?

- Physical examination
  - *Patient is up to date with breast and gyn exams, but on repeat, they do appear normal. No hirsutism or acne. Normal BMI.*
- Laboratory tests
  - *FSH = 55*
  - *Normal TSH and PRL*
- Additional testing
  - *E2 = <20*
  - *Genetic testing: 46XX*
  - *Fragile X testing: Positive*
- Diagnosis?
  - *Fragile X syndrome*
  - *Concern for her son to have inherited this disorder*
- Treatment?
  - *For fertility, can consider donor oocytes to optimize chance for pregnancy*
  - *If not attempting pregnancy, can consider hormone therapy for bone and CV protection*

Case Presentation

Bringing Knowledge to Action through interactive, case-based discussions

Participant presents the case and poses the question(s) for the group

↓

Clarifying questions about the case from group to case presenter

↓

Ideas, suggestions, recommendations from participants

↓

Ideas, suggestions, recommendations from ECHO faculty team

↓

Full group discussion

↓

Summary and wrap-up by facilitator

Case Presentation

DO <u>NOT</u> INCLUDE:

Names, Address, DOB, Phone/Fax #, Email address, Social Security #, Medical Record #

Consider the level of detail necessary. Go with less when possible.

The discussion and materials included in this conference are confidential and privileged pursuant to 26VSA Section 1441-1443. This material is intended for use in improving patient care. It is privileged and strictly confidential and is to be used only for the evaluation and improvement of patient care.

Case

Session Date	Session Topic	Speaker
December 7, 2022	Contraception: Beyond the basics	Lauren MacAfee, MD
December 21, 2022	Management of abnormal PAP testing	Ellie Wegner, MD
January 4, 2023	Endometriosis/Pelvic Pain	Misty Blanchette Porter, MD
January 18, 2023	Abnormal Uterine Bleeding	Jenn Dundee, MD
February 1, 2023	Preconception/Early Pregnancy	Justin D'Angelis, MD
February 15, 2023	Adnexal Masses	Charles Ashley, MD
March 1, 2023	Vulvovaginal disorders	Tracey Maurer, MD
April 5, 2023	Sexual function	Jane Conolly, MD
April 19, 2023	Menopause/Amenorrhea	Julia Johnson, MD
May 3, 2023	**High Risk Breast Screening**	**Kara Landry, MD**
May 17, 2023	Gender-based Violence/Trauma-informed Care	Abigail Garrett, Kiona Heath and Anne Dougherty

Closing Announcements

- Confirm case presenter(s) for next session
- Slides are posted at www.vtahec.org
- Recording of didactic portion will be sent by email to the full cohort
  - For the use of registered participants only
- Please complete evaluation survey after each session
- CE information and QR Code will be sent once evaluation is received
- Please contact us with any questions, concerns, or suggestions:
  - Mark.Pasanen@uvm.edu
  - Patti.Smith-Urie@uvm.edu