Amenorrhea

Tischelle Gatlin, PGY3
Mercy Hospital and Medical Center

Disclosures

None

Objectives

1. Describe the classification of amenorrhea
2. List the major causes of primary and secondary amenorrhea
3. Identify pertinent history and physical exam
4. Discuss diagnostic testing for the evaluation of amenorrhea
5. Determine the long-term follow-up

Definitions

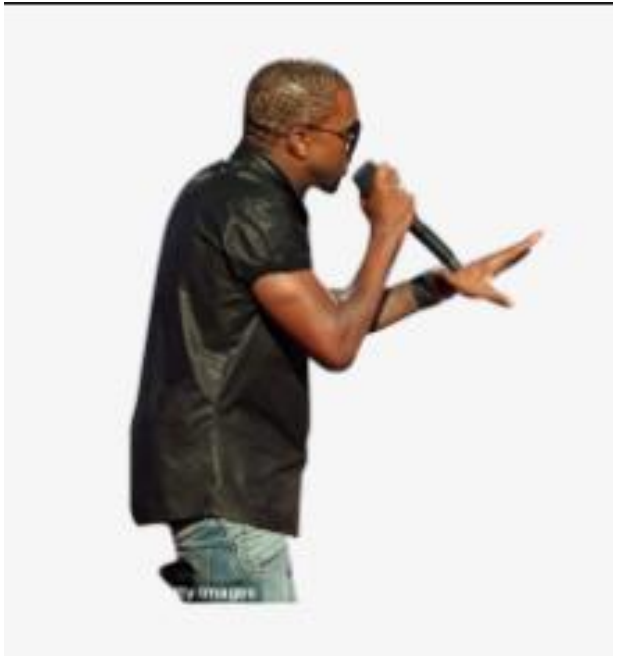
Primary Amenorrhea

- failure to menstruate by age 15 in the presence of normal growth and secondary sexual development
- Failure to menstruate 5 years after breast development if that occurs before age 10
- If by the age of 13 no menses or secondary sex characteristics have occured

Secondary amenorrhea

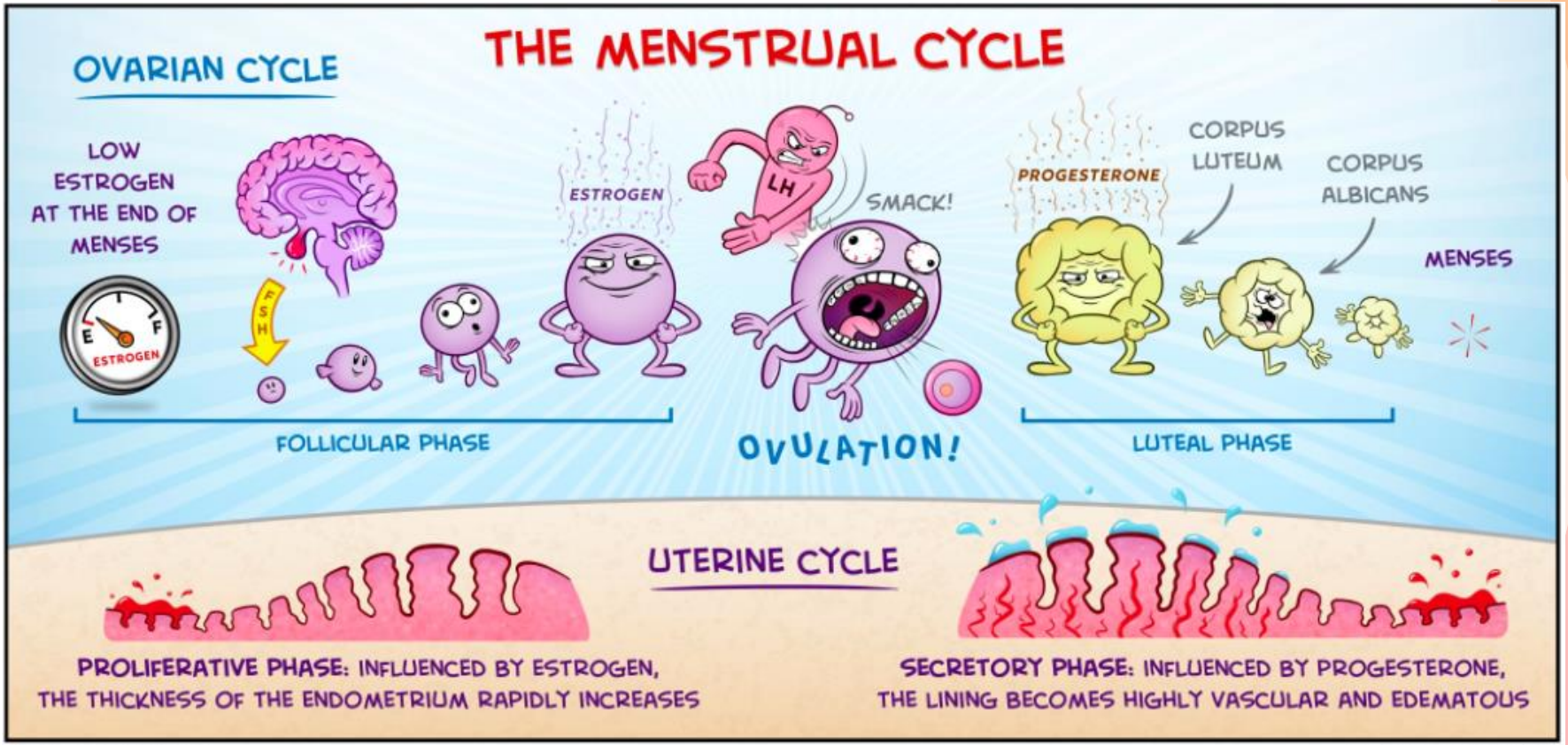
- Absence of menses > 3 months in those with regular menses or absence of menses > 6 months in those with irregular menses

But first…..



The Menstrual Cycle

The Menstrual Cycle

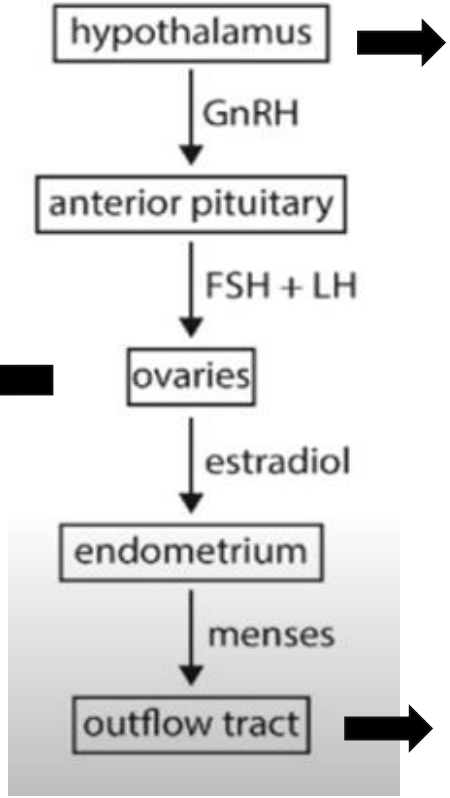


1.
Primary Amenorrhea

Menstrual Cycle

Constitutional Delay

Chromosomal Androgen Insensitivity Syndrome



Kallmann syndrome

Turner syndrome
Gonadal dysgenesis

Imperforate hymen
Absent vagina
Absent Uterus
Transverse vaginal septum
Mullerian agenesis

Physiological Delay

- Accounts for 14%
- Includes constitutional delay, chronic systemic disease, and acute illness
- Includes delayed adrenarche and gonadarche
- Less common in girls

Chromosomal: Androgen Insensitivity Syndrome

- X-linked recessive disorder
- 46,XY subjects have a normal female phenotype.
- These patients are resistant to testosterone due to a defect in the androgen receptor ---> fail to develop all of the male sexual characteristics that are dependent upon testosterone.
- The external genitalia are typically female in appearance, but testes may be palpable in the labia or inguinal area.
- At puberty, breast development occurs, but the areolae are pale and pubic and axillary hair is sparse.

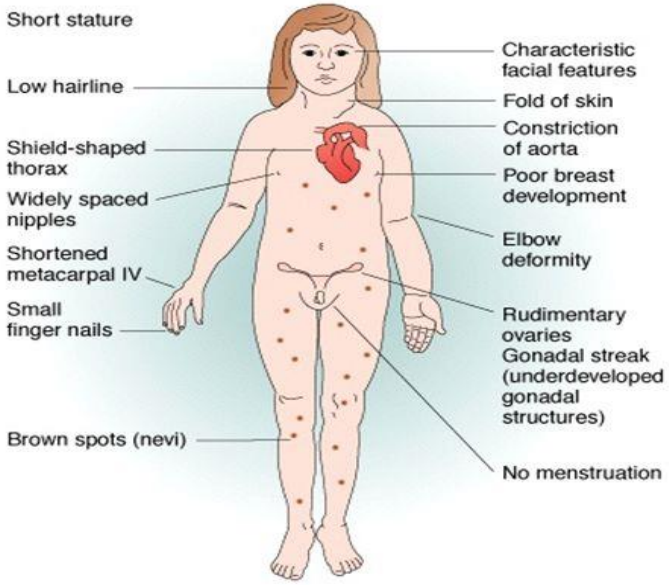
Hypothalamic Failure: Kallmann' syndrome

- Complete gonadotropin releasing hormone deficiency
- Associated with ansomnia
- Apulsatile and prepubertal low gonadotropin concentrations due to absence of GnRh

Gonadal Dysgenesis:

- Accounts for 43 %
- Turner’s syndrome =most frequent
- Complete or partial absence of the second sex chromosome
- Spontaneous puberty and menstruation occur more commonly in women with mosaic type

Turner's Syndrome



Outflow tract disorders

- 20 % of primary amenorrhea
  - Imperforate Hymen
  - Transverse vaginal septum
  - Mullerian agenesis
  - Androgen Insensitivity syndrome

Outflow Tract Disorders: Imperforate Hymen

Figure 1: Imperforate hymen

- Failure of complete canalization of vagina canal

- Presentation: Primary amenorrhea and associated cyclic abdominal pain
  - physical exam significant for abdominal swelling and bluish bulging membrane at introitus

Outflow Tract Disorder:
Mullerian Agenesis Mayer-Rokitansky-Kuster-Hauser

- Congenital absence of vaginal with variable uterine development
- Present in late teens; normal breast development
- Usually accompanied by cervical or uterine agenesis
  - 2-7% have rudimentary müllerian structures with functioning endometrium
- Associated with renal abnormalities and skeletal abnormalities

Assessment: Primary Amenorrhea

A good history and physical can direct your workup

Primary Amenorrhea: History

Timing of other stages of puberty:

- growth spurt
- Axially hair
- pubic hair
- breast development

Family history of delayed or absent puberty

Primary Amenorrhea: History

Stress

Changes in weight, diet, or exercise habits

Medications

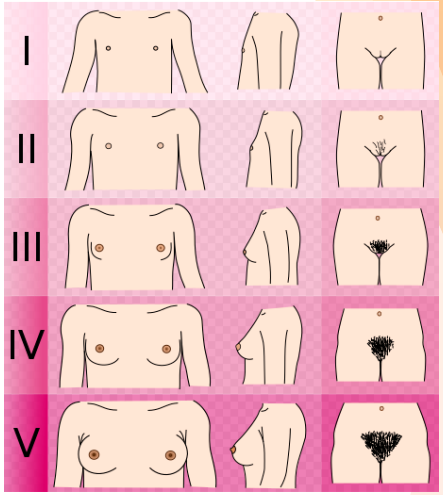
Headaches visual defects

Fatigue

Cyclic pain

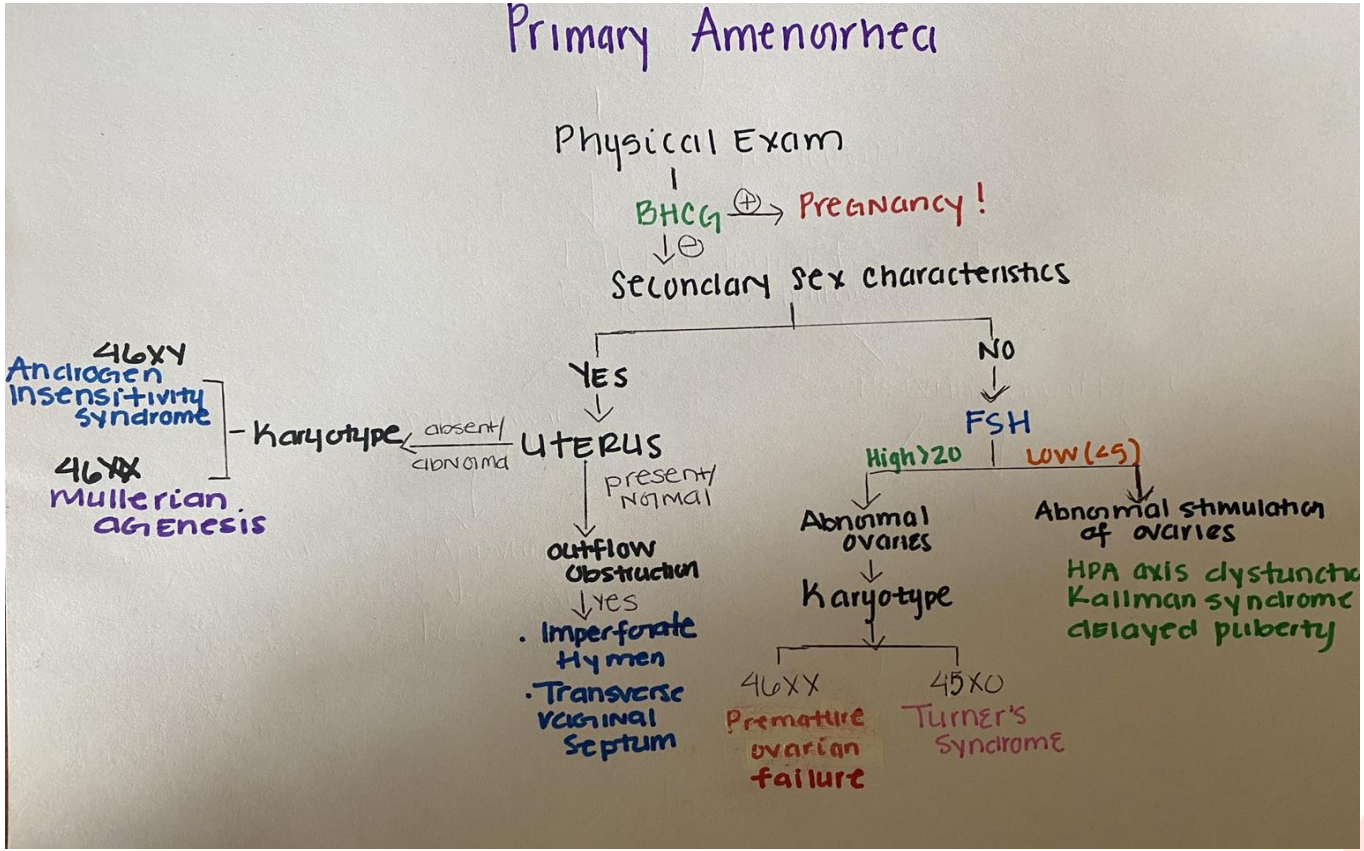
Primary Amenorrhea: Physical

- BMI
- Growth
- Secondary sex characteristics
  - Breast development
  - Axillary hair
  - Pubic hair
- Signs of hirsutism
- Pelvic exam



STAGE	BREAST	PUBIC HAIR
1 Preadolescent	Only papillae are elevated.	Vellus hair only and hair is similar to development over anterior abdominal wall (ie. no pubic hair).
2	Breast bud and papilla are elevated and a small mount is present; areola diameter is enlarged.	There is sparse growth of long, slightly pigmented, downy hair or only slightly curled hair, appearing along labia.
3	Further enlargement of breast mound; increased palpable glandular tissue.	Hair is darker, coarser, more curled, and spreads to the pubic junction.
4	Areola and papilla are elevated to form a second mound above the level of the rest of the breast.	Adult-type hair; area covered is less than that in most adults; there is no spread to the medial surface of thighs.
5 Adult	Adult mature breast; recession of areola to the mound of breast tissue, rounding of the breast mound, and projection of only the papilla are evident.	Adult-type hair with increased spread to medial surface of thighs; distribution is as an inverse triangle.

Primary Amenorrhea Evaluation



Mental break: Questions?

Case 1:

A 17-year-old female presents to the pediatrician with a concern of not yet beginning menses. Her friends in high school have already begun menses a few years ago, and this brings the patient great distress. She reports being sexually active and uses condoms consistently. She does not use any other form of contraception. She denies pelvic pain. On physical exam, there is normal breast development; however, her uterus is not palpable.

What would be your next step?

Case 2

A 16-year-old female presents to your office due to lack of menstruation. She has never had a period and is anxious that she is not “keeping up” with her friends. She states that her breasts began developing when she was 13, and she had a growth spurt around the same time. Review of systems reveals that every month, the patient experiences abdominal pain that last for 3 days but then resolves. Her vitals are stable. Both breasts are Tanner IV with no expressible discharge. Pelvic and axillary hair growth is also Tanner IV. The patient is unable to tolerate a full pelvic exam, but the part of the vaginal canal that is examined is unremarkable.

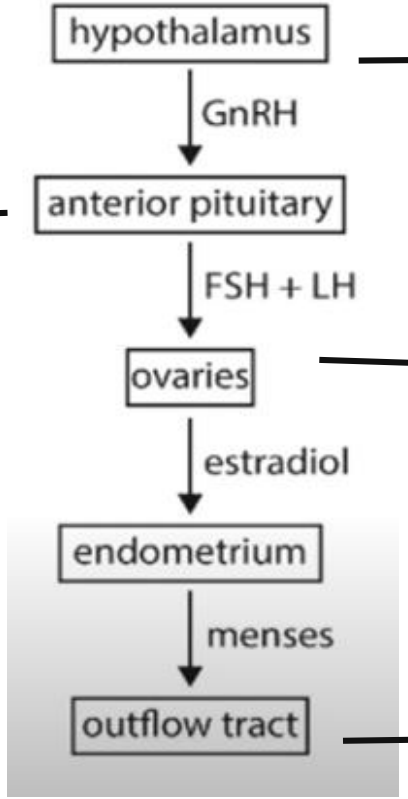
What do you believe is the cause of this patient’s amenorrhea?

2.
Secondary Amenorrhea

Absence of menses= Pregnancy

Until proven otherwise

Refresher: Menstrual Cycle



Hypothalamic dysfunction
Weight related

Pituitary Adenoma
Sheehan's syndrome
Hyperprolactinemia
Hypothyroidism

PCOS
Premature ovarian failure

Asherman's syndrome
Cervical stenosis

Secondary amenorrhea: Hypothalamic Cause

- Causes 30-35% of amenorrhea
- Often seen as a result of stress, weight loss, and eating disorders
- Need minimum of 18% body fat to have menses

Secondary Amenorrhea: Pituitary disorders

- Pituitary lesion: Prolactinoma
- Hyperprolactinemia
  - Medications: Antipsychotics, antidepressants, metoclopramide
- Sheehan’s disorder

Secondary Amenorrhea: Ovarian Insufficiency

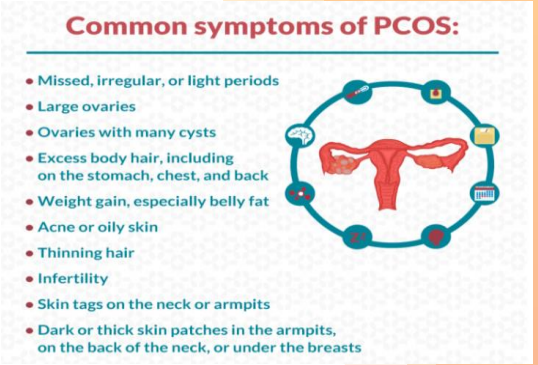
- Menopause < 40 years old
- May be secondary to chemotherapy, radiation, or Fragile X Syndrome
- May suffer from vasomotor symptoms secondary to estrogen deficiency

Secondary amenorrhea: PCOS

- Most cases are oligomenorrhea and in some cases secondary amenorrhea

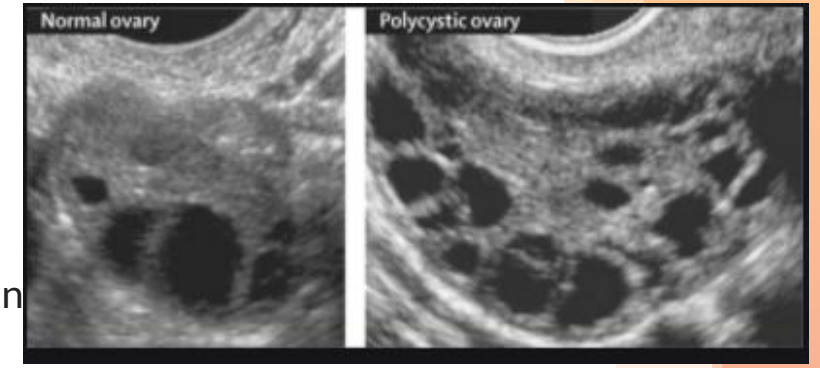
- Most common cause of oligomenorrhea

PCOS Etiology



- Alterations in GnRH pulsatility -->↑LH pulse frequency + ↓ FSH stimulation and action
- ↑↑ LH:FSH ratios
  - Ovary (theca) ->↑↑ androgen = ↑↑ testosterone and androstendione
    Aromatase = Peripheral conversion to Estrone
    - Adipose – Estrone (monocyclic) =>Uterus => Endometrial hyperplasia
    - Follicular atresia => Anovulation/Amenorrhea
    - Skin :Hirsutism, Acne, Acanthosis Nigricans
  - Will have ↑free testosterone

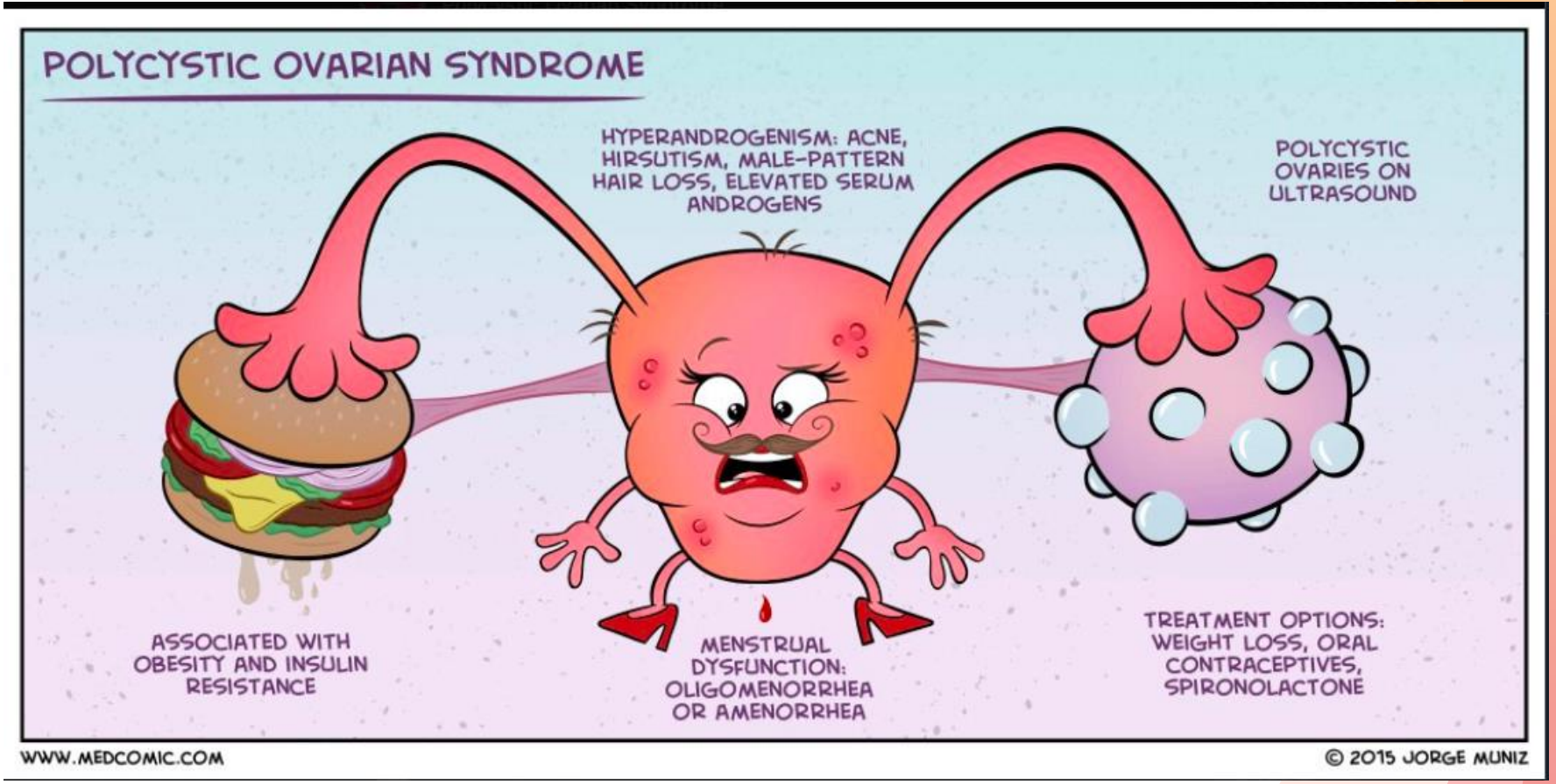
PCOS Diagnostic Criteria



- 2 out of the following 3 criteria
  - Polycystic ovaries on transvaginal ultrasoun
    - >12 follicles in each ovary
  - Clinical or biochemical evidence of hyperandrogenism
    - Clinical
      - Acne
      - Male pattern baldness
      - Hirustiums
    - Biochemical
      - Increased free testosterone, DHEAS
  - Oligomenorrhea or Amenorrhea/other signs of anovulation.

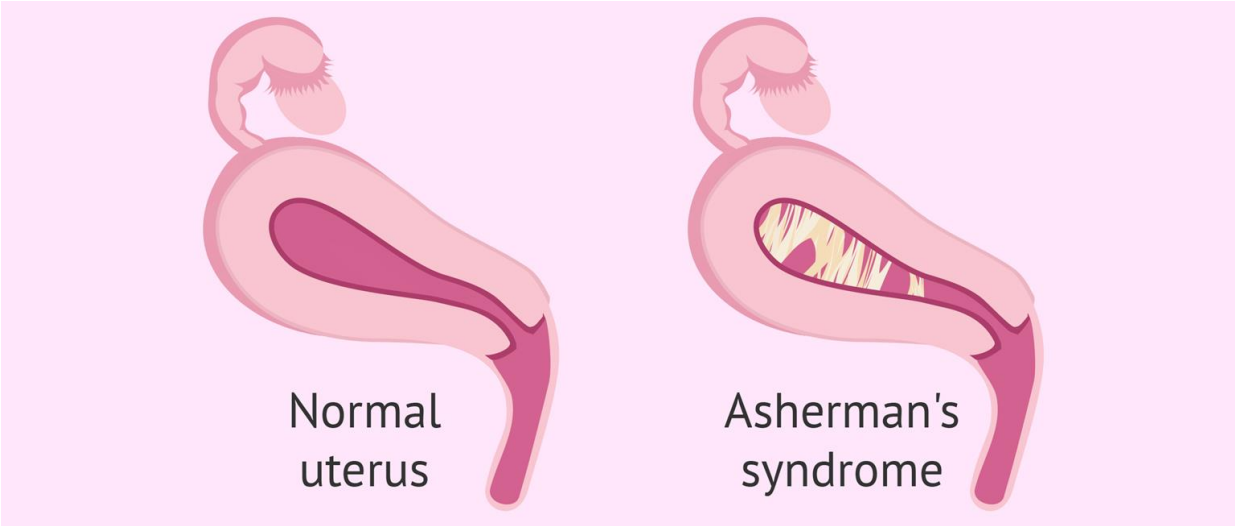
PCOS Treatment

- Restore regular cycles!
  - Purpose? Prevent endometrial hyperplasia
  - Weight reduction
    - 5-7% loss can restore spontaneous ovulation in approx. 75%
  - OCPs


POLYCYSTIC OVARIAN SYNDROME
HYPERANDROGENISM: ACNE, HIRSUTISM, MALE-PATTERN HAIR LOSS, ELEVATED SERUM ANDROGENS
POLYCYSTIC OVARIES ON ULTRASOUND
ASSOCIATED WITH OBESITY AND INSULIN RESISTANCE
MENSTRUAL DYSFUNCTION: OLIGOMENORRHEA OR AMENORRHEA
TREATMENT OPTIONS: WEIGHT LOSS, ORAL CONTRACEPTIVES, SPIRONOLACTONE
WWW.MEDCOMIC.COM
© 2015 JORGE MUNIZ

Secondary Amenorrhea: Asherman's Syndrome

-intrauterine synechiae secondary to curettage or abortive procedures



Assessment: Secondary Amenorrhea

Remember: A good history and physical is KEY

History

- Menstrual cycle
  - Age of menarche
  - Previous menstrual history
- Sexual activity
- Previous pregnancies
- Hot flashes, decreased libido
- Weight change
- Medications
  - Contraception
- Associated symptoms
  - Hypothyroidism
  - Cushing's disease
- Previous surgeries
- Chronic illness

Examination

BMI

Blood pressure

Signs of excess androgen: Hirsutism

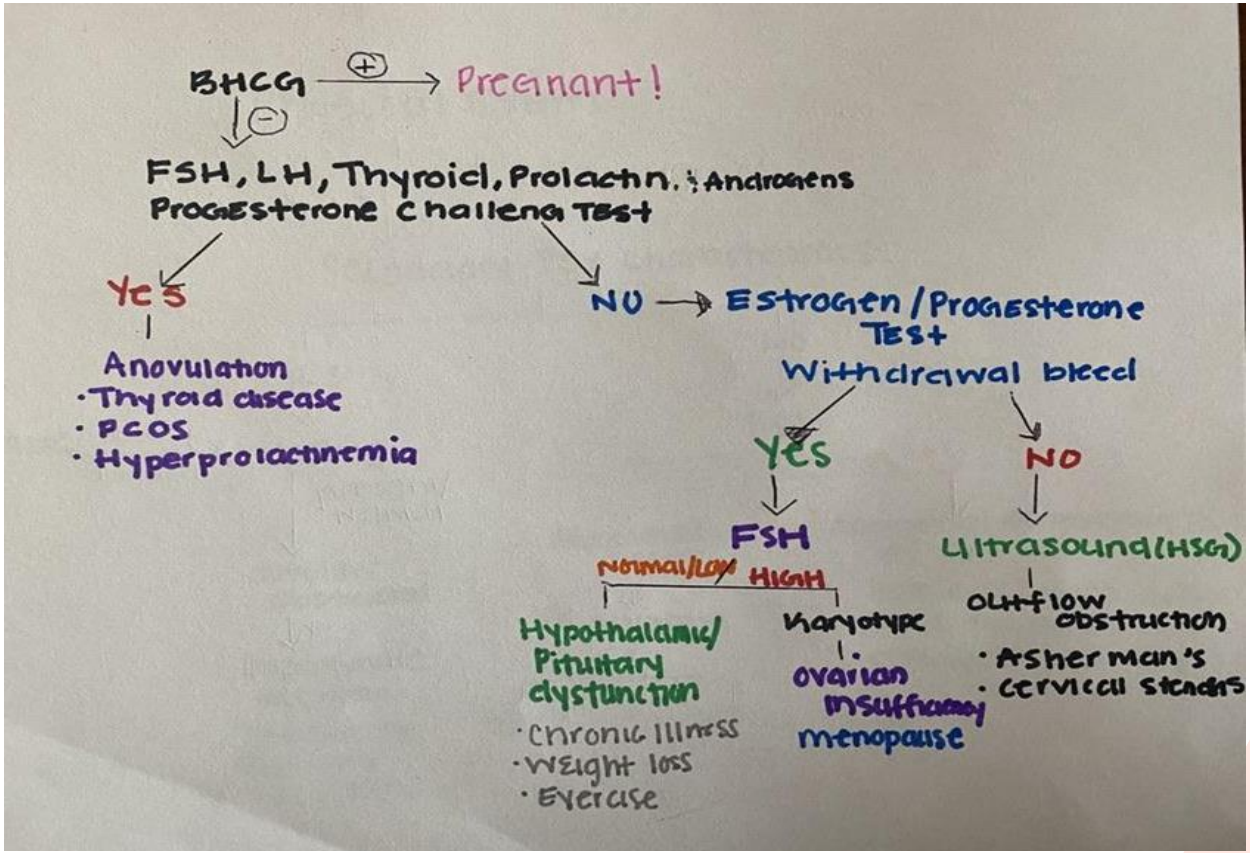
Breast examination : galactorrhea

Abdominal exam

Pelvic exam

Secondary sex characteristics

Evaluating Secondary Amenorrhea



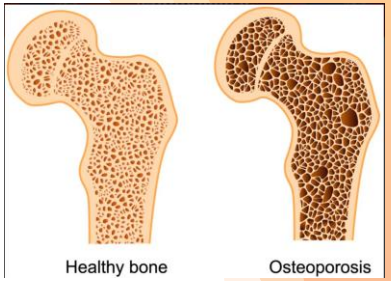
Amenorrhea Treatment

Anatomic abnormalities → Imperforate Hymen
Asherman's syndrome

Ovarian Failure → Hormonal therapy

Hypothalamic/ pituitary dysfunction → Correct underlying cause

Consequences of Amenorrhea



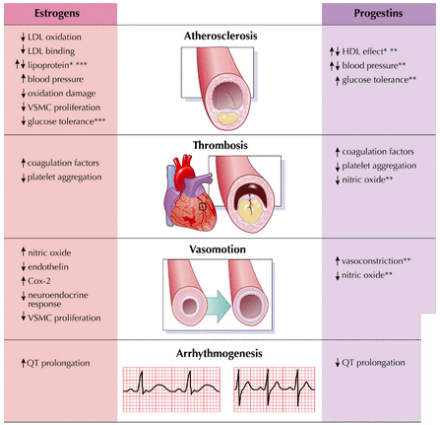
Osteoporosis

Cardiovascular disease

Endometrial cancer

Germ cell tumor

Infertility



Case 3

A 19-year-old female presents to the doctor with a concern of not have a period for 6 months.. She previously had normal menses, with menstruation starting at the age of menses at the age of 15. Patient is competitive cheerleader at Navarro college. She has multiple practices a day and aspires to perform at the national competition at the end of the year. She states that she is not sexually active. The patient emphasizes that it is important for her to maintain her weight as she can't get fat or it will affect her performance. The patient is 5 feet, 4 inches tall and weighs 100 pounds (BMI 17.2 kg/m^2). Temperature is 98.4°F (36.9°C), blood pressure is 98/59 mmHg, pulse is 98/min, and respirations are 14/min. On exam, the patient appears pale and has thinning hair. She has Tanner stage IV breasts and Tanner stage III pubic hair.

What do you believe is the cause of this patient's amenorrhea?

Case 3 continued

Your workup confirms the patient's diagnosis.

How do you go about counseling the patient?

Case 4

A 27-year-old G0 presents to your office for her annual visit. For the past 5 years she has noted irregular menses, but now she has not had a period in 7 months and wonders if this is abnormal.She has been married for the past 3 years and despite having unprotected intercourse with her husband every other day, has failed to have any children.

Physical exam reveals an obese female with, male pattern hair growth around her chin with no evidence of clitoromegaly. Her BMI is 35 and her BP is 150/102. You also noted hyperpigmented lesions under the patient's neck, breasts, and axilla

What is the likely diagnosis?

Case 5:

A 39 yo F presents with mood swings and amenorrhea for the past year. Patient reports that for the past year, she has been having severe episodes of intense sweating, irritability, and vaginal dryness .

What is most likely this patient’s diagnosis?

Case 5 continued

What labs abnormalities are you likely to see with this patient?

Case 6

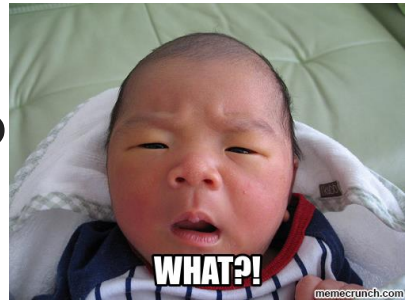
A 33 yo G2P2 female presents you office with complaints of no menses for one year. Her last pregnancy was one year ago and required an emergency c-section and was complicated by an intraoperative hemorrhage. Patient states that she lost 3L of blood and went into DIC. Afterwards recovering, she states that she did not breastfeeding secondary to postpartum depression and her milk supply did not come in .

Review of system include: Dry skin, weight gain, cold sensitivity, fatigue, decreased libido, breast shrinkage, dyspareunia,

What is the most likely diagnosis?

Thanks You!

Any questions?



You can find me at:

- tischelle.gatlin@mercy-chicago.org

References

- Polycystic ovary syndrome. ACOG Practice Bulletin No. 194. American College of Obstetricians and Gynecologists. Obstet Gynecol 2018;131:e157–71.
- Sheehan syndrome. Uptodate. Bariberi et al. March 25, 2019
- The Menstrual Cycle. Medcomic. Muniz, Jorge. https://medcomic.com/medcomic/the-menstrual-cycle/
- Polycystic Ovarian Syndrome. Medcomin, Muniz, Jorge. 2015
- Current Evaluation of Amenorrhea. ASRM. Vol 90, Suppl 3, November 2008
- Wood, Ellen, Amenorrhea. October 2016. https://www.acoog.org/web/Online/PDF/FC16/Thu/08-Wood10616.pdf. Powerpoint presentation