ARE U BLEEDING?

(ABNORMAL BLEEDING IN THE PEDIATRIC AND ADOLESCENT PATIENT)

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OBJECTIVES

Recognize a normal prepubertal external genital exam

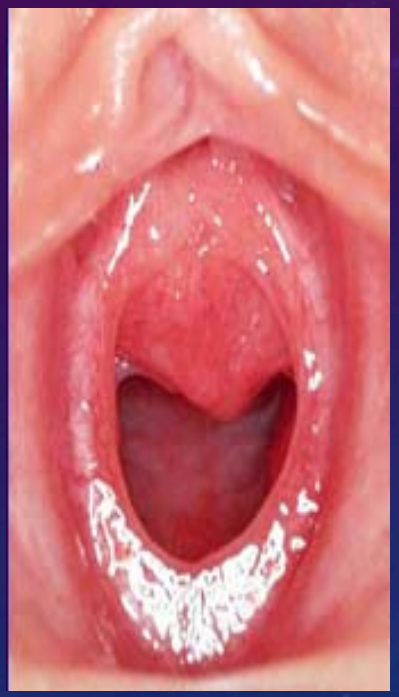
Recognize, evaluate and diagnose common causes of vaginal bleeding

- Prepubertal
- Post pubertal

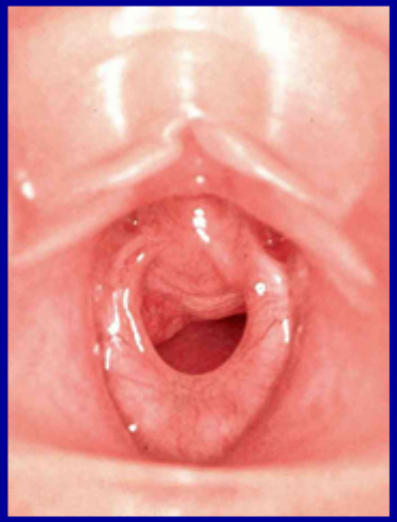
VULVOVAGINAL TISSUE CHANGES OVER TIME

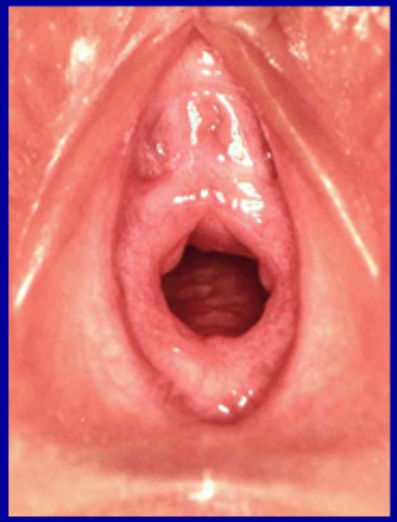
- **<u>Prepubertal exam</u>**
  - Vagina is relatively alkaline with a pH 6.5-7.5
  - Vaginal epithelium is thin
  - Hymen is highly vascularized
  - Labia minora are small, flush with the vulva
  - Labia majora lack underlying adipose tissue and hair

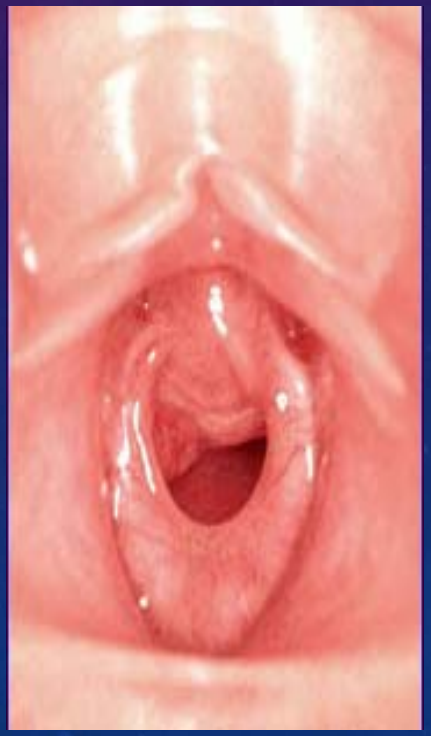
PREPUBERTAL EXAM

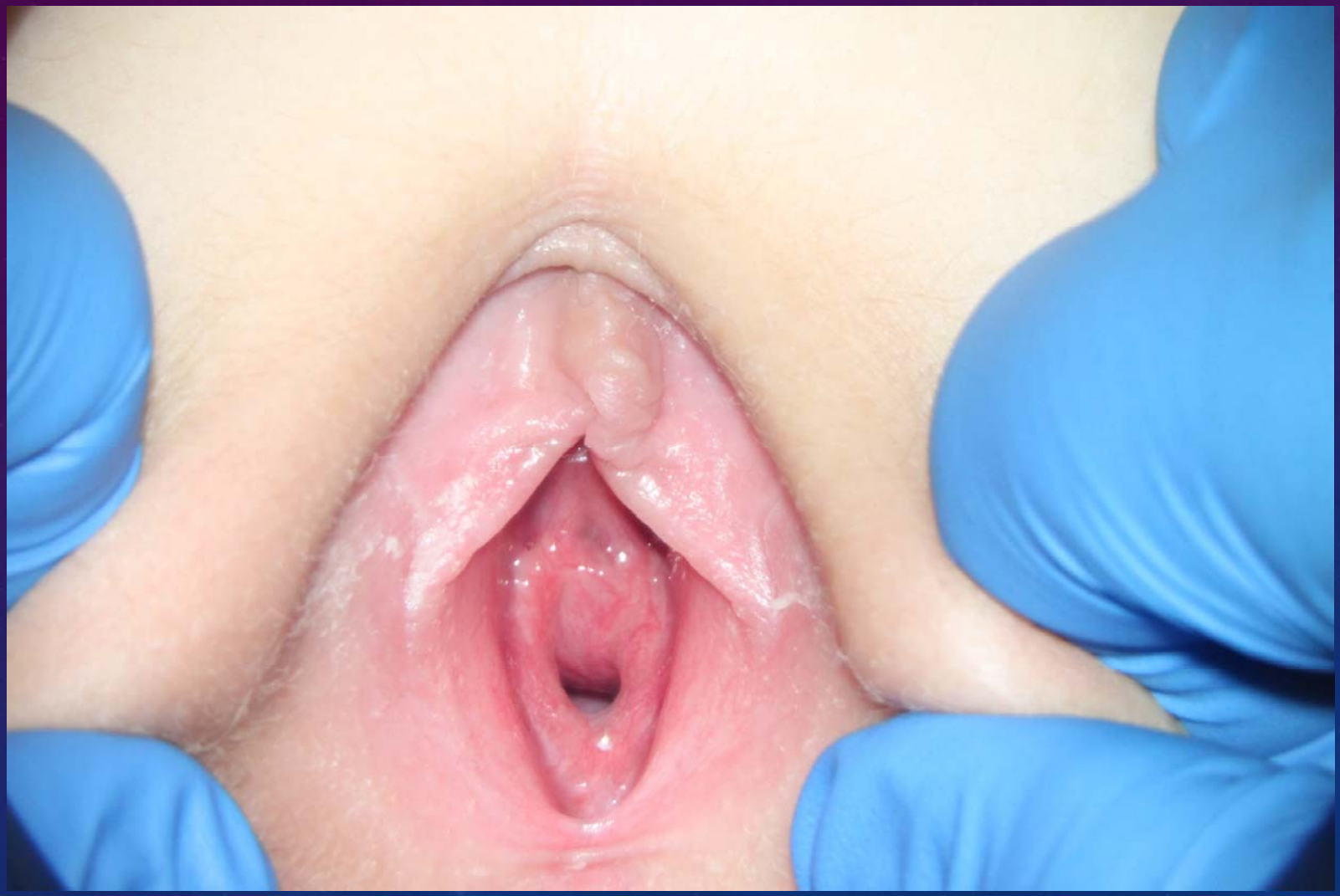


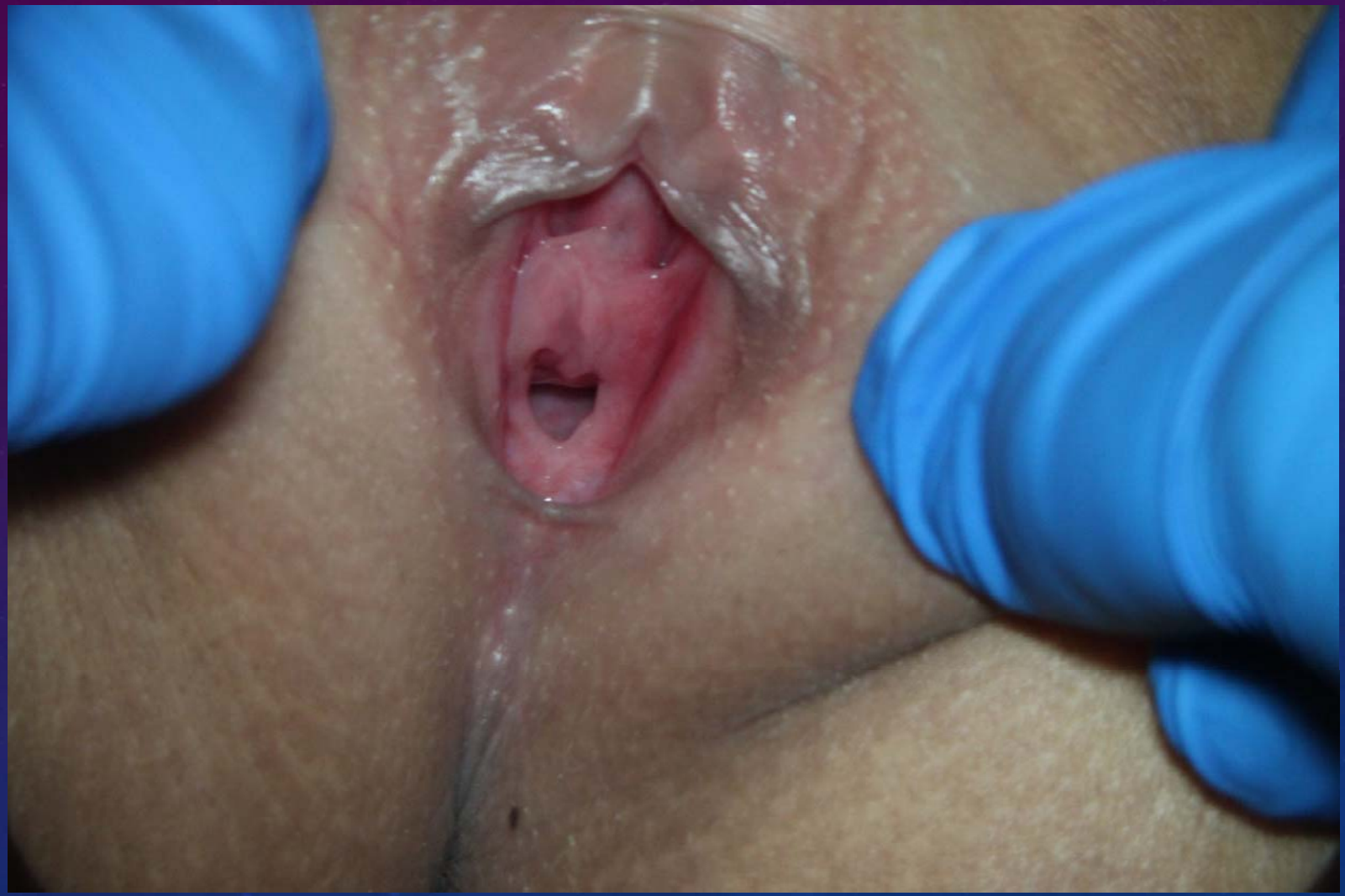
Normal variants











WHERE IS THE BLEEDING COMING FROM?

Prepubertal

-Rarely uterine in etiology unless cancer or precocious puberty

-Most etiologies can be seen externally

Post pubertal

-Same as adults

AUB
POST PUBERTAL

Normal menstrual length and interval for the adolescent ranges from 21-45 day interval and 2-7 day duration.

-Establish not pregnant

-International Federation of Gynecology and Obstetrics (FIGO) grading scale classified AUB into structural and nonstructural causes of irregular bleeding using the acronym PALM-COEIN.

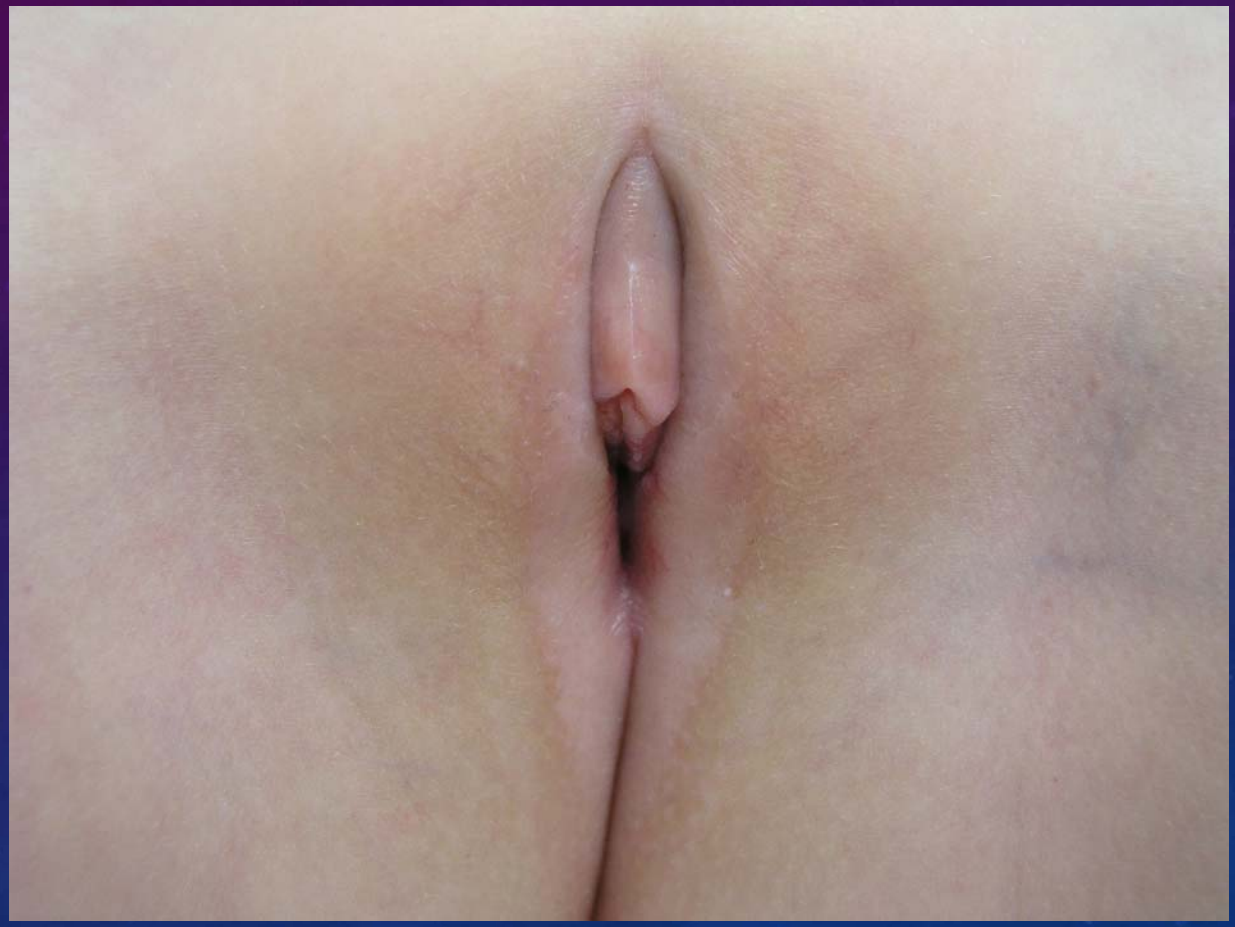
PALM (polyp, adenomyosis, leiomyoma and malignancy) refer to structural abnormalities which are uncommon with adolescents.

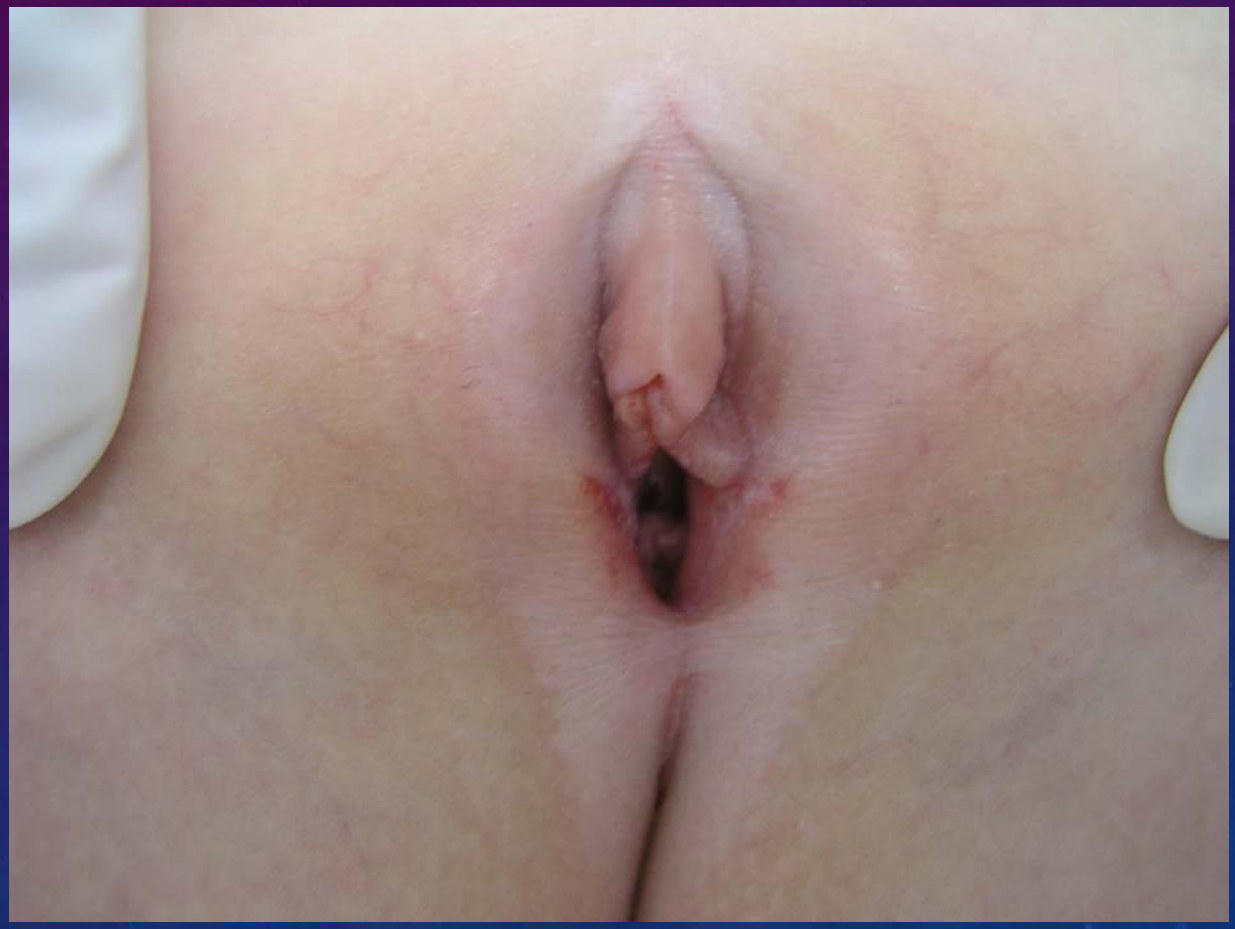
AUB-POST PUBERTAL

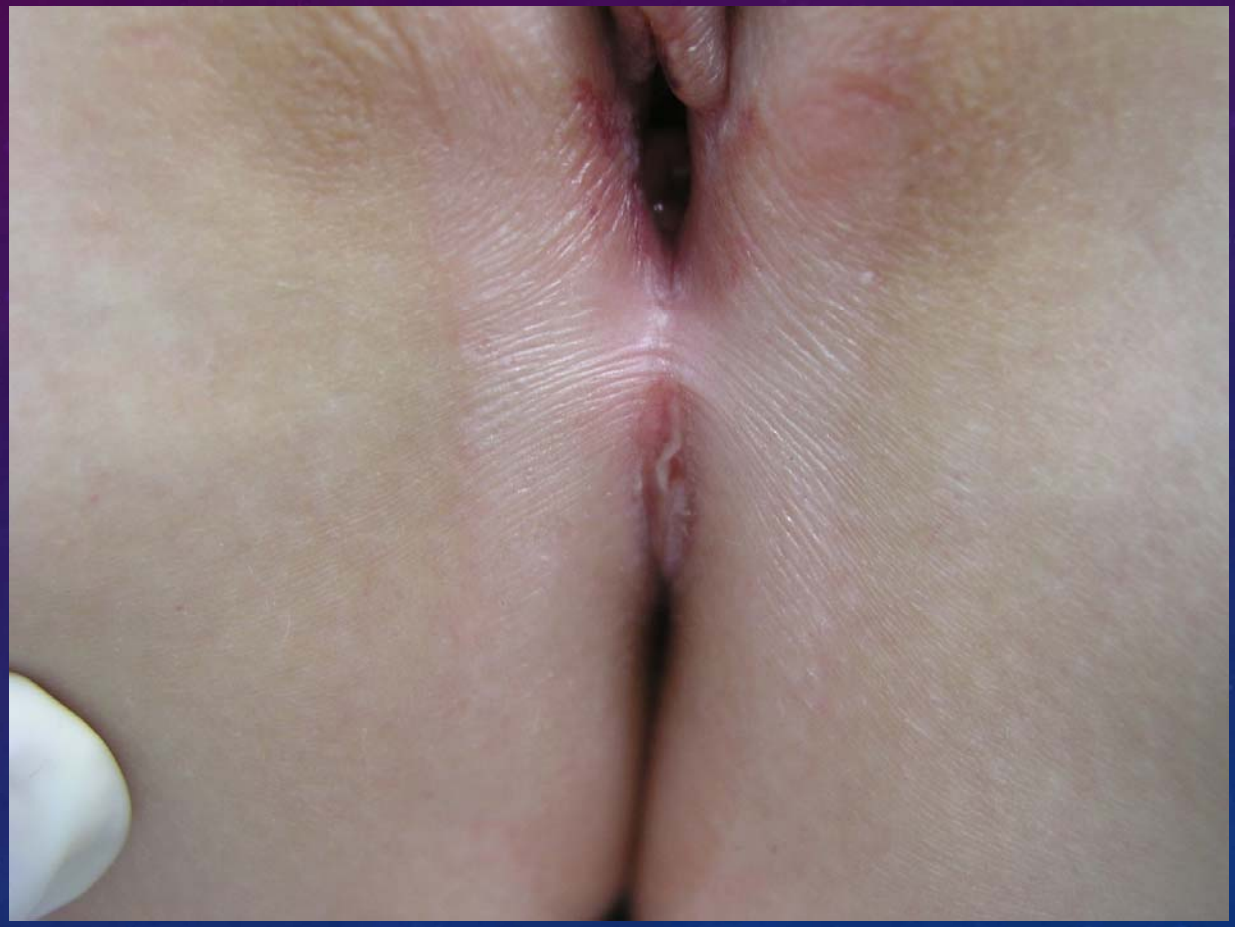
- COEIN (coagulopathy, ovulatory, endometrial, iatrogenic and not classified) are more prevalent with adolescents.
  - "C "for **coagulopathy**
    - most commonly inherited disorder encountered is Von Willebrand's Disease
    - 13% prevalence in adolescents.
    - Up to 33 % of adolescents presenting with heavy menstrual bleeding requiring transfusion will have other underlying bleeding disorders (ITP, leukemia, iron abnormalities).
  - "O" for **ovulatory** dysfunction
    - most commonly due immaturity of the HPO axis during the first 1-2 years of menstruation. Diagnosis of exclusion as laboratory values are needed to rule out other etiologies.
    - PCOS is can be etiology after the first 2 years of menarche.
  - "E" for **endometrial**
    - Endometrial disorders that are seen in the presence normal ovulation. In these instances, mechanisms affecting local endometrial hemostasis are affected. Currently there is no laboratory testing to measure such abnormalities.
  - "I" for **iatrogenic**
    - not uncommon in those patients managed with oral contraceptive pills, intrauterine devices, or other systemic medications which may interfere with gonadotropin release.
  - "N" for **not otherwise classified**
    - encompass arterio-venous malformations of the uterus.

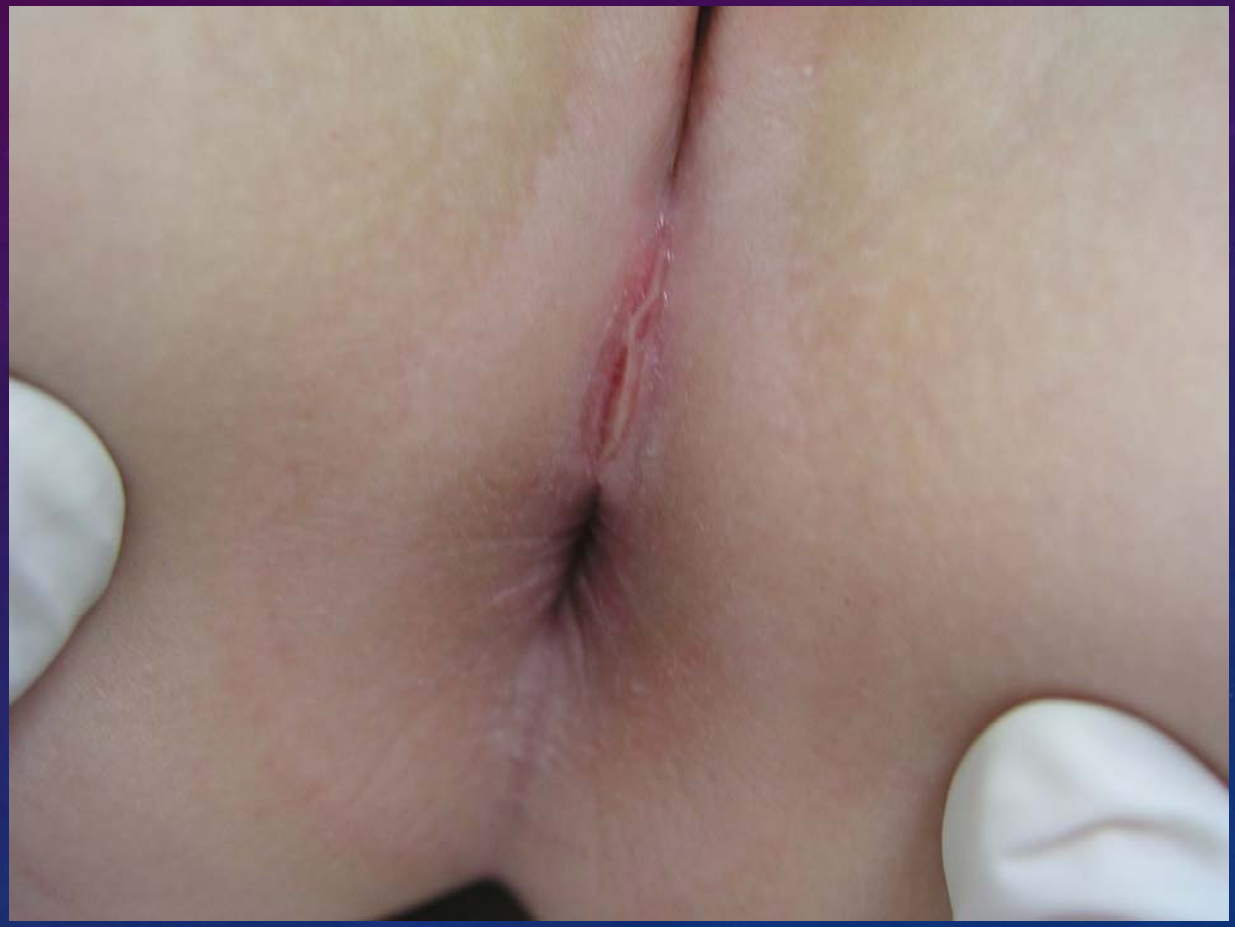
CASE 1

- 4 yr. old presents with a several month history of itching and pain in “ her privates.” She has been seen by her pediatrician and prescribed courses of topical antifungals without remission of symptoms. Now mother has noticed some blood tinge in her underwear and is concerned “something else is going on.”









DIAGNOSIS?

A: sexual assault

B: vulvo vaginitis

C: lichen sclerosus

D: urinary tract infection

LICHEN SCLEROSUS IN THE PREPUBERTAL CHILD

- Chronic inflammatory skin condition, autoimmune process
- Incidence of 1:300-1:1000, most present before age 6
- Presents with itching, irritation, bleeding, dysuria
- Dx clinically by visual inspection
  - Findings of white, atrophic, parchment-like skin
  - May also have ulceration, inflammation, and hemorrhages
  - If progresses, may lose secondary sexual characteristics
  - Figure of eight or hour glass configuration
  - Intermittent flares
- Treatment is with high potency clobetasol 0.05% ointment taper, if unresolved consider biopsy

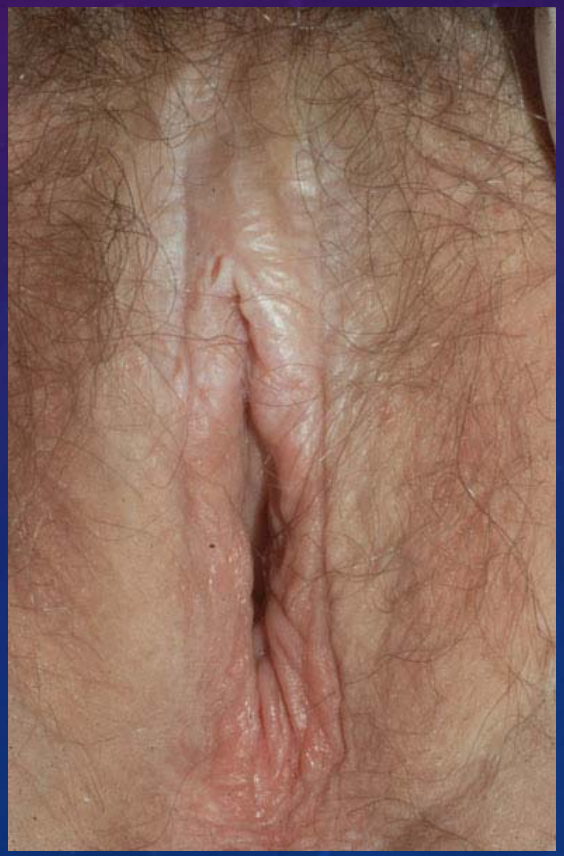
LICHEN SCLEROSUS (POSTMENOPAUSAL)

- Autoimmune disease with characteristic morphology; white with cellophane paper, crinkled, or waxy texture

- Late scarring, loss of labia minora, loss of clitoral hood

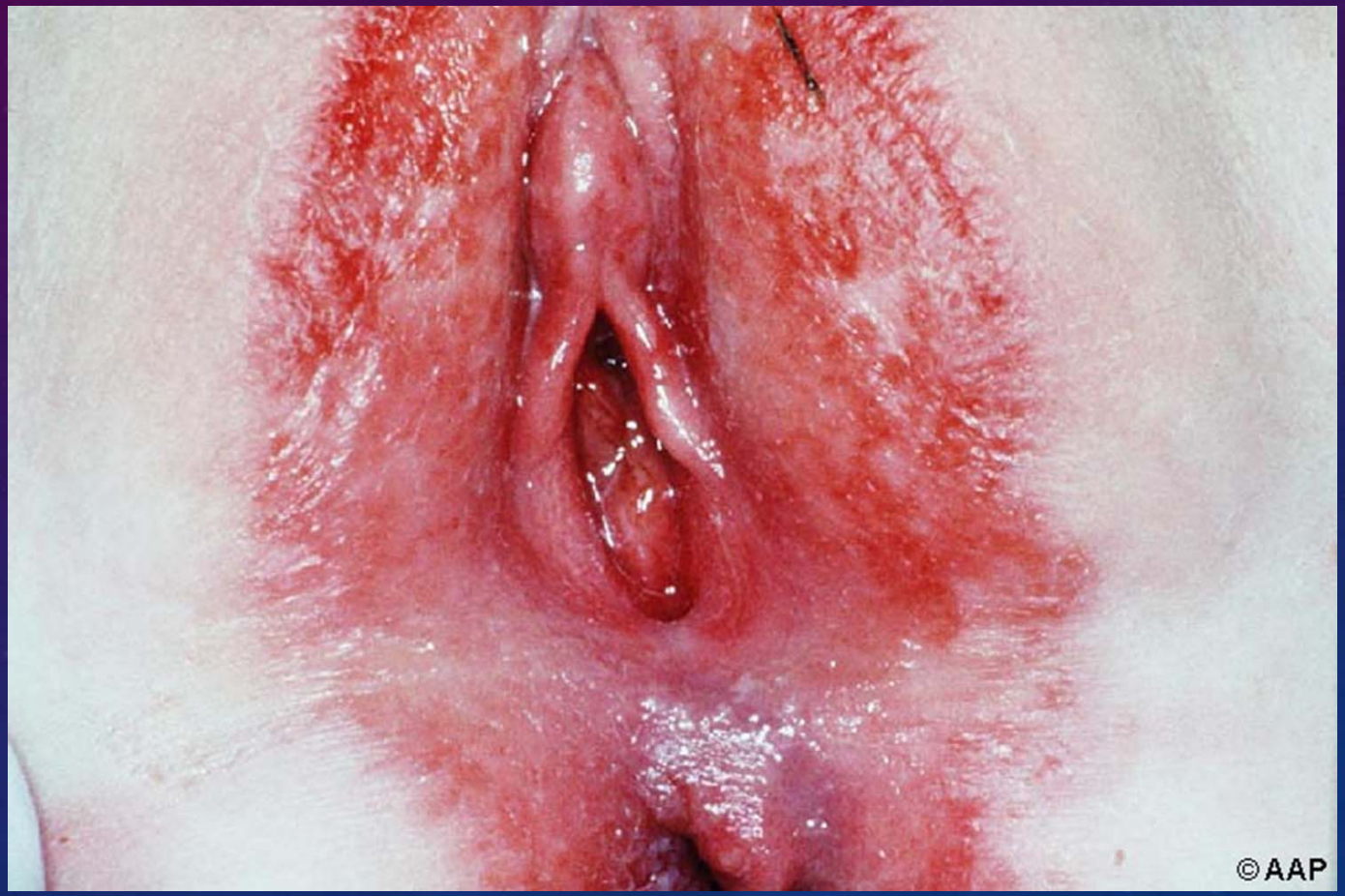
- Spares mucous membrane (vestibule, vagina, rectal mucosa)

- Can be associated with squamous cell carcinoma so continued steroid use is required, not sure if children affected will carry this risk



CASE 2

- 3 yr old presents to her pediatrician. Her guardian noticed acute bright red vaginal bleeding after spending the weekend with her father. Her parents are divorced and share custody. She complains of pain with urination as well.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DIAGNOSIS?

A: non specific vulvovaginitis

B: urinary tract infection

C: sexual trauma

D: bacterial vaginitis

GROUP A BETA-HEMOLYTIC STREPTOCOCCI IN THE PREPUBERTAL CHILD

- Mean age of onset 4.24 years
- Incidence of 1:218-1:2000,
- Well defined, tender lesions
- Beefy red, inflamed appearance
- May present with vaginal bleeding
- Treatment is with first generation cephalosporin

CASE 3

15-year-old presents with complaints of "irregular cycles." She reports her periods have never "been regular" and she "never knows when they are coming." Menarche was age 12. Intervals are every 2–3 months and periods last approximately 1-2 weeks. She denies any heavy bleeding or passing clots. When you speak with her in confidence, she reports she is sexually active and uses condoms regularly. She denies changes in voice, weight, skin pigmentation, vision or bowel movements. Her review of systems is positive for cystic acne and increased hair growth on her abdomen, denies chest or gluteal hair growth.

MORE INFORMATION...

- Physical Exam:
- BP 115/76, HR 70, weight 115 lbs, height 64 inches
- HEENT: scarring from acne noted along cheeks and chin line, excessive chin hair growth, no thyromegaly
- Chest: no male pattern hair growth noted
- Abdomen: shaved pattern noted in a diamond shape from umbilicus to suprapubic bone
- Pelvic exam: normal external female genitalia w/o clitoromegaly, patent appearing hymen, extremely apprehensive about internal examination but does allow cotton swab applicator with gel to pass to 7 cm length. No discharge noted or pain on examination

WANT ANYTHING ELSE?
OR CAN YOU DIAGNOSE?

OK SOME LABS….

Laboratory evaluation:

HCG negative

TSH normal

PRL normal

Random blood glucose normal

Free testosterone/Total testosterone
High/normal range for age

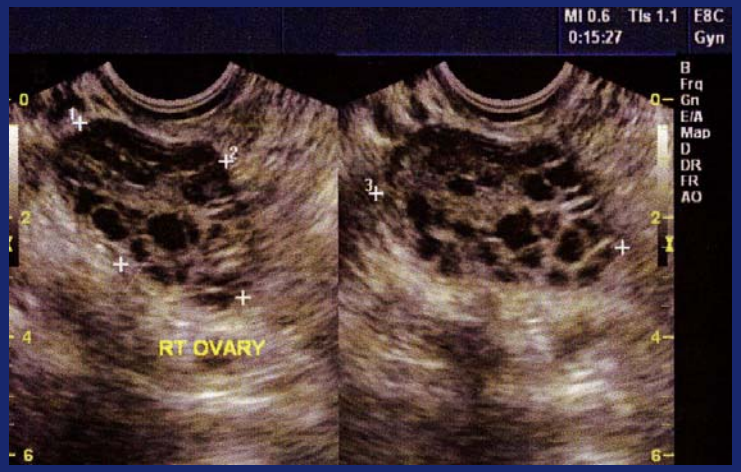
DHEAS normal

Androstenedione normal

17 OHP normal

DIAGNOSIS?

- A: polycystic ovarian syndrome
- B: virializing tumor
- C: cystic acne
- D: hirsutism



WHICH OF THE FOLLOWING IS TRUE ABOUT THE DIAGNOSTIC CRITERIA FOR PCOS IN THE ADOLESCENT?

A: DIAGNOSIS OF PCOS CAN BE MADE WITHIN FIRST 2 YEARS POST MENARCHE

B: ADOLESCENTS MUST HAVE POLYCYSTIC OVARIES ON ULTRASOUND EXAMINATION TO BE GIVEN A DIAGNOSIS OF PCOS.

C: CRITERIA INCLUDE IRREGULAR PERIODS PLUS CLINICAL OR LABORATORY EVIDENCE OF HYPERANDROGENISM.

D: MILD NONCYSTIC ACNE RESPONDING TO TOPICAL TREATMENT IS A CRITERION FOR HYPERANDROGENISM.

AUB-O

Evaluation for irregular periods should be initiated when menstrual irregularities persist 2 years post menarche and/or when girls have had amenorrhea for at least 12 weeks.

Obesity, insulin resistance/impaired glucose tolerance and hyperinsulinemia are not part of the diagnostic criteria for PCOS although they may often be present in overweight girls with PCOS.

Rotterdam Criteria are often used to diagnosis PCOS in adolescents.

These criteria include irregular periods PLUS clinical or laboratory evidence of hyperandrogenism.

- Clinical hyperandrogenism is diagnosed when an adolescent has moderate/severe hirsutism, and /or inflammatory acne nonresponsive to topical dermatologic therapy.
- Biochemical hyperandrogenism is based on serum androgens, though again, can vary during early puberty.

TREATMENT FOR PCOS IN ADOLESCENTS

Tailored to the patient's needs and concerning symptoms.

If sexually active, consider and oral contraceptive pill that targets her hyperandrogen symptoms and provide contraception.

Monotherapy is recommended for 6 months before adding additional agents.

Adherence in this group can be challenging. Consideration of a progestin containing LARC to provide contraception and decrease risk of endometrial hyperplasia can improve compliance, These patients may need additional medication, like spironolactone and/or OCP, to target hyperandrogen symptoms.

For those with impaired glucose tolerance as indicated by an elevated HbA1C and/or abnormal glucose tolerance test, addition of metformin may be considered in addition to lifestyle modification.

WHAT WOULD BE THE INITIAL MOST APPROPRIATE TREATMENT OPTION FOR THIS PATIENT?

- A: Lifestyle modification and exercise
- B: Combined oral contraceptives
- C: Spironolactone
- D: Metformin

Level of activity	Androgenic generic name(s)
High	Norgestrel (Cryselle, Lo-ovral)
	Levonorgestrel (Altavera)
Middle	Norethindrone (Loestrin)
	Norethindrone acetate
Low	Ethynodiol
	Norgestimate (Ortho products)
	Desogestrel (Desogen)
	Drospirenone (Yaz, Yasmin)
	Dienogest

CASE 4

- Lucy is a 13-year-old female who presents with prolonged periods. She had menarche 1 year ago and has had 4 periods since menarche. Previously, periods have lasted anywhere from 5-14 days and have been painless. However, this current period started 35 days ago and now she is having some cramping. The bleeding was initially heavy and then lightened over the last week until 2 days ago when it became much heavier. Lucy now reports having to change her pad every 2 to 3 hours. Mom also reports she passed a blood clot when she used the restroom this morning. Her review of systems is otherwise negative for any changes in weight, appetite or other systemic symptoms. She has no personal history of easy bruising, nose bleeds or gum bleeding.

MORE INFO…

- On exam her vital signs are within normal limits. Her physical examination is unremarkable, and her genitourinary examination shows normal external female genitalia at Tanner Stage V.
  Urine pregnancy test negative.

WHAT WOULD BE THE MOST APPROPRIATE NEXT STEP IN MANAGEMENT FOR THIS PATIENT?

A: Pelvic ultrasonography

B: Complete blood count (CBC) and TSH

C : Follicle stimulating hormone (FSH)

D: STI screening

WHY?

Given the duration of her bleeding symptoms a CBC and TSH would be next most appropriate lab test. Assesses acute anemia and evaluates other cell lines ruling out other processes which can cause heavy menstrual bleeding (for example ITP or new onset leukemia). Also given that many adolescents do not present with classical signs of hypothyroidism, a TSH can rule out underlying endocrinopathy….

Hb 13.8, normal differential and TSH 1.72

WHY NOT THE OTHER STUDIES?

Given the rarity of structural causes of prolonged menses in adolescents, an ultrasound would not be an appropriate next step.

Checking gonadotropin levels are useful if there is concern for premature ovarian insufficiency or delayed puberty but not in this patient with prolonged menstruation.

STI screening may be useful if concerned for exposure and illicit a cause AUB due to chronic endometritis. Seeing as she is not sexually active would not be necessary as initial evaluation.

FINAL DIAGNOSIS?

A: Abnormal Uterine Bleeding (AUB) –O (Ovulatory)

B: AUB – M

C: AUB –C

D: AUB-L

AUB-O

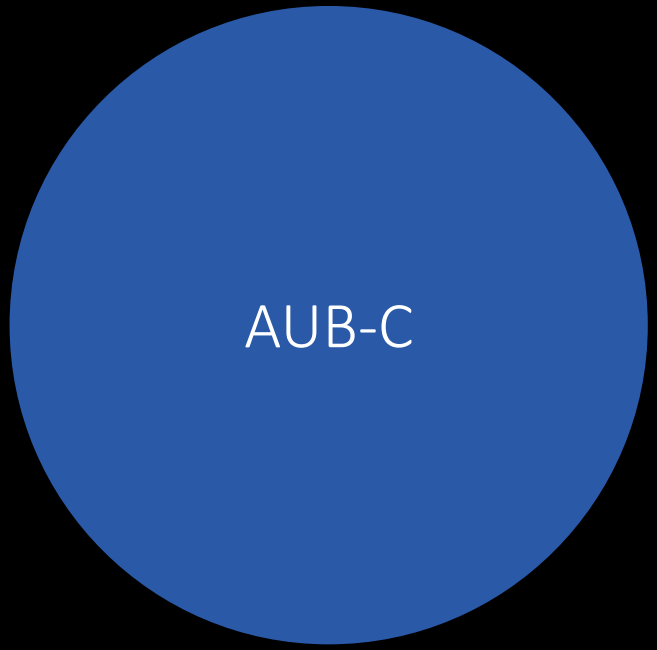
AUB-O is abnormal vaginal bleeding caused by anovulation.

Most commonly caused by immaturity of the hypothalamic pituitary ovarian axis, hence subsequent anovulatory cycles.

Adolescents may have irregular periods for the first 1 to 2 years following menarche.

These patients respond well to either cyclic progestin to stabilize the endometrium or combined oral contraceptive pills.

In any patient who presents with prolonged periods it is important through history and laboratory evaluation to rule out an underlying bleeding disorder.



- Lets say last patient and hemoglobin 4.2 and positive orthostatic

AUB-C

Assessment of hemodynamic status is most prudent.

In adolescents, a low threshold for coagulopathy evaluation with CBC, activated partial thromboplastin time and partial thromboplastin time (aPTT/PTT), prothrombin time, VWD screening, thyroid and prolactin screening should be on the fore front of evaluation.

Screening studies for bleeding disorders are most accurate prior to transfusion if possible.

Of note, exogenous estrogens do not elevate VWF and can be obtained at initial presentation if on hormonal suppression.

VWB screening includes von Willebrand factor antigen, von Willebrand factor activity (risocetin cofactor activity) and Factor VIII activity.

ACUTE HMB

- Treatment
  - Known bleeding disorder?
  - Unknown if has bleeding disorder?

Box 1. Clinical Screening for an Underlying Disorder of Hemostasis in the Patient With Excessive Menstrual Bleeding

Initial screening for an underlying disorder of hemostasis in patients with excessive menstrual bleeding should be structured by the medical history. A positive screening result* comprises the following circumstances:

- Heavy menstrual bleeding since menarche
- One of the following conditions:
  - —Postpartum hemorrhage
  - —Surgery-related bleeding
  - —Bleeding associated with dental work
- Two or more of the following conditions:
  - —Bruising, one to two times per month
  - —Epistaxis, one to two times per month
  - —Frequent gum bleeding
  - —Family history of bleeding symptoms

*Patients with a positive screening result should be considered for further evaluation, including consultation with a hematologist and testing for von Willebrand factor and ristocetin cofactor.

Modified from Kouides PA, Conard J, Peyvandi F, Lukes A, Kadir R. Hemostasis and menstruation: appropriate investigation for underlying disorders of hemostasis in women with excessive menstrual bleeding. Fertil Steril 2005;84:1345–51. [PubMed] [Full Text]

AUB-C

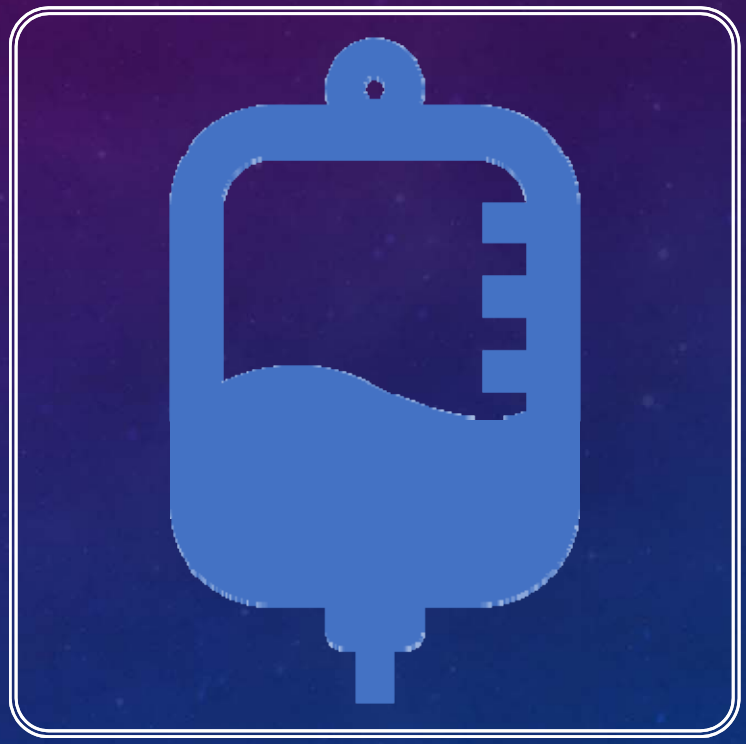
- Patients with a positive screening result should be considered for further evaluation
- Adolescents with heavy menses since menarche who present with acute AUB should undergo testing for von Willebrand disease

TREATMENT

- In patients WITHOUT known or suspected bleeding disorders:
  - **Hormonal therapy is first line**
    - Options include IV conjugated equine estrogen, combined estrogen-progestin contraceptives (OC) and progestins
  - **Consider antifibrinolytic agents**
    - Tranexemic acid
      - 1300mg orally three times a day for up to 5 days
      - IV dose if unable to tolerate oral: 10mg/kg every 8 hr
      - Avoid in patients with increased risks for thromboembolism
    - Alternative therapy: Aminocaproic acid orally or intravenously
      - Avoid in patients with renal impairment
  - **Consider balloon tamponade**
    - May provide a temporary measure to limit bleeding while further investigations are ongoing
  - **Dilation and curettage and other surgical procedures is rarely required in adolescents**

TREATMENT

- In patients WITH known or suspected bleeding disorders:
  - As described in previous slide but with special consideration
  - Measures to control uterine bleeding should be implemented while correcting deficiencies of clotting factors or abnormalities of platelet number or function
  - Heme consult
  - Choose treatment option depending on etiology



RECAP

Pre pubertal bleeding

- Usually external etiologies

Post pubertal AUB

- Use PALM COEIN
- Usually ovulatory causes