

OBSTETRICS AND GYNECOLOGY

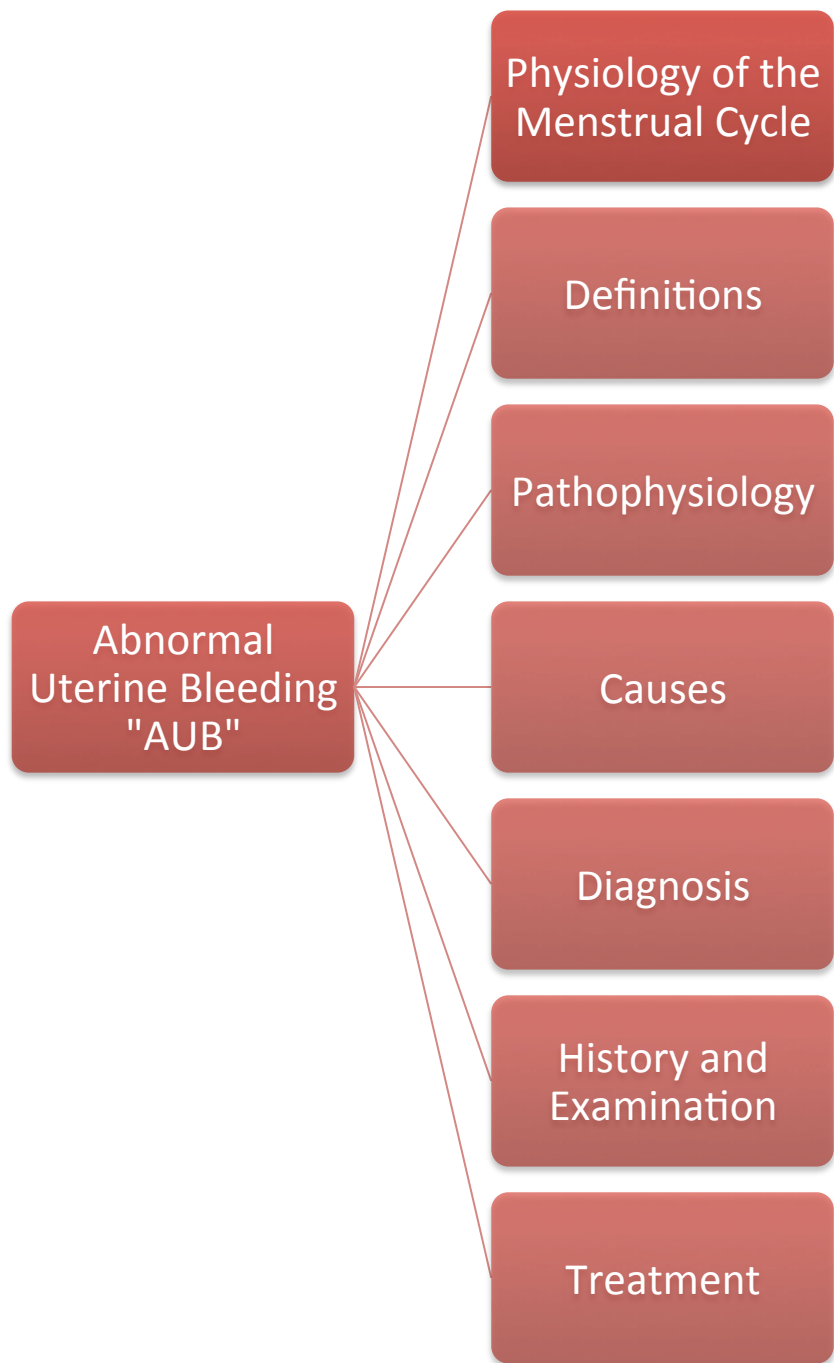
(22) Abnormal uterine bleeding

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Physiology of the Menstrual Cycle

Events of the menstrual cycle ⁽¹⁾

1. Follicular or proliferative phase. The follicular phase occurs from day 0 until day 14. During this period, a primordial follicle develops into a graafian follicle, and neighboring follicles become atretic (degenerate or regress). The remaining follicle is called the **dominant follicle**. Gonadotropins stimulate the synthesis of estradiol; thus the follicular phase is dominated by **17 β -estradiol, which cause proliferation of the endometrial lining.**

2. Ovulation. Ovulation occurs on day 14 of a 28-day menstrual cycle prior to menses, regardless of the cycle length. The burst of estradiol has a positive feedback on follicular stimulating hormone “**FSH**” and luteinizing hormone “**LH**” secretion by the anterior pituitary. **The FSH and LH surge cause ovulation of the mature ovum.** At ovulation, the cervical mucus become watery and more penetrable by sperm. Estradiol levels decrease just after ovulation, but will increase again during the luteal phase.

3. Luteal or secretory phase. The luteal phase occurs from days 14 to 28, ending with the onset of menses. During the luteal phase, the corpus luteum develops and begins synthesizing estradiol and progesterone. The high levels of progesterone stimulate secretory activity of the endometrium and its vascularity. Thus in the follicular phase, estradiol causes the endometrium to proliferate; in the luteal phase, progesterone is preparing the endometrium to receive a fertilized ovum. **Basal body temperature increases during the luteal phase because progesterone increases the hypothalamic temperature set-point.**

4. Menses. If there is no fertilization, the corpus luteum will regress, the the levels of progesterone and estradiol will drop, which will slough the endometrial lining and menses will start. During this time, primordial follicles for the next cycle are being recruited and are beginning to develop.

- In the first 10 days of the menstrual cycle, the low concentration of estrogen increases the secretion of FSH and decreases the secretion of LH.

- After the first 10 days, the increasing levels of estrogen will increase the secretion of LH and decrease the secretion of FSH.

- Progesterone prevents the release of GnRH and stimulates the endometrium growth.

- Check this video: https://www.youtube.com/watch?v=2_owp8kNMus

Some definitions and Facts

- Normal duration of menstrual cycle is (28 to 35) days, but it might be shorter or longer in some girls and it is considered to be normal.
- Ovulation time= 2 weeks + expected day of period.
- The luteal phase is always fixed (2 weeks after ovulation), the changes are in the follicular phase.
- Intermenstrual bleeding: between periods.

To say this is a normal cycle you need to ask about these parameters: 1) Duration of the flow 2) Amount of the blood loss “In clinical setting it is a descriptive variable either heavy or light” 3) Pattern “Regular vs irregular

It is normally 29 days +/- a week.

Abnormal uterine bleeding: General definition	Is change in the frequency of menses, the duration of flow (>7days), and the amount of blood loss (>80ml).
Menorrhagia:	Is heavy or prolonged, but regular bleeding.
Metrorrhagia:	Is irregular bleeding, intermenstrual bleeding, spotting , or breakthrough bleeding
Menometrorrhagia:	is prolonged bleeding at irregular intervals
Polymenorrhea:	Is menstrual interval <21 days .
Oligomenorrhea:	is menstrual interval >35 days .
Dysfunctional Uterine Bleeding: (idiopathic)	is excessive uterine bleeding with no demonstrable organic cause ; most often endocrinologic in origin.

Pathophysiology (2)(3)

- **Pregnancy:** in a patient who has abnormal uterine bleeding during the reproductive age group, pregnancy or a complication must first be considered. Complications of early pregnancy include incomplete abortion, threatened abortion, ectopic pregnancy or hydatidiform mole.
- **Anatomic lesion:** like sub-mucous myomas (fibroids) or endometrial polyps. If the pregnancy test was negative, then an anatomic cause of vaginal bleeding should be considered. **The classic history is that of unpredictable bleeding (without cramping) occurring between normal, predictable menstrual periods (with cramping).**
- **Inherited coagulopathy:** should be considered in the adolescent age group, specially if there are other bleeding symptoms including epistaxis, gingival bleeding, and ecchymoses, with a significant family history. **Von Willebrand's disease is the most common hereditary coagulation abnormality.**
- **Dysfunctional uterine bleeding (DUB):** is defined as abnormal uterine bleeding in women between menarche and menopause that cannot be attributed to medications, blood dyscrasias, systemic diseases, trauma, uterine neoplasms, or pregnancy. **It mostly caused by aberrations in the hypothalamic-pituitary-ovarian hormonal axis resulting in anovulation "unopposed estrogen". The classic history is that of bleeding that is unpredictable in amount, duration, and frequency without cramping occurring.**

During the perimenopausal years, the anovulatory bleeding is mainly caused by the declining capacity of the ovary. In adolescences, the anovulatory bleeding may be caused by a failure of the hypothalamic-pituitary system to respond to the positive feedback effects of estrogen.

Adenomyosis is endometrial tissue growing inside the muscular layer of the uterus, you should differentiate it from endometriosis, which is endometrial tissue outside the uterus.

Diagnosis (2)(3)

- **Pregnancy:** serum or urine β -hCG is required to confirm pregnancy. If it was positive, do vaginal ultrasound to assess any complication.
- **Anatomic lesion:** to exclude lower genital tract lesions do pelvic and speculum exam, and to exclude upper genital tract lesions do saline sonogram, endometrial biopsy, or hysteroscopy.
- **Inherited coagulopathy:** family history, systemic review, complete blood count "CBC", platelet count, PT and aPTT and vWF antigen.
- **DUB:** anovulatory cycles can be usually diagnosed from a history of irregular, unpredictable bleeding without cramping, **since there is no prostaglandin release to cause myometrial contractions. Basal body temperature (BBT) chart will not show a midcycle temperature rise due to the absence of the thermogenic effect of progesterone.** Endometrial biopsy will show a proliferative endometrium.

So, two investigations are most useful for confirming DUB: **a pelvic ultrasound and endometrial biopsy.**

Correctable causes of anovulation: Hypothyroidism (high TSH, treated with thyroid replacement), and Hyperprolactinemia.

- Endometrial thickness is pathological in postmenopausal women, because there might be an unknown source of estrogen.
- It is better to do US after the menstrual period to assess the endometrial thickness.
- Polyps are best diagnosed with HSG but it is time consuming so we do hysteroscopy, US is not accurate.
- If you are planning to do histopathology, don't give the patient hormonal therapy before taking the biopsy.
- Postmenopausal woman + uterine bleeding = do biopsy for every patient to exclude malignancy.
- Young female (premenopausal) with menstrual irregularities and/or anovulation = do biopsy after considering other risk factors.
- Indications for endometrial biopsy in AUB:
 - 1-Every post menopausal woman who is bleeding
 - 2-Women who are older than 40 with Irregular bleeding
 - 3-Women who are younger than 40 but who have high risk for endometrial cancer (ex. PCOS)

History and Examination:

1- Suggestive symptoms of heavy bleeding:

- Pads (number of pads/day, using maxi size, using 2 together (diapers)).
- Presence of clots, soaking clothes and /or on bed.
- Symptoms of anemia.

2- Bleeding pattern:

- Regularity.
- Postcoital bleeding (bleeding after intercourse)
- Intermenstrual bleeding (between cycles).

3- Other symptoms:

- Dysmenorrhea
- Chronic abdominal pain
- Symptoms of hyperandrogenism, hyperprolactenemia, hypothyroidism

4- Past medical history:

- Bleeding tendency (coagulopathy).
- Medication history (anticoagulant drugs).

5- Vital signs

6- Weight, height and BMI

7- General exam: signs of anemia or hirsutism

8- Thyroid examination

9- Abdominal exam (masses, scars and tenderness)

10- Pelvic exam: using speculum to look for masses uterine size, and bimanual for tenderness.

11- Pap smear and endometrial biopsy

Treatment Modalities:

Treatment of DUB:

Medical treatment:

1-Hormonal estrogens, progestins (systemic or Progesterone releasing IUCD), or combined OCs.

2-NSAIDs (esp. in ovulatory DUB).

3-Antifibrinolytic agents.to prevent bleeding

4-Low-dose Danazol.

5-GnRH agonists.

Surgical:

1-D & C (not permanent treatment)

2-endometrial ablation (burning the uterus)

3-hysterectomy

Treatment of uterine fibroid:

Medical:

-same as DUB

UAE uterine artery embolization

Surgical:

-myomectomy

(laparoscopy hysteroscopy or laparotomy)

-hysterectomy

Always remember:

- 1-stabilize the patient first
- 2-get IV access
- 3-blood group and x-match
- 4-treat anemia

Case 1:

14-year-old female presents with “heavy period” never been sexually active generally healthy. A- What is your DDx? Von Willebrand’s disease-DUB

B-What is your treatment?

In the case of DUB, since the patient is young and still her body is adapting to cycles, you reassure the patient.

Case 2:

38-year-old woman with a history of heavy, infrequent (two per year), menses since menarche at age 12 - Spontaneous pulmonary embolism six years ago.

- O/E - Wt. = 150 kg. Ht. = 145 cm
- Hirsutism involving upper lip, chin, midline chest and abdomen
- Negative speculum exam, bimanual limited by BMI.

A-What is your DDx? PCOS-Hypothyroidism

B-What is your most likely diagnosis? Most likely it is PCOS (High BMI, Hirsutism)

Case 3:

48-year-old obese patient with oligomenorrhea presents with 6 weeks' history of constant bleeding, now it is very heavy.

- O/E - Wt. = 150kg, vitals stable, pelvic; non-contributory except bleeding + + +
- Hb =7, MCV=85

A-What is your most likely diagnosis? Uterine Fibroids

B-Outline your immediate investigations and treatment?

Order CBC, Hormonal Profile, and you might do a biopsy. The treatment is the same as mentioned in the lecture.

Case 4:

43-year-old lady known type 2 DM and uterine fibroid presented with heavy regular vaginal bleeding.

A-What is your management? You start with the medical options; however you have to inform the patient about all available treatments for fibroids.

B- Which investigation you need to do? U/S C-Do u need to do endometrial biopsy?
No, since the patient is having a regular bleeding and has a low chance of cancer

Summary

- The luteal phase is always fixed, two weeks after the ovulation.
- In the premenopausal women with abnormal uterine bleeding, always exclude pregnancy by checking the levels of beta-hCG.
- Polyps in premenopausal women should not be removed if they were asymptomatic, except in postmenopausal women because of the risk of cancer.
- Von Willebrand's disease should be suspected whenever we have an adolescent with abnormal vaginal bleeding.
- With repeated cycles of unopposed estrogen, endometrial hyperplasia or even cancer may develop ⁽²⁾.
- During anovulatory cycles, the resulting nonsecretory endometrium contains less prostaglandin and is less apt to initiate an efficient menstrual period of short duration ⁽²⁾.
- The treatable causes of DUB are hyperthyroidism and hyperprolactinemia.
- The more common and less urgent type of DUB is best managed by cyclic estrogens with a progestin added at the latter 10 to 15 days of the 25-day estrogen cycle ⁽²⁾.
- Cyclic progestin alone may be used for younger patients who are likely to have sufficient estrogens to prime the endometrial progesterone receptors ⁽²⁾.
- For older patients who do not respond to medical therapy and who do not anticipate later pregnancies permanent measures should be considered, like endometrial ablation at the time of hysteroscopy ⁽²⁾.
- Vaginal hysterectomy may be appropriate for women who have associated problems such as pelvic relaxation or severe dysmenorrhea or for patients who are refractory to endometrial ablation ⁽²⁾.

References

1. Linda S. Costanzo Physiology, 4th edition.
2. Hacker and Moore's Essential of Obstetrics and Gynecology, 5th edition.
3. Kaplan USMLE Step 2 CK, Obstetrics and Gynecology Lecture Notes, 2014.

MCQs:

Q1. A 46-year-old G3P3 complains of severe, progressive menstrual cramps and heavy menstrual bleeding. Pelvic examination demonstrates a tender, diffusely enlarged uterus with no adnexal tenderness. Results of endometrial biopsy are normal. Which of the following is the most likely diagnosis?

- a. Endometriosis
- b. Endometritis
- c. Adenomyosis
- d. Uterine sarcoma
- e. Leiomyoma

Q2. A 36-year-old morbidly obese woman presents to your office for evaluation of irregular, heavy menses occurring every 3 to 6 months. An office endometrial biopsy shows complex hyperplasia of the endometrium without atypia. The hyperplasia is most likely due to the excess formation in the patient's adipose tissue of which of the following hormones?

- a. Estriol
- b. Estradiol
- c. Estrone
- d. Androstenedione
- e. Dehydroepiandrosterone

Q3. A 32-year-old morbidly obese diabetic woman presents to your office complaining of prolonged vaginal bleeding. She has never been pregnant. Her periods were regular, monthly, and light until 2 year ago. At that time she started having periods every 3 to 6 months. Her last normal period was 5 months ago. She started having vaginal bleeding again 3 weeks ago, light at first. For the past week she has been bleeding heavily and passing large clots. On pelvic examination, the external genitalia is normal. The vagina is filled with large clots. A large clot is seen protruding through the cervix. The uterus is in the upper limit of normal size. The ovaries are normal to palpation. Her uterine pregnancy test is negative. Which of the following is the most likely cause of her abnormal uterine bleeding?

- a. Uterine fibroids
- b. Cervical polyp
- c. Incomplete abortion
- d. Chronic anovulation
- e. Coagulation defect

Answers

Q1: C

Q2: C

Q3: D

Explanation:

Q1: Adenomyosis is a condition in which normal endometrial glands grow into the myometrium. Symptomatic disease primarily occurs in multiparous women over the age of 35 years, compared to endometriosis, in which onset is considerably younger. Patients with adenomyosis complained of dysmenorrhea and menorrhagia, and the classical examination findings include a tender, symmetrically enlarged uterus without adnexal tenderness. Although patients with endometriosis can have similar complaints, the physical examination of these patients more commonly reveals a fixed, retroverted uterus, adnexal tenderness and scarring, and tenderness along the uterosacral ligaments. Leiomyoma is the most common pelvic tumour, but the majority are asymptomatic and the uterus is irregular in shape. Patients with endometritis can present with abnormal bleeding, but endometrial biopsies show an inflammatory pattern. Uterine sarcoma is rare, and presents in older women with postmenopausal bleeding and non-tender uterine enlargement.

Q2: In premenopausal women, most of the estrogen in the body is derived from ovarian secretion of Estradiol, but a significant portion also comes from the peripheral conversion of androstenedione to estrone in adipose tissue. When there is an increase in fat cells, as in obese persons, estrogen levels – particularly estrone – will be higher provoking anovulation and endometrial hyperplasia.

Q3: The patient presents an example of chronic anovulation in an older woman. She gives a classic history of changing from regular, monthly periods to irregular, infrequent episodes of vaginal bleeding. Patients with chronic anovulation often have underlying medical problems such as diabetes, thyroid problems, or polycystic ovarian syndrome. A patient with uterine fibroids may have heavy periods, but the regularity of the periods is not affected unless the patient has underlying ovulatory dysfunction. A cervical polyp would clearly be seen on physical examination and, like uterine fibroids, would not affect the timing of menstruation. Patients with cervical polyps often complain of bleeding between periods, usually provoked by sexual intercourse. Since the patient's pregnancy test is negative, she cannot have an incomplete abortion. Patients with coagulation defects have problems with heavy periods from the time of menarche.

For mistakes or feedback

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