Vaginal Bleeding (AUB)

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1. In any woman with vaginal bleeding, rule out pregnancy. [1]

- All patients of child-bearing age who present with vaginal bleeding, require testing with either a urine or serum βhCG to rule out the possibility of pregnancy. This includes patients who report no recent sexual activity and in those who report use of contraception. However, once pregnancy is confirmed a quantitative serum βhCG must be ordered, as the βhCG levels can help guide management (such as in cases of ectopic pregnancy)

2. In pregnant patients with vaginal bleeding

a) Consider worrisome causes (e.g., ectopic pregnancy, abruption, abortion), and confirm or exclude the diagnosis through appropriate interpretation of test results.

It's important to remember when creating our differential for vaginal bleeding, that this can include bleeding from several different pelvic structures including the uterus, cervix, vagina, and vulva.

For any patient that comes in with vaginal bleeding (regardless of pregnancy status) you should start by taking a thorough history:

This includes asking the patient about:

- Characteristics of bleeding:
  - Amount and frequency
  - Presence and size of clots
  - Inciting factors such as trauma or intercourse
- Menstrual history:
  - LMP
  - Cycle regularity
  - Cycle length
  - Number of bleeding days and heaviness
  - Presence of dysmenorrhea, premenstrual symptoms, post-coital spotting and intermenstrual bleeding
- Associated Symptoms:
  - Symptoms of anemia or hypovolemia including light-headedness, SOB, or chest pain
  - Abdominal pain/pressure: if present ask about further characteristics including if unilateral or bilateral
  - Infectious symptoms: fever, chills, abnormal vaginal discharge, or odour
  - Dyspareunia
- Sexual and reproductive history including:
  - Sexual activity (oral, vaginal, anal intercourse)
  - Current partner(s)

    - Use of contraception
    - If currently pregnant
    - Desire for future pregnancy, if trying for pregnancy, any use of fertility treatments or history of infertility
- Obstetrical History:
    - GTPAL
    - Including previous early miscarriages
- Gyne History:
    - Previous episodes of abnormal vaginal bleeding
    - History of ovarian cysts, fibroids and if so any investigations or procedures
    - Last pap/abnormal paps
    - Previous STIs/PID
- PmHx or FmHx of coagulopathies, PCOS, endometrial or colon cancer
- Medications: that can interfere with ovulation or cause abnormal vaginal bleeding
    - Anticoagulants, some antidepressants (SSRIs and TCAs) and antipsychotics (risperidone), hormonal contraceptives and tamoxifen[1]

Your physical exam should include:

- Assessment of vitals to ensure hemodynamic stability
- Abdominal exam to assess for masses and signs of peritonitis such as guarding or rigidity
- You also may consider assessment of the vulva, vagina, and cervix by speculum exam
- Note: a manual pelvic examination should **never** be performed on pregnant patients after 20 weeks' gestation until placenta previa has been ruled out definitively by ultrasound)

Your differential for vaginal bleeding in pregnancy varies depending on gestational age.

Ectopic pregnancy [2]

- An estimated 1-2% of pregnancies are ectopic (meaning – a blastocyst *implants at any site other than the uterine cavity)*, however within the first trimester they can account for 75% of maternal deaths and therefore need to be at the top of our differential
- Risk factors for ectopic pregnancy include:
    - Anatomic abnormalities to the fallopian tubes such as:
        - Previous ectopic pregnancies
        - Prior fallopian tubes surgeries
        - Prior pelvic and abdominal surgeries
        - Certain STIs, such as Chlamydia and Gonorrhea
        - PID
        - Endometriosis
        - Exposure to diethylstilbesterol in utero
    - And non-anatomical risk factors such as:
        - Age >35
        - Smoking
        - IUD
        - IVF
- Common symptoms of an ectopic pregnancy include:

  - Abdominal pain
  - Vaginal bleeding
  - And a missed menstrual period and/or positive pregnancy test in a reproductive aged-female

Investigations:

- Blood work
  - CBC, βhCG,
  - G&S to determine blood type and Rh status
  - LFTs and creatinine to assess liver and kidney function , which is necessary to establish a baseline prior to methotrexate use
- TVUS

An IUP can generally be seen on TVUS once the βhCG is over 2000-3000. This is called the discriminatory zone, as this is the βhCG level at which an intrauterine gestational sac can reliably be seen on TVUS.

If βhCG is positive and an ectopic pregnancy is visualized on ultrasound, the diagnosis of an **ectopic pregnancy** is confirmed, and the patient should be sent to the emergency room.

Of important note, the βhCG of an ectopic pregnancy can be above or below the discriminatory zone and still be seen on ultrasound. Therefore, it is always important to get an ultrasound done, even if βhCG levels are low. One of the hallmark features of an ectopic pregnancy is abnormal βhCG rise, so an ectopic can be growing in size and rupture, even before βhCG levels rise over 2000.

However, In some cases, βhCG is positive but there is no IUP or ectopic pregnancy on imaging, this is referred to as a pregnancy of unknown location and requires close monitoring and management

If βhCG levels are above 2000 and no IU gestational sac is seen, then there is a **probable ectopic pregnancy**, and the patient should be sent to the emergency room.

If βhCG is less than 2000 and no IU gestation sac is seen, then there is a **possible ectopic pregnancy**. These patients should be given an ectopic warning and followed closely. These patients may alternatively have an early or failed pregnancy.

Ectopic pregnancies and pregnancies of unknown location should be managed by gynecology.

Although we'll briefly discuss the different management options below, the consulted gynecology team will be the ones to determine the optimal management option and provide said care.

Once a diagnosis of a tubal ectopic pregnancy is confirmed treatment options include expectant management, medical management, or surgical management depending on specific criteria[2]

- Tubal pregnancies are rarely managed expectantly.
- Expectant management does not involve any interventions but requires weekly monitoring of serum βhCG until levels are undetectable. Strict criteria are needed for expectant management to be offered.

Medical management involves treatment with methotrexate.
Methotrexate is a folic acid antagonist that impairs DNA synthesis. It is teratogenic.

Once treated with methotrexate patients should be given serial blood work requisitions to monitor the downward trend of serum βhCG until undetectable.
Patients should also be counselled to avoid folic acid, alcohol, and to stop taking their prenatal vitamins.
They should also refrain from sexual activity and vigorous activities as it can increase the risk of tubal rupture.
Since MTX has teratogenic effects, it is recommended that patients delay pregnancy for at least 3 months after the last dose of MTX. (ACOG bulletin #193)

Patients should undergo surgical management if they elect against or do not meet criteria for safe expectant or medical management, if they fail medical management with methotrexate, or if they develop symptoms consistent with a ruptured ectopic[2]

Next well talk about one of the most common causes of bleeding in early pregnancy: threatened and spontaneous abortions [4, 5]

Threatened abortion:

- Occurs when there is:
  - Vaginal bleeding with a closed cervix
  - Viable intra-uterine pregnancy detected on ultrasound
- Threatened abortions with fetal cardiac activity detected on ultrasound, are only at a 5% risk of progression to complete abortion[4]
- Therefore, these cases are often managed expectantly

Complete abortion:

- Occurs when:
  - a patient either recently had or is still experiencing vaginal bleeding
  - Has a closed cervical os on examination
  - Current ultrasound findings show no evidence of POC within the uterine cavity and no extrauterine gestation
  - And the patient MUST have a previous ultrasound from the currently pregnancy confirming IUP
  - Otherwise, with a positive βhCG and no prior documentation of IUP available, it is considered a PUL until proven otherwise and managed as such
- Once a complete abortion is confirmed, no further management is required

Incomplete abortion:

- Occurs when a patient has:
  - Vaginal bleeding with a dilated cervical os, with some but not all products recently passed
  - Partial retained POC seen within the uterus on ultrasound or within the cervical os on speculum examination

Inevitable abortion:

- Occurs when a patient experiences vaginal bleeding with a dilated cervical os
- Either viable or non-viable POC visualized within the uterus on ultrasound, without any report or evidence of tissue passage

Missed abortion:

- Presents with possible light vaginal bleeding and a closed cervical os
- Ultrasound findings revealing a non-viable POC within the uterus

Incomplete, inevitable and missed abortions all have similar treatment options which include expectant, medical or surgical management

Expectant management:

- Can be considered for patients who are stable, have no signs of infection or hemorrhage, severe anemia or bleeding disorders
- You should counsel patients that passage of retained product can take up to 8 weeks
- With this, patients can expect mild to moderate cramping and bleeding
    - It is important to prescribe pain medications if needed
- Counsel patients to present to ED if they experience heavy bleeding (soaking 2 pads/hour for over 2 hours), signs of infection or hypovolemia
- A follow up ultrasound should be booked to confirm passage of pregnancy tissue
- If ultrasounds are not available, you can order serial serum βhCG

Medical management:

- Can be considered in the same subset of patients meeting criteria for expectant management
- Used to shorten the time to complete expulsion
- Includes:
    - A single dose of misoprostol either vaginally or sublingually
    - If there is no response to this dose, an additional dose can be given after 24-48h
    - Mifepristone can be used 24 hours prior to misoprostol as it has been shown to increase treatment efficacy
    - The same counselling and follow up should be provided as in expectant management

Surgical management:

- Patients who are hemodynamically unstable or have signs of a septic abortion should be managed surgically

Septic abortion:

- Occurs when there is infected RPOC
- Patients often present with:
    - Fever, abdominal cramping, uterine tenderness, purulent vaginal discharge, and hemodynamic instability

- These patients require surgery to remove infected POC and should be started on broad spectrum antibiotics, such as Gentamycin or Clindamycin

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Finally, another rare but important diagnosis to keep on your differential is gestational trophoblastic disease, otherwise known as a molar pregnancy [6]

Molar pregnancies:

- Occur when there is abnormal fertilization of an ovum leading to overgrowth of trophoblastic tissue
- Common symptoms include:
  - Vaginal bleeding
  - Pelvic pain or pressure
  - Enlarged uterus (greater than GA)
  - Due to elevated βhCG would also see:
    - Early pre-eclampsia
    - Hyperemesis gravidarum
    - Signs of hyperthyroidism
- On investigations, you'll see:
  - Significantly elevated βhCG (greater than upper limit of normal for GA)
  - Ultrasound findings reveal an echogenic mass containing multiple hypoechoic cystic spaces
    - Commonly described as a "snowstorm" or "grape" pattern
- Patients with molar pregnancies should be referred to gynecology for management

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Next we'll move along to patients > 20 weeks pregnant with vaginal bleeding:

- Before we review our differential, it's important to remind ourselves that a manual pelvic examination should **never** be performed on pregnant patients after 20 weeks gestation until placenta previa as been ruled out definitively by ultrasound

For patients >20 weeks our differential includes:[7]

- Placental abruption:
  - Involves either partial or complete separation of the placenta from the uterus and can cause subsequent hemorrhage from both maternal and fetal vessels
  - Risk factors for placental abruption include:
    - PPROM, Multiparity, previous abruptions, hypertension, Type 2 diabetes, thrombophilias, fibroids, history of smoking and cocaine use
    - Abruption can also occur after abdominal trauma
  - Patients often present with:
    - Sudden onset painful bleeding
    - Pain is often constant and present in the abdomen and back
    - Increased uterine tone
    - Fetal heart rate may be abnormal
  - At this point you should consult obstetrics for assessment:
    - Management normally includes:
      - Acute stabilization with resuscitation and IVFs if needed

- CBC and coagulation panels to monitor for the development of DIC
- Preterm and stable: they normally will be admitted for monitoring
- Term and stable: induce for vaginal delivery
- Unstable patients: emergency C/S

- Placenta previa: occurs when the placenta implants in the lower segment of the uterus
- Vasa previa: occurs when fetal vessels are located close to the internal cervical os
    - Some patients may be asymptomatic, with findings of placenta previa or vasa previa discovered incidentally on anatomy ultrasound
    - If symptomatic patients with either condition will normally present with painless vaginal bleeding
    - For more information on the assessment and management of placenta previa and vasa previa check out Episode 7 on Placental Abnormalities

- It's also important to keep non-obstetrical causes of bleeding on the differential in pregnant patients
- This includes:
    - Vaginal or cervical lesions (i.e. polyps, ectropion), infections or trauma
    - Rectal bleeding
    - Urinary tract bleeding

a) Do not forget blood typing and screening, and offer Rh immunoglobulin treatment, if appropriate. [8]

Rh alloimmunization:

- Order a blood type and antibody screen to determine Rh status
- This should be done in all cases of maternal bleeding or trauma as there is a risk of alloimmunization
    - This includes miscarriages, threatened abortions, induced abortions, placental abruption, placenta previa
- If this is a known pregnancy and a blood type and a recent antibody screen has already been completed and Rh status is known, you do not need to repeat the testing

Treatment:

- For all patients who are Rh negative ensure that you treat then with Rho (D) immune globulin
- This should be given within 72 hours of all sensitizing events
- Since this is a blood product, ensure that written or verbal consent is obtained prior to administration

b) Diagnose (and treat) hemodynamic instability. [1]

Acute vaginal bleeding with hemodynamic instability can be life threatening and therefore needs to be managed similarly to other cases of acute bleeds.
This includes:

- Acute resuscitation including continuous monitoring of vitals, review of ABCs, assessment of cognition
- Patients should receive IV fluid resuscitation and blood transfusion when needed

- All pregnant patients should be given O negative blood to reduce further risk of alloimmunization
- Abdominal PoCUS can be done to assess for free fluid in abdomen
- Blood work should be ordered to assess for anemia and DIC
- Pregnant patients can be given tranexamic acid to help slow the rate of bleeding
- An urgent consult should be made to either gynecology or obstetrics depending on gestational age

2. In a non-pregnant patient with vaginal bleeding:

a) Do an appropriate work-up and testing to diagnose worrisome causes (e.g., cancer), using an age-appropriate approach. [1, 9]

We can use the pneumonic PALM-COEIN to help work through our differential diagnosis for abnormal uterine bleeding.

PALM: refers to structural causes of abnormal uterine bleeding, including polyps, adenomyosis, leiomyomas (otherwise known as fibroids) and uterine hyperplasia or malignancy.

- Polyps are often asymptomatic, however can at times cause irregular menstrual bleeding
- Adenomyosis is a benign growth of endometrial tissues within the myometrial layer of the uterus
  - Although some patients may be asymptomatic
  - Others experience: abnormal uterine bleeding, dysmenorrhea, and chronic pelvic pain
  - Additionally, you may notice a soft, boggy uterus on exam that is often tender to palpation

- Fibroids: are a benign growth of smooth muscle within the uterus
  - Common symptoms include:
    - AUB as in heavy painful periods. It is important to note that fibroids generally do not cause irregular bleeding.
    - Pelvic pressure
    - Obstructive symptoms such as urinary frequency or urgency (if the fibroid is large and obstructing the bladder)
    - Bowel dysfunction (if the fibroid is large and proximal to the bowels)
    - History of infertility
  - On exam you may notice an enlarged, mobile uterus with irregular contours

- Endometrial hyperplasia and endometrial cancer
  - Risk factors for endometrial cancer can be assessed on history and physical exam and include
    - Age
    - BMI > 30
    - Nulliparity
    - Chronic anovulation
    - PCOS
    - Diabetes
    - HPNCC (hereditary non-polyposis colorectal cancer): which is a genetic condition that increased an individual's risk of endometrial, colon and several other cancers
    - Tamoxifen use

Now let's move to the COIENs part of the PALM-COIEN pneumonic
This side of the pneumonic considers medical disturbances that could cause AUB.

- Coagulopathies:
    - VWD is the most common inherited bleeding disorder accounting for around 70% of AUB secondary to coagulopathies
    - Other less common disorders include factor XI, VII and XIII, carrier status for hemophilia A and B and other inherited disorders of platelet dysfunction
    - Patients with coagulopathies as the cause of their bleeding often report heavy, regular, cyclic menses without intermenstrual bleeding
        - In adolescents, heavy menstrual bleeding starting at menarche is often a sign of an underlying bleeding disorder
    - Patients may also report:
        - Easy bruising, frequent nose bleeds, and prolonged bleeding with minor injuries or following dental procedures
        - A family history of bleeding disorders
    - Referral to hematology should be made for definitive diagnosis

- Ovulatory dysfunction:
    - Patients with ovulatory dysfunction will often present with irregular, unpredictable bleeding
    - Causes for ovulatory dysfunction include:
        - PCOS, hyperthyroidism, hyperprolactinemia, anorexia, mental stress and excessive exercise
    - If your patient shows signs of hirsutism, acne and alopecia, has a history of infertility or irregular menses consider ordering labs for FSH and LH and an ultrasound to assess for enlarged or polycystic ovaries
    - If your patient is showing signs of hypothyroidism, consider ordering thyroid function tests
    - If your patient has galactorrhea, impaired renal function, or is taking medications such as estrogens, antipsychotics or SSRIs consider hyperprolactinemia
    - Ovulatory dysfunction can also occur when the body experiences extreme stress
        - This can occur in patients with anorexia, excessive mental stress, or with extreme exercise
    - Finally abnormal bleeding in adolescents is commonly caused by ovulatory dysfunction due to immaturity of the hypothalamic-pituitary-ovarian axis

- Endometrial: refers to primary disorders of the endometrium.
    - Often a diagnosis of exclusion for patients who experience heavy bleeding during their regular and predictable menstrual cycles
    - This can only be made when other causes have been ruled out

- Iatrogenic:
    - Includes:
        - Breakthrough bleeding for patient who use hormonal therapies
        - Abnormal bleeding associated with hormonal or copper intrauterine devices
- Not yet classified: such as chronic uterine inflammation (e.g. chlamydia, PID), foreign body and AV malformations

Finally, it is important to consider non-uterine causes of vaginal bleeding.

- This includes cervical dysplasia, lesions or inflammation such as secondary to infection
- Genital lesions or cervical polyps
- Vaginal laceration: ensure you do a speculum examination and inquire about recent trauma

And it's important to consider alternative sources of bleeding such as perianal, rectal and urinary tract bleeding

Now knowing what we would include on our differential we can now review appropriate history, physical and investigations to order:

History:

- A general history should be taken for all patients with vaginal bleeding
- This will look similar to the history discussed in objective 2 and should include characteristics of bleeding, menstrual history (including signs and symptoms of menopausal if appropriate), associated symptoms, sexual and reproductive history, obstetrical history, gynecological history, past medical history and medications
- It's also important to screen for symptoms of hypothyroidisms, hyperprolactinemia, coagulation disorders, PCOS, adrenal or hypothalamic disorders, as these are all systemic causes of abnormal uterine bleeding.

Physical Examination:

- Physical exam would include:
    - Assessment of vitals
- An abdominal exam should be completed to assess for masses, HSM or signs of peritonitis
- Gynecological exam includes:
    - Assessment of the vulva, vaginal, cervix (via a speculum exam), anus and urethra
    - A bimanual examination to assess the uterus and adnexal structures
    - A rectal exam including DRE should be considered if bleeding from the rectum is suspected
- You can also consider (for completion sake):
    - Weight and calculating BMI
    - Assess the thyroid gland for signs of hypothyroidism
    - Assess the skin to look for changes including
        - Pallor: as sign of anemia
        - Bruising or petechia: signs of possible bleeding disorders
        - Striae: which is found in Cushing's disease
        - Hirsutism: which is seen in PCOS

Putting it all together, investigations for AUB in non-pregnant patients include:

- CBC, TSH, swabs for GC/CHL, pap test and a TVUS for all
- INR if heavy bleeding
- PRL, LH, FSH, estradiol if oligomenorrhea
- +/- endometrial biopsy

b) Diagnose (and treat) hemodynamic instability. [1]

Acute resuscitation measures should be made to manage hemodynamic instability in non-pregnant patients. Patients should be referred to the emergency department for this care
This includes:

- Continuous monitoring of vitals, review of ABCs, assessment of cognition
- IV fluid resuscitation and blood transfusion when needed
- PoCUS can be done to assess for anatomic causes of bleeding in uterus as well as assess for free fluid in abdomen
- Blood work to assess for anemia and DIC

Medical management for unstable non-pregnant patients include:

- IV or PO estrogen
- Nausea is a common side effect of high dose estrogens therefore consider concurrently giving an anti-emetic such as Ondansetron
- Tranexamic acid

Once an acute episode of bleeding has resolved, the patient can continue to receive daily OCPs or tranexamic acid until further workup is completed.

Some contraindications to high dose estrogens and TXA include:

- Acute PE or DVT
- Inherited thrombophilias
- Recent MI or stroke
- Or Active malignancy

Surgery should be considered only when there are known contraindications to medical treatment or if medical treatment fails

c) Manage hemodynamically stable but significant vaginal bleeding (e.g., with medical versus surgical treatment). [1]

Once endometrial cancer is ruled out medical management with both non-hormonal and hormonal treatment options should be the first line of therapy. Additionally, treatment for underlying medical conditions such as hypothyroidism, should be provided prior to use of non-hormonal and hormonal treatment.

Non-hormonal:

- They can be used monthly during menses to reduce blood loss
    - They are more effective in treating heavy bleeding that is regular and predictable.
- Options include: NSAIDs and antifibrinolytics such as TXA
    - It's important to note that NSAIDs affect platelet function and therefore are contraindicated in patients with bleeding disorders

Hormonal treatment options:

- Helpful treatment option for both patients with predictable cyclic heavy menstrual bleeding and irregular or prolonged bleeding as it helps to regulate cycles and lighten bleeding
- First line includes: COC, depot medroxyprogesterone acetate and the IUS, Mirena
    - Great choices for patients who want a method of contraception
- Danazol and GnRH agonists can also be used to treat heavy menstrual bleeding if there are contraindications to COC, shots or IUDs. These often require a referral to gynecology.

Surgical management:

- Indicated when:
    - failed response to medical therapy
    - Side effects or contraindications to medical therapy
    - Significant anemia/hemodynamic instability
    - Concomitant uterine pathology such as a significantly enlarged uterine fibroid or uterine hyperplasia

At this time referral to gynecologist should be made.
It is important to have the conversation with your patient around desire for further pregnancy as this can influence surgical management

3. In a post-menopausal woman with vaginal bleeding, investigate any new or changed vaginal bleeding in a timely manner (e.g., with endometrial biopsy testing, ultrasonography, computed tomography, a Pap test, and with a pelvic examination). [10, 11, 12]

Endometrial cancer must be ruled out in all post-menopausal patients with new vaginal bleeding.
A complete and thorough history and physical examination including abdominal, speculum and bimanual exam should be completed
Initial investigations for suspected endometrial cancer can include both a transvaginal ultrasound and endometrial biopsy.
On transvaginal ultrasound:

- The ACOG states that a TVUS is sufficient for initial evaluation of PMB if the ultrasound reveals a clear and thin endometrial lining (less than or equal to 4 mm), given that an endometrial thickness of 4 mm or less has a greater than 99% negative predictive value for endometrial cancer. (ACOG opinion #734).
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- If the TVUS images are not clear, or there is recurrent/ongoing postmenopausal bleeding, then it is necessary to proceed with an endometrial biopsy.

Endometrial biopsy:

- Abnormal findings on endometrial biopsy such as endometrial carcinoma and atypical endometrial hyperplasia, warrant a referral to gynecology.

CT scans are not recommended for diagnosis of endometrial cancer

Pap smears:

- You should ensure that your patient is also up to date on their pap smears, for cervical cancer screening. All asymptomatic patients who have ever been sexually active should have pap smears for cervical cancer

screening. This should be completed every 3 years and can stop at the age of 70 given their most recent 3 pap smears were negative.
- Pap smears are screening tests and therefore not indicated for diagnosis in symptomatic patients.
- If there are abnormal findings on cervical assessment or high suspicion for cervical pathology as the source of bleeding, colposcopy and cervical biopsy may be indicated as well as referral to gynecology.

One last thing to note, vulvovaginal atrophy is one of the most common causes of post-menopausal bleeding.
This diagnosis can only be considered once endometrial cancer and hyperplasia has been ruled out.
Vulvovaginal atrophy is caused by lower systemic levels of estrogen, leading to atrophy after onset of menopause. This occurs in up to 50% of females within 3 years of menopause.

- This condition can often by treated with routine application of topical estrogen creams, suppositories, or vaginal rings as well as encouraging lubrication during sexual intercourse

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