Abnormal Uterine Bleeding Primary Care Pathway

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Normal cyclical bleeding refers to a regular bleed occuring at 24-38-day intervals (cycle length may vary)

1. History

- Evaluate bleed (pattern and quantity)
- Pregnancy risk / sexual history
- Risk factors for endometrial cancer

Risk factors for endometrial cancer:
- Age > 40 years
- Obesity (BMI > 30 kg/m2)
- Nulliparity
- Diabetes
- Current Tamoxifen use
- Polycystic ovarian syndrome w/irregular cycles
- Hereditary non-polyposis colorectal cancer
- Unopposed estrogen exposure

2. Assessment / red flags

- Vitals / general appearance
- Vulva / vagina: Atrophic change or trauma
- Bimanual
- Speculum exam / inspect cervix

Consider:
- Pap test, if due
- STI screen (C/G and Trich) if intermenstrual bleeding, vaginal discharge, post-coital bleeding

More details

Red flags
- Patient looks unwell
- Hypotension / tachycardia
- Flooding through >1 pad each hour

Red flags

Yes → Call RAAPID or 911 if urgent

3. Investigations

For all patients, please consider the following:

- Pregnancy test — If positive → Manage pregnancy, as appropriate
- CBC/Ferritin — If low → Iron therapy, as appropriate
- Transvaginal pelvic ultrasound — More details

4. Treat / manage

Normal ultrasound or fibroid < 5cm

- Cyclical heavy bleeding — More info
  - No abnormal findings; trial medical management — More info
- Non-cyclical heavy bleeding — More info
  - >40 years old, high risk of cancer; irregular bleed for 3-6 months → Start medical management, refer to gynecology
  - Oligoovulatory / irregular bleed → Trial medical management — More info
  - Intermenstrual / post-coital bleed — More details
    - Screen, treat STI → If symptoms persist → Trial medical management — More info
    - Cervix Friable? → Treat for mucopurulent cervicitis — More info → If symptoms persist → Refer to gynecology

Polyp or submucosal fibroid or large / multiple fibroids

Start medical management, refer to gynecology — More info

Patients > 40 years old, with history of amenorrhea > 1 year and new episode of bleeding

Follow post-menopausal pathway

Essential information to include with referrals: History exam, inc. Pap results; Lab & DI results; Attempted treatments & outcome

PATHWAY PRIMER

- Normal cyclical bleeding refers to a regular bleed occurring at 24-38 days intervals.[1] Abnormal uterine bleeding (AUB) is bleeding that occurs outside of the normal 24-38 -day pattern. Post-menopausal bleeding is defined as bleeding occurring in a woman older than 40 years of age with new onset of bleeding after one year of no bleeding (amenorrhea). See Post-Menopausal Bleeding pathway for information on managing this condition.
- This pathway applies to any female who has had menarche. The pathway facilitates the prompt management of abnormal uterine bleeding in the patient's medical home and provides primary care clinicians with guidance on evidence-based diagnosis, investigations, and management. The pathway also establishes guidelines for when to make a referral to Gynecology or to RAAPID for urgent evaluation. The Society of Obstetricians and Gynecologists of Canada (SOCG) generally recommend that treatment of AUB should start with medical management, followed by the least invasive surgical interventions to achieve results for patients.[1] This principle is also re-iterated in a Choosing Wisely Canada recommendation that surgical interventions should be avoided for abnormal uterine bleeding until medical management (including progesterone intra-uterine system) has been offered and either declined or found unsuccessful.[2]
- Abnormal uterine bleeding is a common condition that affects many women of reproductive age and can result in significant health and economic burdens. For example, a 2007 systematic review on AUB assessed the prevalence of heavy bleeding, one type of AUB, at between 10% to 30% in women of reproductive ages.[3]

EXPANDED DETAILS

1. History

A thorough patient history and physical examination will, in most cases, identify the cause(s) of abnormal uterine bleeding and provide direction for investigation and management.

- Evaluate the bleeding pattern, including quantity and timing:
  - Do cycles occur between 24-38 days apart? Cycles may vary in length month to month, but a normal cycle will average between 24-38 days in length.
  - Is there bleeding between cycles?
  - Is there bleeding with intercourse?
- **Assess pregnancy risk and sexual history**
  - All pre- or peri-menopausal patients with abnormal bleeding should have a pregnancy test if there is potential for pregnancy. See Important Treatment Considerations - Confirmed Pregnancy for more information on managing pregnancy with abnormal bleeding.
- **Review the risk factors for endometrial cancer[1]:**
  - Age > 40 years
  - Obesity (BMI > 30 kg/m2)
  - Nulliparity
  - PCOS (polycystic ovarian syndrome) with irregular cycles
  - Diabetes
  - Current Tamoxifen use
  - HNPCC (hereditary non-polyposis colorectal cancer)

- Unopposed estrogen exposure
- The average age for women with endometrial cancer is 61 years, but 5% - 30% of cases can occur in premenopausal women.[1] Women younger than 50 years of age can share many of the same risk factors for endometrial cancer as older women.

- **Rule out urinary or bowel as the source for bleeding**

2. Assessment / red flags

The physical examination should identify evidence of any systemic conditions that can cause bleeding, as well as evaluate any anatomical causes, such as fibroids or cervical polyps.

- In stable patients, conduct a physical examination for structural abnormality: vulva, vagina, speculum (cervix) and bimanual examinations.
- If the patient is due, include a PAP test (TOP Cervical Cancer Screening Guideline).
- If there is intermenstrual, post-coital bleeding or vaginal discharge, initiate STI testing for:
  - Chlamydia
  - Gonorrhea
  - Trichomonas
- STI test can be performed with swab or as a urine test.
- If STI testing is positive, treat as per provincial guidelines (STI Treatment Guidelines)
- If STI testing is negative, but the cervix appears friable, initiate a trial treatment for mucopurulent cervicitis (STI Treatment Guidelines). Persistent symptoms that do not respond to treatment should be referred to Gynecology.

Alarm features / red flags

- Patient looks unwell
- Hypotension or Tachycardia
- Hemorrhage or heavy bleeding defined as soaking through a pad or tampon every hour

If alarm features are present or the patient is medically unstable, call RAAPID for an urgent referral to Gynecology for immediate hospital evaluation.

3. Investigations

Laboratory tests

- Confirm Pregnancy: For all patients with abnormal uterine bleeding, perform a sensitive urine or serum pregnancy test if there is any possibility of pregnancy. If the test is positive, see Important Treatment Considerations – Confirmed Pregnancy for information on management.

- CBC/Ferritin: For all stable patients, order a CBC/Ferritin if there are concerns of possible anemia or iron deficiency. Treat as appropriate with iron therapy, especially if there is continued menstrual bleeding.
- Free Androgen Index: Consider the addition of Free Androgen Index testing if the patient has historical features of polycystic ovarian syndrome. There is no utility to requesting FSH / LH / estradiol or progesterone levels.[2]
- Thyroid: Thyroid functioning testing is not indicated unless there are clinical findings suggestive of an index of suspicions of thyroid disease.[1]

- Coagulation Disorders: Testing for coagulation disorders should only be considered in women with heavy bleeding since menarche or who have a family history/personal history of abnormal bleeding.[1]
- Transvaginal Pelvic Ultrasound: A Transvaginal Pelvic Ultrasound should be the first line for imaging abnormal uterine bleeding.[1] For all stable patients, perform a Transvaginal Pelvic Ultrasound to rule out uterine structural causes for abnormal bleeding (e.g. fibroids). A transvaginal ultrasound allows for assessment of anatomical abnormalities of the uterus and endometrium. Do not assess endometrial thickness in a pre-menopausal patient.

4. Treat / manage

- For patients older than 40 years with a history of amenorrhea for > 1 year and have a new episode of bleeding, consult the Enhanced Primary Care Pathway – Post-Menopausal Bleeding.
- If a small fibroid (<5cm) that is not submucosal is present: continue with pathway to manage abnormal uterine bleeding
- If a polyp or submucosal fibroid is present, or there is a large fibroid (>5cm) or multiple fibroids, start medical therapy for cyclical bleeding (below) and complete an initial referral to Gynecology

Treatment considerations: Protocols apply to women with normal ultrasound findings or fibroids < 5cm:

Cyclical heavy bleeding

- For women with regular monthly bleeding (24-38 days) that is heavy and who have no bleeding in between cycles.
- For a normal ultrasound or small (<5cm) non-submucosal fibroid, attempt medical therapy. Ensure no contraindications prior to prescribing:
  - Tranexamic acid with menses: 1000mg po QID or 1500mg PO TID x 5 days with menses, taken with food.
  - NSAIDS with menses (e.g. Advil® 400mg po q6h x5 days or naproxen 500mg po BID x5 days)
  - Progesterone-only methods (e.g. Prometrium® 100-200 mg PO OD at bedtime daily, or Micronor® /Visanne® progesterone-only pills, or Depo-Provera®)
  - Mirena® IUD (referral to Gynecology or GP with IUD experience)
  - Combined contraceptive to decrease the amount of bleeding:
    - Monophasic oral pill, patch or ring
    - Contraindications: History of or current VTE, CAD/cerebrovascular disease, breast cancer, other estrogen-dependent malignancy, known or suspected pregnancy, benign or malignant liver tumor/disease, smoking and > 35 years old, uncontrolled hypertension, or migraines with focal neurologic symptoms.

Non-cyclical bleeding

Consider performing an endometrial biopsy if the patient is > 40 years old with risk factors for endometrial cancer and is experiencing irregular periods for >3-6 months at a time. Refer to a GP with expertise in endometrial biopsy or to Gynecology for biopsy if necessary.

- **Oligo-ovulatory/irregular bleeding:** For a normal ultrasound, attempt medical therapy. Ensure no contraindications prior to prescribing:
  - Stop current bleeding with tranexamic acid: 1000mg po QID or 1500mg PO TID x5 days
  - Progesterone-only methods:
    - Prometrium® 100-200 mg PO OD (perimenopausal group) at bedtime (NOT CYCLIC – daily only)
    - Micronor® or Visanne® progesterone-only pills
    - Depo-Provera®
  - Mirena® IUD (referral to Gynecology or GP with IUD experience)
  - Combined contraceptive for cycle control:
    - Monophasic oral pill, patch or ring
    - Contraindications: History of or current VTE, CAD/cerebrovascular disease, breast cancer, other estrogen-dependent malignancy, known or suspected pregnancy, benign or malignant liver tumor/disease, smoking and > 35 years old, uncontrolled hypertension, or migraines with focal neurologic symptoms.
- **Intermenstrual bleeding or post-coital bleeding**
  - For women with regular monthly cycles (24-38 days) who experience bleeding in between cycles or after sexual intercourse.
  - Complete a screening for STIs and treat if positive, according to provincial guidelines (STI Treatment Guidelines)
  - For a normal ultrasound and structural/infectious causes ruled out, attempt medical therapy. Ensure no contraindications prior to prescribing:
    - 3 to 6 months of oral monophasic contraceptive pill/ring/patch
    - 3 to 6 months of a progesterone-only method (e.g. Depo-Provera®, Micronor®, Visanne®)
  - If the cervix is friable, treat for mucopurulent cervicitis. If symptoms persist, refer to Gynecology for management.

Confirmed pregnancy

- Confirm the patient's Rh status for a positive pregnancy.
  - If the patient is Rh negative and negative for Anti-D antibodies on type and screen, give the Anti-D antibody (e.g. WinRho®/RhoGam® in 300mcg IM injection)
- If the patient has a positive pregnancy test and is bleeding, ensure the pregnancy is viable and intrauterine with a pelvic ultrasound.
- Link to an Early Pregnancy Loss clinic if the pregnancy is NOT viable and intrauterine and the patient is stable.
- If this is a possible ectopic pregnancy or the patient is bleeding heavily or is medically unstable, call RAAPID for referral to Gynecology.

Polycystic Ovarian Syndrome (PCOS)

A patient requires 2 of 3 criteria to make a diagnosis of PCOS:

1. Pelvic ultrasound findings of polycystic ovaries
2. Clinical presentation (e.g. Hirsutism) **OR** laboratory confirmation (e.g. Free androgen index) of high androgens.
3. Oligo-ovulation / irregular menstrual cycles (not occurring 24-38 days apart).

There is no indication for Free Androgen Index testing if the patient has clinical signs (e.g. hirsutism) of high androgens. There is no need for FSH/LH/estradiol testing as this does not change the diagnosis or management of PCOS.[2] PCOS can occur at any BMI and the patient does not have to be obese.

Issues with PCOS separate from abnormal uterine bleeding:

- Acne: This is a feature of hyperandrogenism. Treatments include skin care, combination oral contraceptive and/or antiandrogen. Consider referral to Dermatology for the refractory cases.
- Hirsutism: This refers to the increased hair growth in the androgen-dependent area of the skin. This is a feature of hyperandrogenism. Treatments include depilation treatment, combination oral contraceptive, Vaniqa® cream and/or antiandrogen e.g. spironolactone. Consider referral to Medical Endocrinology for the refractory cases.
- Infertility: Patient with irregular menses or oligo-ovulation does have ovulatory dysfunction, which is a cause of infertility. Patient and her partner should be assessed for other additional causes(s) of infertility, such as tubal factor and male factor. Treatment is based on all the identified causes if ovulatory dysfunction is the only identified cause, ovulation induction will be the first-line treatment.
- Metabolic syndrome: Patient should be screened for diabetes mellitus and impaired glucose tolerance by 2-hour oral glucose tolerance test and dyslipidemia. Patient should also be counselled for lifestyle change.
- Risk of endometrial hyperplasia.

BACKGROUND

About this pathway

This pathway is intended to provide evidence-based guidance to support primary care providers in caring for patients with common gynecological conditions within the medical home.

Authors and conflict of interest declaration

This pathway was reviewed and revised under the auspices of the Calgary Zone Department of Gynecology in 2020 by a multidisciplinary team led by family physicians and gynecologists. Names of participating reviewers and their conflict of interest declarations are available on request.

Pathway review process, timelines

Primary care pathways undergo scheduled review every year if there is a clinically significant change in knowledge or practice.

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DISCLAIMER

This pathway represents evidence-based best practice but does not override the individual responsibility of health care professionals to make decisions appropriate to their patients using their own clinical judgment given their patients' specific clinical conditions, in consultation with patients/alternate decision makers. The pathway is not a substitute for clinical judgment or advice of a qualified health care professional. It is expected that all users will seek advice of other appropriately qualified and regulated health care providers with any issues transcending their specific knowledge, scope of regulated practice or professional competence.

PROVIDER RESOURCES

Advice options, referral guidelines

When to refer to specialty or contact RAAPID or Specialist LINK/eReferral Advice Request:

- Severe bleeding or medical instability (i.e. soaking through a pad an hour or abnormal vital signs). This patient needs to be directed to hospital through RAAPID or the ER. Call RAAPID for the on-call Gynecologist or **911**.
- If there is a possible ectopic pregnancy, call RAAPID for referral to Gynecology.
- Failure of medical therapy for abnormal uterine bleeding, initiate a referral to Gynecology.
- For any Gynecology referral please include: A complete patient history, results from Pap test, laboratory and diagnostic imaging investigations, and any attempted treatments with outcomes. This information allows for the appropriate triage of your patient.

Contact information

- For RAAPID South, call **1-800-661-1700** or **403-944-4486**. Visit https://www.albertahealthservices.ca/info/Page13345.aspx for more details.
- Family physicians can request non-urgent advice online at specialistlink.ca or by calling **403-910-2551**. The service is available from 8 a.m. to 5 p.m. (with some exceptions), Monday to Friday (excluding statutory holidays). Calls are returned within one hour.
- Obstetrics and Gynecology advice is available via Alberta Netcare eReferral Advice Request (responses are received within five calendar days). Visit https://www.albertanetcare.ca/eReferral.htm for more information.

Resources	Link
TOP Guideline – Cervical Cancer Screening	https://actt.albertadoctors.org/CPGs/Lists/CPGDocumentList/Cervical-Cancer-Screening-Summary.pdf
Alberta STI Treatment Guidelines	https://open.alberta.ca/publications/6880386
SOGC Clinical Practice Guideline No. 292 - Abnormal Bleeding in Pre-Menopausal Women	https://www.jogc.com/article/S1701-2163(18)30117-8/abstract
Choosing Wisely Canada – Recommendations from the Society of Obstetricians and Gynecologists of Canada	https://choosingwiselycanada.org/obstetrics-and-gynaecology/ #6: Don't routinely order hormone levels including estradiol, progesterone, follicle-stimulating hormone and luteinizing hormone in postmenopausal women or after a hysterectomy, either to diagnose menopause or to manage hormone therapy. #9: Don't do any surgical intervention, including ablation, for abnormal uterine bleeding until medical management (including the progesterone intra-uterine system) has been offered and either declined or found unsuccessful.

PATIENT RESOURCES

Information

Resources	Link
My Health.Alberta.ca > Health Information & Topics> **Abnormal Uterine Bleeding.** Information on causes, symptoms, treatments and resources for women with abnormal uterine bleeding.	https://myhealth.alberta.ca/health/pages/conditions.aspx?Hwid=aa76597
Online menstrual tracking tools (smartphone compatible) E.g. Clue - free application launched in 2013	https://helloclue.com/
Menstrual Diary to Monitor Premenstrual Symptoms (available from My Health Alberta). Print off a paper-based diary to track your menstrual cycle, along with symptoms and other factors pertinent to your health.	Menstrual Diary to Monitor Premenstrual Symptoms https://myhealth.alberta.ca/health/Pages/conditions.aspx?hwid=aa151402

[1] Sing, S, Best, C, Dunn, S et al. SOGC Clinical Practice Guideline No. 292 – Abnormal Uterine Bleeding in Pre-Menopausal Women. *J Obstet Gynaecol Can*. 2018;40(5):e391-e415

[2] Choosing Wisely. Society of Obstetricians and Gynecologists of Canada: *Nine Things Physicians and Patients Should Question.* Choosing Wisely Canada; 2019. https://choosingwiselycanada.org/obstetrics-and-gynaecology/

[3] Liu, Z, Doan, QV, Blumenthal, P and Dubois, RW. A Systematic Review Evaluating Health-Related Quality of Life, Work Impairment, and Health-Care Costs and Utilization in Abnormal Uterine Bleeding. Value in Health. 2007;10(3):183-194.