

This primary care pathway was co-developed by primary and specialty care and includes input from multidisciplinary teams from all five zones in Alberta Health Services, the Provincial Pathways Unit, and Patient and Family Advisors. It is intended to be used in conjunction with specialty advice services, when required, to support care within the medical home.

## **EXPANDED DETAILS**

# **Pathway Primer**

- This clinical pathway was created to provide primary care clinicians with guidance on evidence-based diagnosis, investigations, medical management, and appropriate referral to gynecology for patients with postmenopausal bleeding. This pathway does not apply to premenarchal persons with a uterus who have abnormal uterine bleeding please refer to the <a href="Provincial Primary Care Pathway for Abnormal Uterine">Provincial Primary Care Pathway for Abnormal Uterine</a>
   Bleeding instead for that guidance.
- Post-menopausal bleeding is defined as new onset bleeding that occurs after at least one year of amenorrhea an individual with a uterus older than 40 years of age. Post-menopausal bleeding occurs in between 4% -11% of women and is usually attributable to an intrauterine source. <sup>1</sup> However, bleeding can occur from the cervix, vagina, vulva, fallopian tubes, the bladder, or bowel.
- Abnormal uterine bleeding should be evaluated promptly, as it is the presenting sign of endometrial cancer in 90% of women. <sup>2</sup> Endometrial cancer is a very common gynecological malignancy, with an incidence in Canada of 19 cases per 100,000 women. <sup>3</sup>

## 1. History

The patient history obtained from the individual who presents with vaginal bleeding after menopause should focus on a review of risk factors for gynecological cancers and on eliminating other possible causes for bleeding as listed in the differential diagnosis. Use pronouns and names appropriate to the patient's gender identity and use gender-inclusive language throughout the interaction.

- . Evaluate the bleeding pattern, including quantity and timing
- · Assess pregnancy risk and sexual activity
- · Review the risk factors for gynecological cancer

### **Endometrial Cancer Risk Factors**

The average age for women with endometrial cancer is 61 years, but 5% - 30% of cases can occur in premenopausal women. <sup>4</sup> Women younger than 50 years of age can share many of the same risk factors for endometrial cancer as older women.

- o Age > 40 years
- Obesity (BMI > 30 kg/m2)
- Nulliparity
- o PCOS (polycystic ovarian syndrome)
- o Irregular cycles
- o Diabetes
- Lynch syndrome or HNPCC (hereditary non-polyposis colorectal cancer)- the most common hereditary form of hereditary colorectal cancer
- o Current tamoxifen use
- Unopposed estrogen exposure

## **Cervical Cancer Risk Factors**

- o Suboptimal cervical screening
- Multiparity
- o HPV Infection
- Sexual Activity:
  - Becoming sexually active at a young age (especially younger than 18 years old)
  - Multiple sexual partners
  - Having one partner who is considered high risk (someone with HPV infection or who has many sexual partners)
- o Weakened immune system
- o Chlamydia infection
- o Long-term use of oral contraceptives
- o Family history of cervical cancer

## **Ovarian Cancer Risk Factors**

- o Hereditary
  - Family history of ovarian cancer
  - Personal history of breast cancer
  - Alteration in BRCA1 or BRCA2
  - Lynch Syndrome
- o Reproductive
  - Advanced Age
  - Nulligravity
  - Infertility
- Hormonal
  - Early age at menarche
  - Late age at natural menopause
  - Hormone replacement therapy
  - Estrogen
  - Androgens
- $\circ \ \, \text{Inflammatory}$ 
  - Perineal talc exposure
  - Endometriosis
  - Pelvic inflammatory disease
- o Lifestyle
  - Obesity
- o Geography
  - Extremes in latitude

### Review Differential Diagnoses

Other potential causes for post-menopausal bleeding include:

- o Non-gynecologic sources of bleeding: bladder/kidney, urethral caruncle, and bowel as a source
- o Endometrial or cervical polyp
- o Proliferative endometrium, or endometrial hyperplasia (with atypia and without atypia)
- o Endometrial carcinoma
- Cervical dysplasia or cervical cancer
- o Vulvar, vaginal or endometrial atrophy
- o Submucosal fibroid
- o Sexually transmitted infection
- o Foreign body in the vagina (e.g. a retained pessary)

## 2. Assessment

The physical examination should identify evidence of systemic conditions or anatomical causes of bleeding.

- Providing Trauma-Informed Care is critical. Providers are encouraged to refer to the <u>Canadian Public Health</u>
   <u>Association Guide</u> for providing trauma informed exams.
- It is highly recommended that patients should receive a pelvic exam, including inspection of external genitalia, speculum and bimanual exams.
- Examine the external genitalia for ulcers or atrophic tissue, which could be the source of the bleeding.
  - If ulcers are present, initiate an urgent referral to gynecology for biopsy and medical management. A biopsy can be taken by the primary care provider if skilled in this area.
- Inspect and palpate internally for abnormalities such as fibroids, masses or cervical polyps. If concerning lesion or mass present, initiate an urgent referral to gynecology for biopsy and medical management. A biopsy can be taken by the primary care provider if skilled in this area.

## 3. Red flags

- · Patient looks unwell
- Tachycardia / hypotension
- Flooding through >1 high protection product (pad/tampon/menstrual cup) per hour
- Fever

If red flags are present or the patient is medically unstable, call <u>RAAPID</u> for an urgent referral to gynecology for immediate hospital evaluation or call 911.

## 4. Investigations

- If the patient is due, include a PAP test (TOP Cervical Cancer Screening Guideline).
- If there is post-coital bleeding or vaginal discharge, initiate testing for:
  - o Chlamydia
  - o Gonorrhea
  - o Trichomonas
  - o Bacterial Vaginosis
  - o Yeast
- If STI testing is positive, treat as per provincial guidelines (<u>Alberta STI Guidelines</u>).

If STI testing is negative, but the cervix appears friable, initiate a trial treatment for mucopurulent cervicitis (Alberta STI Guidelines). Persistent symptoms that do not respond to treatment should be referred to gynecology.

### Rule out and/or manage pregnancy:

- o Perform a sensitive urine or serum pregnancy test if there is any possibility of pregnancy.
  - If the patient has a positive pregnancy test and is bleeding, ensure the pregnancy is viable and intrauterine with a pelvic ultrasound.
  - If the pregnancy is NOT viable and intrauterine and the patient is stable, link to early pregnancy loss clinic, if available or local hospital. You can search the Alberta Referral Directory to find an early pregnancy loss clinic in your zone.
- o If this is a possible ectopic pregnancy or the patient is bleeding heavily or is medically unstable, call RAAPID for referral to gynecology.
- CBC/ Ferritin: For all stable patients, consider ordering a CBC/Ferritin. Treat as appropriate:
  - o Follow the Using Blood Wisely Guidelines when considering a transfusion
  - o Follow the Iron deficiency anemia pathway
  - o There is no utility to requesting FSH / LH / estradiol or progesterone levels. 5
- Thyroid testing: Thyroid functioning testing is not indicated unless there are clinical findings suggestive of an index of suspicions of thyroid disease. 3
- 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.
- Transvaginal Pelvic Ultrasound: For all stable patients, perform transvaginal pelvic ultrasound to rule out uterine structural causes for abnormal bleeding (e.g., polyp).
  - o You can refer to the Canadian Public Health Association Guide for providing trauma informed exams.
  - o If a Transvaginal pelvic ultrasound is not available or appropriate for the patient, please complete a trans abdominal ultrasound.

## 5. Management

A post-menopausal endometrial thickness assessment is best evaluated with a transvaginal ultrasound, so please encourage the patient to be prepared for this assessment.

### **Ultrasound findings:**

### • Fibroids / Polyps:

- o If a polyp or submucosal fibroid is present, these findings may cause post-menopausal bleeding and a referral to Gynecology is indicated.
- o Intramural fibroids and serosal fibroids do not usually cause post-menopausal bleeding, but if your patient is experiencing pressure symptoms or pain, a referral to gynecology is indicated.

## • Endometrial Thickness Assessment:

- o Endometrial thickness <5mm: If endometrial thickness <5mm with vaginal bleeding due to atrophy, attempt medical therapy.
  - Trial of topical moisturizer (e.g. Replens®)
  - Trial of topical vaginal estrogen (insertion)
    - For 14 days, applied at night daily, then two to three times/week for maintenance if symptoms improve.
  - o If the patient is taking tamoxifen, initiate a referral to Gynecology for any vaginal bleeding. Do not prescribe vaginal estrogens for atrophy, but you may trial Replens® or a non-hormonal vaginal moisturizer while awaiting referral.

Back to algorithm Updated: Oct 11, 2023 Page 5 of 9



#### ○ Endometrial thickness ≥5mm:

- o Counsel patient to stop any hormone therapies if taking estrogen.
- If endometrial thickness ≥5mm with vaginal bleeding, refer to gynecology or skilled community primary care physician for endometrial sampling.

## - Hyperplasia without atypia <sup>6</sup>\_:

- If sampling suggests hyperplasia without atypia, begin progesterone treatment (levonorgestrel IUD or progesterone 200mg PO QHS).
- A minimum treatment duration of 6 months is usually necessary. Repeat endometrial sampling is indicated in three to six months to ensure resolution of endometrial hyperplasia even if bleeding has ceased. If IUD is in place, endometrial sampling can be completed. Consider referral to gynecology if collection of repeat endometrial sampling support is needed.
- If bleeding persists, refer to gynecology.

#### Proliferative endometrium,

- No hyperplasia or malignancy, start medical treatment with Progesterone-only methods (e.g. Progesterone 100-200mg or levonorgestrel IUD).
- **Hyperplasia with atypia or malignancy:** If sampling suggests hyperplasia with atypia or endometrial carcinoma, make an urgent referral to Gyne-ONCOLOGY.

## Follow-up

- If there is successful cessation of bleeding on progesterone therapy, discontinue the therapy after one year.
- If there is successful cessation of bleeding with levonorgestrel IUD, remove after duration of device (~five years).
- If the patient has any further bleeding, they will need to be re-assessed again with transvaginal ultrasound, endometrial sampling, and should have a referral to gynecology for consideration of hysteroscopic sampling.

### 6. Advice Options

Severe bleeding or medical instability (i.e. soaking through a protective product per hour or abnormal vital signs). This patient needs to be directed to hospital through RAAPID or the ER. Call RAAPID for on-call gynecologist or 911.

Zone	Program	Online Request	Phone Number	Hours of operation	Anticipated Turnaround Time	
Urgent Telephone						
North, Edmonton, Central, Calgary, South	RAAPID  (+) RAAPID  Refural, Access, Advice, Placement, Information & Destination	N/A	North: 1-800-282-9911 780-735-0811 South: 1-800-661-1700 403-944-4486	7 days per week 24 hours	1 hour	
Non-Urgent Electronic						
Calgary, Edmonton	eReferral (FAQ)  eReferral		N/A	Mon - Fri	5 business days	
Non-Urgent Telephone - on next page						

Non-Urgent Telephone						
Edmonton, North	ConnectMD	Online Request	1-844-633-2263	<b>Mon - Fri</b> 9am – 6pm*	2 business days	
Calgary	Specialist Link Specialist Link Connecting Personal and Expecually Care	Online Request	403-910-2551	Mon - Fri 8am – 5pm*	1 hour	

<sup>\*</sup>There are some exceptions to non-urgent telephone program hours of operation and exclusion

## 7. Referral Process

- Referral pathways are guidelines to help referring providers know what information, labs and diagnostic imaging are required with their referral to a specialty.
- Referral pathways are co-designed with Primary and Specialty Care, AHS Operations, and patients to ensure the
  right amount of information is included throughout the referral process to triage the patient as quickly as
  possible.
- For all referrals to gynecology please ensure to follow the <u>Provincial Adult Gynecology Referral Pathway</u> and use the <u>Provincial Referral Form</u> (if available)
  - o If provincial referral pathway is not yet available Send referral to Gynecology; see Alberta Referral Directory for referral information.
- For hyperplasia with atypia or malignancy, send referral to Gyne-**Oncology**; see <u>Alberta Referral Directory</u> for referral information.

# **BACKGROUND**

### About this pathway

- This pathway was developed in collaboration with gynecologists, primary care physicians, patient and family advisors, and the Alberta Health Services (AHS) Provincial Pathways Unit.
- · Condition-specific clinical pathways are intended to offer evidence-based guidance to support primary care providers in caring for patients with a range of clinical conditions.

#### Authors and conflict of interest declaration

- This pathway was initially developed 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.
- In March 2023, in collaboration with gynecologists, primary care physicians, patient and family advisors, and the Alberta Health Services (AHS) Provincial Pathways Unit the Calgary Zone pathway was reviewed and revised in order to make it a provincial primary care clinical pathway for use in Alberta.

### Pathway review process, timelines

• Primary care pathways undergo scheduled review every two to three years, or earlier if there is a clinically significant change in knowledge or practice. The next scheduled review is October 2025. However, we welcome feedback at any time. Please email comments to AlbertaPathways@ahs.ca.

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## PROVIDER RESOURCES

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

## **PATIENT RESOURCES**

Resources	Link	
Patient Pathway on MyHealth Alberta > A webpage and two PDF formats are available to allow for easy printing, download, or scanning a QR code with the patient's smart phone for more information at their convenience	https://myhealth.alberta.ca/HealthTopics/post- menopausal-bleeding-pathway/Documents/ post-menopausal-bleeding-pathway- summary.pdf	
MyHealth.Alberta.ca - Menopause and Perimenopause: Information on causes, symptoms, treatments and resources for women	https://myhealth.alberta.ca/health/pages/ conditions.aspx?Hwid=hw228763#hw228868	

# **REFERENCES**

Back to algorithm Updated: Oct 11, 2023 Page 9 of 9

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<sup>&</sup>lt;sup>2</sup> ACOG Committee Opinion No. 734 Summary: The Role of Transvaginal Ultrasonography in Evaluating the Endometrium of Women With Postmenopausal Bleeding, Obstetrics & Gynecology: May 2018 - Volume 131 - Issue 5 - p 945-946 doi: 10.1097/AOG.0000000000002626

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<sup>6</sup> Auclair MH, Yong PJ, Salvador S, Thurston J, Colgan TTJ, Sebastianelli A, Guideline No. 390-Classification and Management of Endometrial Hyperplasia. J Obstet Gynaecol Can. 2019 Dec;41(12):1789-1800. doi: 10.1016/j.jogc.2019.03.025. Erratum in: J Obstet Gynaecol Can. 2020 Oct;42(10):1287. PMID: 31785798.