

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

PATHWAY PRIMER

- This pathway aims to achieve a provincial standard of care when referral from the primary care setting to specialty care should be made using standardized testing and referral triggers. This pathway is limited to the care of Albertans over the age of 18 years of age with hematuria.
- Hematuria is defined as the presence of red blood cells in urine. This is further subcategorized into microhematuria (nonvisible) and gross hematuria (visible). (5,8,9,12)
- Hematuria is present in 20% of all diagnosed urological disorders. (9) There are numerous medical conditions that may present with hematuria however there is a heterogenous group of patients with a broad range of risk factors for genitourinary cancers (10). It is important that these patients are referred to specialty care when required.
- There is an association of both gross hematuria and microhematuria with bladder and kidney cancer, the focus of evaluation has been excluding cancer. "Cancer is more likely to be identified in men than in women when they are evaluated for microhematuria. Worldwide, estimates of the incidence of kidney cancer are 6.0 cases per 100,000 person-years for men and 3.1 cases per 100,000 person-years for women, and estimates of the incidence of bladder cancer are 9.0 cases per 100,000 person-years for men and 2.2 cases per 100,000 person-years for women, according to GLOBOCAN, a registry of data on the global incidence of cancer,⁹ a result also found in a 2020 meta-analysis". (12)
- Primary care providers should rule out and treat nonmalignant causes of hematuria and perform risk stratification by following the pathway.
- Use of anti-coagulants or anti-platelet therapy does not exclude a patient from evaluation of hematuria. (5,8,9,12)

EXPANDED DETAILS

1. History

Rule Out Treatable and/or Identifiable Cause - Evaluation performed by primary care providers.

- Urinary Tract Infections (UTI) Effective treatment, retest. If hematuria persists, continue on pathway Evidence based criteria for urinary infection testing Algorithm (albertahealthservices.ca). (6)
- Renal Colic (Suspected) Order CT Renal Colic Protocol if symptoms of renal colic present. If no stones identified, continue on pathway.
- Gynecologic cause.
- Traumatic catheterization/ instrumentation.
- Exercise induced hematuria Proceed on hematuria pathway.
- Myoglobinuria Differentiating blood from myoglobin in the urine is important. This is one of the reasons why a urinalysis is required even with gross hematuria. A dipstick alone cannot distinguish the difference. (12)

2. Microhematuria

- Defined as ≥3 red blood cells per high-power field on microscopic evaluation on urinalysis. It should not be defined by a positive dipstick test alone. A positive urine dipstick test indicates the need for prompt formal microscopic evaluation. (8)
- The probability of diagnosing malignancy in a patient with microhematuria is influenced by the presence or absence of known cancer risk factors. (8,9)
- The overall rate of urologic malignancy in patients with microhematuria is low. (8)

Risk factors for urothelial carcinoma

The major risk factors for urothelial cancers are listed below:

- **Smoking** history >10 pack-years Tobacco use is the most significant risk factor of urothelial carcinoma, being the attributed cause of 50% of bladder cancer cases. (2)
- Men age >40 years. (5)
- Women age >50 years. (5)
- **Cyclophosphamide or ifosfamide** Having previous treatment with these drugs can increase risk of bladder cancer as they are bladder irritants. (1)
- **Prior radiation to pelvis** People who have treatment with radiation therapy to the abdomen or pelvis have increased risk of bladder cancer. Exposure to radiation at work or surviving an atomic bomb or nuclear accident increases risk of bladder cancer. (1)
- Lynch Syndrome The National Cancer Institute defines Lynch Syndrome as "An inherited disorder that increases the risk of developing colorectal cancer, endometrial cancer, ovarian cancer, and many other types of cancer, such as cancers of the stomach, small intestine, pancreas, bile duct, urinary tract, and brain, often before age 50." (4)
- Schistosomiasis A parasitic worm that infects the bladder and causes irritation, found more commonly in developing countries. (1)
- Chronic bladder irritation From frequent infections, prolonged catheterizations. (1)
- Workplace exposures Despite manufacturing and legislative changes to improve workplace safety standards many bladder cancers still arise through occupational carcinogen exposure. These include exposures to aromatic amines, and polycyclic aromatic hydrocarbons (PAHs) which are a class of chemicals that occur naturally in coal, crude oil, and gasoline. They also are produced when coal, oil, gas, wood, garbage, and tobacco are burned.

Examples of higher risk professions:

- o Industry and manufacturing: rubber, plastic, and dye workers
- o Leather workers (e.g., shoe repairers)
- o Plumbers, Electricians, Mechanics, Autobody Repair

- o Telephone linespersons, cable workers
- o Electrical Engineers
- o Janitorial Workers
- o Food preparation workers who are exposed to organic solvents (benzene, toluene, and xylene)
- o Healthcare professionals exposed to certain inhalants
- Firefighters can be exposed to combustion products PAHs, and polyhalogenated dibenzodioxins or dibenzofurans from flame-retardants. (3)
- Arsenic exposure Sometimes found in drinking water, naturally occurring, leeching from rocks, and soil. Can also be present because of industry such as mining, manufacturing etc. (1)

If No Risk Factors are Present:

- The risk of upper tract malignancy for these patients is considered exceedingly low. (8) Furthermore, there is limited evidence in relation to the evaluation of the risk/benefits of the urologic work up with imaging and cystoscopy (this would be offered by urology referral). (8)
- Therefore, the next step that these patients have a **urinalysis repeated in one month.** If the patient does have persistent hematuria on that urinalysis they should proceed with testing and referral. Patients with persistent microhematuria have been shown to have a higher rate of cancer on upon evaluation when compared to those with negative repeat urinalysis. (8) Patients without persistent microhematuria do not require evaluation.

If Risk Factors are Present:

- A second urinalysis should be repeated in one month. If microhematuria persists, the patient should proceed for testing. If no hematuria remains, the patient may be retested in one year. A practitioner may consider eAdvice if they feel a patient is of particular concern or risk of cancer.
- Patients with a second positive urinalysis for microhematuria are considered intermediate to high risk for urothelial tract cancer however this is dependent on the type and number of risk factors present. (8)

3. Gross hematuria

- Blood is visible in urine.
- Gross hematuria frequently has a clear explanation that aligns with the patient's history, signs, and symptoms (e.g., the passage of a kidney stone, acute hemorrhagic cystitis, or a sickle-cell crisis). (12)
- An unexplained episode of gross hematuria may be an indication urothelial cancer and further work up via Diagnostic Imaging and Urology consult is warranted. (12)

4. 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. These 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. To ensure referring providers have referral information at their fingertips, referral pathways may link to clinical pathways when available. AHS manages referral pathways and extensive work is ongoing as part of the <u>Alberta Surgical Initiative</u>. If you have questions or want to know more about the referral pathway development process, please email access.ereferral@ahs.ca.

- Urgent Referral Call surgeon on call via RAAPID or call 911.
- Follow the Provincial Urology, Adult Referral Pathway.
- <u>Alberta Referral Directory</u> is also a helpful resource for all referral information.

5. Advice Options

You can request non-urgent advice at any point when uncertain about medications, next steps in treatment, investigations, or resources available.

For emergency medical attention call RAAPID for on-call surgeon, or 911.

Zone	Program	Online Request	Phone Number
Urgent Telephone			
All Zones	RAAPID CHD RAAPID Identif. Access. Advice. Pleasmark. Marchadian & Destination	N/A	North: 1-800-282-9911 or 780-735-0811 South: 1-800-661-1700 or 403-944-4486
Non-Urgent Electronic			
All Zones	Netcare eReferral		N/A
Non-Urgent Telephone			
Edmonton, North	ConnectMD ConnectMD	Online Request	1-844-633-2263

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BACKGROUND

About this pathway

- This pathway was developed in collaboration with Urologists, Oncologists, Radiologists, Primary Care Providers, Patient and Family Advisors, Alberta Health Services Provincial Pathways Unit, and the Cancer Strategic Clinical Network.
- 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 reviewed and revised under the auspices of the Cancer System Innovation and Integration Team in Alberta, by a multi-disciplinary team.
- Names of the content creators and their conflict-of-interest declarations are available on request by emailing <u>AlbertaPathways@ahs.ca</u>.

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 2027. However, we welcome feedback at any time. Please email comments to <u>AlbertaPathways@ahs.ca</u>.

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PATIENT RESOURCES

Information/ Services available

Blood in the Urine: Care Instructions (alberta.ca)	See Red? - Bladder Cancer Canada
Hematuria (Blood in Urine) National Kidney Foundation	Bladder cancer Canadian Cancer Society
Symptoms & risk factors - World Bladder Cancer	<u>What is Upper Tract Urothelial Carcinoma</u>
Patient Coalition	(UTUC)? (bcan.org)
Quit with Confidence: Deciding to quit -	<u>Get help to quit smoking Canadian Cancer</u>
Canada.ca	<u>Society</u>

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