Bladder Cancer

PATIENT Fact Sheet

Introduction

The urinary bladder is a muscular organ that stores urine made by the kidney. Urine flows from the kidney through tubes called *ureters* to the bladder. As the bladder fills, the muscular wall of the bladder stretches. Sensors in the muscle wall sense fullness and send a signal through your nervous system to the brain making you aware of the need to void (urinate). The bladder usually feels full when it is holding about two cups of urine. You empty your bladder of urine through a tube, called the *urethra,* when it is socially acceptable.

The muscle wall of the bladder is made up of three layers. The inner layer lining inside the kidney, ureters, bladder, and urethra is made up of transitional cells. A support or basement membrane separates the inner lining from the middle layer. The middle layer is made up of connective tissue, and the outer layer is muscle tissue. Most (90%) bladder cancer in the United States is found in the inner lining (transitional cell lining) of the bladder.

Bladder cancer is the fourth most common cancer among men and the 11th most common cause of cancer among women. More than 80,000 new cases will be diagnosed in 2019 with an estimated 17,000 deaths. Bladder cancer occurs two to three times more often in men than women and is more common in Caucasians than African Americans or Hispanics. The average age at diagnosis is 73 years.

Risk Factors Associated with Increased Chance for Developing Bladder Cancer

- Smoking or secondhand smoke exposure is the leading risk factor for development of bladder cancer. Smokers are three times more likely to get bladder cancer than nonsmokers.
- Increasing age.
- Family history or genetic defects.
- Occupational exposure, especially in those who work with dyes (aromatic amines), rubber, leather, textiles, certain paint products, and printing.
- Chronic inflammation, chronic urinary tract infections caused by parasites (common outside the United States) or chronic kidney stones.
- Chronic inflammation associated with chronic indwelling urinary catheter.
- History of previous bladder cancer.
- Previous pelvic radiation.
- Previous chemotherapy.

What Are the Signs and Symptoms of Bladder Cancer?

Often people have no symptoms of bladder cancer. The most common sign of bladder cancer is visible blood in the urine, or blood that is only visible on microscopic examination of the urine (microscopic hematuria). There is often no pain associated with the blood in the urine. Some symptoms that may be present include urinary urgency (strong sensation of the need to urinate), frequency, and difficulty with urination or emptying the bladder. There may be pain when urinating, flank pain, back or abdominal pain, and loss of appetite or weight loss. Many of these symptoms can also be due to other causes such as bladder stones or infection.

How is Bladder Cancer Detected?

- If your healthcare provider thinks your symptoms might be due to bladder cancer, then he/she will review your medical history including smoking history or secondhand smoke exposure along with a physical examination. The healthcare provider may also order laboratory tests such as cytology to look for cancer cells under the microscope.
- A cystoscopy is a minor procedure performed under local anesthetic, often in the urology office, which involves the use of a cystoscope, a small thin tube with a light at the end. The cystoscope is gently inserted into the urethra and allows the healthcare product look inside the bladder and visualize the

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bladder wall. A local anesthetic is used to numb the urethra prior to the cystoscopy.
- Imaging studies are also done to examine the kidneys, ureters, bladder, and urethra. A CT urogram will likely be ordered by the healthcare provider, especially if there is visible blood in the urine or microscopic blood. To look for spread of cancer, the healthcare provider might also order a chest x-ray and bone scan.

Diagnosis of Bladder Cancer

To diagnose bladder cancer, the physician will perform a procedure called *transurethral resection of bladder tumor* (TURBT) or bladder biopsy. A TURBT or bladder biopsy is typically done in the operating room where a cystoscope is inserted along the urethra into the bladder to visualize the bladder wall lining. Any abnormal-appearing tissue is removed for examination under a microscope. Removal and examination of tissue is the only way to know if bladder cancer cells are present. To grade the cell growth, a pathologist will examine the cancer cells for how fast the cells are growing. The more aggressively the cancer cells are growing, the higher the grade of cancer. The more slowly they are growing, the lower the grade.

Low grade: This type of cancer can recur but rarely spreads to the bladder muscle.

High grade: This type does not look like normal tissue; it is more likely to grow quickly and invade the bladder muscle wall.

Carcinoma in situ (CIS) describes high-grade, flat tumors that sit on top of the lining of the bladder. The tumor cells are flat and sometimes appear as inflamed, reddened areas within the lining of the bladder.

Another type of bladder tumor commonly seen is a *papillary tumor*, which is a raised tumor that lies on a stalk, with a shape similar to cauliflower. A papillary tumor can be a low-grade or high-grade tumor.

Once bladder cancer is diagnosed, the physician needs to determine the extent of disease and whether or not it has spread to other areas of the body. This is done through staging:
- T0: No tumor present.
- Tis (CIS): Carcinoma in situ.
- Ta: Papillary tumor without invasion into the bladder wall.
- T1: Tumor has invaded the connective tissue under the surface of the bladder lining (lamina propria).
- T2: The cancer has spread into the muscle layer of the bladder.
- T3: The cancer has spread to perivesical fat, which is a lining of fatty tissue that surrounds the bladder.
- T4: The cancer has spread into the organs near the bladder; for men this is usually the prostate, and for women, this is often the uterus and vagina. In men or women, it can also spread to the pelvic area, lymph nodes, and beyond.

Treatment of Bladder Cancer

Decisions about what treatment is best will be made by you and your healthcare provider based on the stage and grade of tumor. It will also be important to consider your age, general health, and benefits and side effects of the treatment options. No matter what kind of bladder cancer is found it may require lifelong monitoring.

Generally, for superficial bladder cancers (Tis, Ta, or T1), the following treatment options are suggested alone or in combination with one another:
- Surgery is the most common treatment for bladder cancer. Transurethral resection (TUR) is done to remove all the superficial cancer cells. Using a cystoscope inserted along the urethra, the physician will insert a tool with a small wire loop at the end to remove the cancer and to burn (fulgurate) the base of the tumor, or he/she might use a high-energy laser to destroy any remaining cells.
- Intravesical chemotherapy involves placing a drug into the bladder. It can be a single dose instilled right after the tumor is removed to kill any remaining cancer cells. It can also be given at weekly intervals for up to 6 weeks. These 6 weekly treatments are not started until 2 to 4 weeks after the surgery and are used to prevent the cancer from recurring. Intravesical chemotherapy agents include Mutamycin® (mitomycin C), Gemzar® (gemcitabine), Valstar® (valrubicin), and Taxotere® (docetaxel).
- Bacillus Calmette-Guerin (BCG) is a drug used for intravesical immunotherapy treatments. It is instilled into the bladder through a catheter. BCG is a weakened tuberculosis vaccine that uses the body's own immune system to attack the cancer cells on the lining of the bladder. It is usually administered in clinic once a week for 6 weeks. Patients are instructed to hold the instillation for 1 to 2 hours then urinate at home. Interferon-alpha is sometimes used in combination with BCG.
- If the intravesical chemotherapy or BCG treatments are effective, additional bladder instillations may be given periodically for maintenance to prevent recurrence of the cancer.

For muscle-invasive bladder cancer (T2- T4), the physician might recommend the following options:

- Bladder saving surgery, also called a segmental or partial cystectomy, removes only the part of the bladder affected by cancer, along with nearby lymph nodes. (This is rarely performed.) This is only an option when it is the patient's first tumor and the tumor is in a good location that can spare the important parts of the bladder to save function. No carcinoma in situ can be present for the patient to be a candidate for partial cystectomy with removal of nearby lymph nodes, as well as any organs in the area where the cancer may have spread.
- If the tumor has invaded the muscle, transurethral resection and/or intravesical therapy is unlikely to cure the cancer. Radical cystectomy is the gold standard treatment for muscle-invasive bladder cancer. If the patient is not a good candidate for major surgery due to other illnesses, then bladder-preserving therapy including chemotherapy and radiation can be used but with lower cure rates.
- Radical cystectomy for men requires removal of the prostate gland and seminal vesicles. For women, this may include removal of the cervix, ovaries, uterus, urethra, fallopian tubes, and a portion of the vagina.
- When removing the bladder, the physician will need to create a new way to store and/or drain urine. This is called a *urinary diversion.* There are three types of urinary diversions: continent, incontinent, or neobladder. For the continent diversion, the physician might use part of the small intestine to create an internal pouch with a valve that allows drainage of urine several times a day using a catheter. An incontinent diversion, also known as an ileal conduit or urostomy, uses a section of small bowel to create a passageway for urine to flow from the ureter to the outside through an opening (stoma) in the skin. The urine drains through the stoma into a bag or pouch worn on the outside of the body. A neobladder is created using a portion of the intestines and placing it in the same place as the original bladder. The neobladder will be connected to the urethra allowing the patient to urinate more normally by tightening the abdominal muscles and relaxing the pelvic floor muscles to push urine through the urethra. With a neobladder, there are risks of urinary incontinence or urinary retention requiring catheterization of the urethra intermittently to empty the bladder.
- External beam radiation therapy is usually offered if the patient is not a surgical candidate or the tumor cells cannot be removed without more risk. Side effects from radiation include bladder infection, infection of the prostate, diarrhea, and local skin irritation
- Chemotherapy can either be given before surgery (neoadjuvant) or after surgery (adjuvant). Many clinical trials are evaluating the benefit of both these treatment options.
- In some situations, a combination of TURBT, chemotherapy, and radiation can be used to preserve the bladder if the patient is not a candidate for the gold standard treatment of radical cystectomy.

Prevention of Bladder Cancer

- Stop smoking and avoid tobacco smoke in your environment. There are multiple programs and medications available to help with quitting smoking.
- Drinking plenty of water, at least 8 glasses a day, and eating a diet high in fruits and vegetables may help prevent bladder cancer.
- Adding antioxidants to the diet may play a role in cancer prevention. Sources of antioxidants include broccoli, kale, berries, nuts, beans, coffee, russet potatoes, and artichokes, to name a few.

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