

THE UROLOGY GROUP

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BLADDER CANCER

HOW COMMON IS BLADDER CANCER?

It was estimated that in 2010 approximately 70,000 Americans would be diagnosed with bladder cancer and 15,000 would die of this cancer. Male patients outnumber female patients three to one, making bladder cancer the fourth most common cancer in men.

The **kidneys** make urine, which is transported to the **bladder**. Urine is stored in the bladder until the bladder is full. During urination, the bladder empties the urine through the **urethra**, the urinary pathway. The lining of the bladder and urinary tract is composed of specialized cells called **urothelium** or **transitional cells**. Over 90% of bladder cancer cases involve this lining and are referred to as **urothelial cancer** or **transitional cell carcinoma**.

WHAT ARE RISK FACTORS FOR BLADDER CANCER?

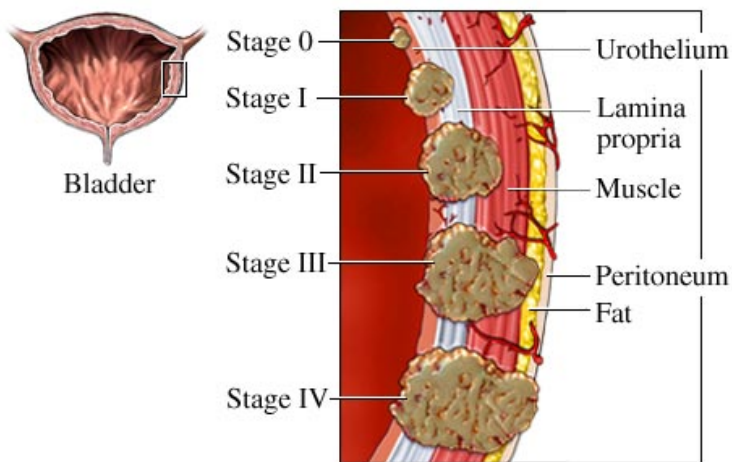
Smoking is the most important risk factor for bladder cancer. There is an approximate threefold increased risk of bladder cancer among current and former smokers. Exposure to certain chemicals such as **aniline dyes** in the fabric industry and **aromatic amines** used in various industrial processes, is also linked to bladder cancer. **Radiation** to the pelvis and the chemotherapy agent, **cyclophosphamide**, have also been linked to bladder cancer.

HOW IS THE STAGE AND GRADE DETERMINED?

STAGE

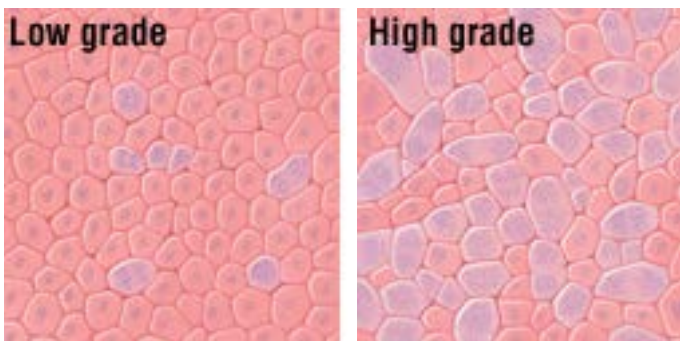
Stage refers to the anatomic extent of the cancer. The bladder is comprised of the three layers: epithelium, connective tissue and muscle. The **stage** of the bladder cancer is determined by how deep the cancer invades into the layers of the bladder.

Non-muscle invasive bladder cancer (which includes Ta, T1 and carcinoma in situ) is confined to the epithelium and underlying supporting connective tissue. In contrast, **muscle-invasive bladder cancer** (T2) or beyond the bladder (T3-4) and represents more advanced disease.



GRADE

Grade refers to the microscopic appearance of the bladder cancer cells. Bladder cancer is assigned a **grade** based on how aggressive the tumor appears on pathologic exam once the cancer has been removed and examined by the pathologist. Grades include Papillary Urothelial Neoplasm of Low Malignant Potential (PUNLMP), low grade and high grade. The higher the grade, the more likely the cancer is to recur and progress deeper into the bladder layers.



WHAT ARE THE SYMPTOMS OF BLADDER CANCER?

Most people with bladder cancer are diagnosed after an episode of blood in the urine (**hematuria**). Hematuria may be referred to as gross hematuria (seen by the naked eye) or microscopic hematuria (seen on a urine study). In some cases, symptoms may only be irritative voiding symptoms, such as urinary urgency and frequency.

Patients who have had gross hematuria should have a full urological evaluation. Patients with microscopic hematuria who are older than 40 years of age or younger than 40 years with risk factors for bladder cancer, should undergo a complete urological evaluation. Evaluation includes a **cystoscopy** (look in the bladder with a camera), **cytology** (check the urine for cancer cells) and imaging of the kidneys and collecting system with contrast enhanced computerized tomography (CT scan or CT Urogram).

HOW IS BLADDER CANCER TREATED?

Transurethral Resection of Bladder Tumor (TURBT) is the standard of care for initial management of bladder cancer and serves a diagnostic and therapeutic purpose. It is done in the operating room under regional (spinal or epidural) or general anesthesia. An instrument

called a cystoscope is placed through the urethra into the bladder and the bladder tumor is resected (removed). In some cases, a **catheter** may be left in place to drain the bladder and allow the bladder to heal for several days. Hazards of the procedure include bleeding, perforation of the bladder, damage to surrounding organs, fluid absorption and complications from anesthesia.

A single dose of chemotherapy with **mitomycin C** may be used following TURBT. This chemotherapy solution is placed in the bladder at the end of the operation and typically stays in the bladder for one hour after surgery and is then drained in the recovery room.

WHAT HAPPENS AFTER THE TUMOR IS REMOVED?

Subsequent management depends on the stage and grade of the tumor. Low grade, superficial tumors (Ta) can be followed with office cystoscopy and cytology every three months, with gradually increasing intervals. High grade tumors are often managed with a **re-staging TURBT**, a procedure to resect more deeply at the site of the tumor, as up to 60% of these tumors may be understaged, or have grown further into the bladder layers than seen on the first surgery.

WHAT IS BCG IMMUNOTHERAPY?

Bladder cancer has the potential to **recur** such that new bladder tumors form. Bladder cancer can also **progress**, such as becoming a higher grade or invading deeper into the bladder wall. **Bacille Calmette Guerin (BCG)** is a bacteria that triggers the body's immune system when placed in the bladder. It is first line treatment for carcinoma in situ (CIS) and is used to help prevent recurrence and progression of bladder cancer. BCG is instilled into the bladder via a catheter 2 to 4 weeks after TURBT, once the bladder has had a chance to heal. **BCG induction therapy** consists of 6 weekly instillations in the bladder. The BCG is allowed to remain in the bladder for one hour.

After the initial six-week course of BCG is treatment is complete, additional **maintenance therapy** may be given for the next one to three years.

Side effects of the BCG treatment may include bladder irritation with urinary urgency and frequency and blood in the urine. Other local side effects may include inflammation of the prostate, testicle and epididymis (gland above the testicle). Systemic side effects may include fever and malaise (feeling ill). Serious side effects occur in less than 5% of patients and include blood infection requiring antibiotics or hospitalization. BCG therapy may not be used in patients with immunosuppression or those on steroid (prednisone) treatment. BCG treatment may be withheld if there is catheter trauma, urinary tract infection or recent gross hematuria.

WHAT IF BCG DOESN'T WORK?

If the bladder cancer recurs after induction therapy or the stage or grade of the tumor worsens while on BCG, the cancer is not responding to BCG therapy. In this case bladder removal (**radical cystectomy**) may be considered in patients healthy enough to undergo this surgery. Performing a radical cystectomy within two years of the start of BCG therapy can improve survival compared to waiting.

HOW IS MUSCLE-INVASIVE BLADDER CANCER TREATED?

If the bladder cancer has grown into the muscle layer of the bladder or beyond, bladder removal

(radical cystectomy) and lymph node dissection is indicated for those healthy enough to undergo the surgery. Preoperative evaluation includes blood work, urine studies and chest x-ray and CT scan to be sure the cancer has not spread. In men, the surgery involves removal of the bladder, and typically the prostate and glands behind the prostate (seminal vesicles). In women, the surgery involves removal of the bladder, typically uterus and part of the vagina. The surgery can be done using open, laparoscopic (“keyhole surgery”) or robotic surgery. Surgery typically lasts 4 to 8 hours and involves a 5 to 8 day hospitalization.

When the bladder is removed, a new route for urine to leave the body is created. Options include an **ileal conduit**, which uses a loop of bowel to bring urine outside the body to be collected in a bag. A **neobladder** uses intestine to make a bladder substitute.

HOW IS BLADDER CANCER MONITORED?

Because there is a risk of recurrence and progression of bladder cancer, ongoing follow-up is needed including **cystoscopy** and **cytology** (as described above). These surveillance procedures are done three months after surgery and then at repeated intervals according to the tumor grade. High grade tumors often require lifelong surveillance. Imaging of the collecting system (such as contrast CT scan) may be done at periodic intervals depending on the tumor grade and risk factors.

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Reference: Gorin MA, Ayyathurai R and Soloway MS: Transurethral management of urothelial carcinoma of the bladder. American Urologic Association Update 2011, Lesson 23, Volume 30. © 2011 American Urological Association, Education and Research Inc., Linthicum, MD.

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