BLADDER CANCER: PATIENT INFORMATION

The *bladder* is the balloon like organ located in the pelvis that stores and empties urine. Urine is produced by the *kidneys*, is conducted to the bladder by the *ureters,* and is discharged from the body through the *urethra*.

In the United States, the incidence of bladder cancer has increased greatly over the last few decades, with more than 60,000 new cases diagnosed each year. It is the fourth most common cancer in men and the eighth in women. The incidence of bladder cancer increases with age and is three times more common in men than women. 80% of newly diagnosed individuals are 60 years of age or older. At present, about 20% of patients die each year, but when the disease is diagnosed and treated in an early stage, the chances of survival are excellent, highlighting the importance of a timely and accurate diagnosis. More than 90% of newly diagnosed bladder cancers are *uothelial carcinomas*. Approximately 75% of patients present with superficial cancer; 20% with invasive disease; and the remaining 5% with metastatic disease (spread beyond the confines of the bladder) at initial diagnosis.

The highest incidence of bladder cancer is in industrialized countries. Cancer-causing agents (carcinogens) are often responsible for bladder cancer. Bladder cancer is highly associated with **cigarette smoking**—even if one stopped smoking years ago, the risk is related to the *quantity* of cigarettes smoked over the years. The carcinogens that are present in cigarettes are absorbed through the lungs into the bloodstream and are filtered through the kidneys directly into the bladder, where the prolonged contact time with the lining of the bladder leads to cancerous changes. Certain occupations are also at higher risk for bladder cancer because of exposure to chemicals—these include: hairdressers, painters, machinists, printers, and those who work with dyes, textiles, rubber, leather, and petrochemicals.

Bladder cancer most commonly presents with symptoms of *hematuria* (blood in the urine), either *visible* or *microscopic* (seen only under microscopic magnification). It may also cause *irritative lower urinary tract symptoms* including urgency, frequency, discomfort with urinating, and incontinence.

The evaluation for hematuria includes *imaging, cytology,* and *cystoscopy*. Imaging tests are means of scrutinizing the anatomy of the urinary tract, typically through ultrasonography, computerized tomography (CT), or magnetic resonance imaging (MRI). Cytology is a microscopic inspection of a urine sample by a pathologist for the presence of abnormal or cancerous cells that slough off the lining of the bladder, very much similar to a Pap smear done to screen for cervical cancer. Cystoscopy is a visual inspection of the entire *lower urinary tract* (bladder and urethra) using a tiny, flexible, lighted instrument attached to a camera and monitor. When a bladder tumor is identified on cystoscopy, attention

is directed to the number of tumors present, their size, location within the bladder, and physical appearance. A *papillary* appearance consists of *fronds* (finger-like projections floating in the bladder) with a narrow attachment to the bladder lining versus a *sessile* appearance, in which the tumor appears solid and is widely attached to the bladder lining.

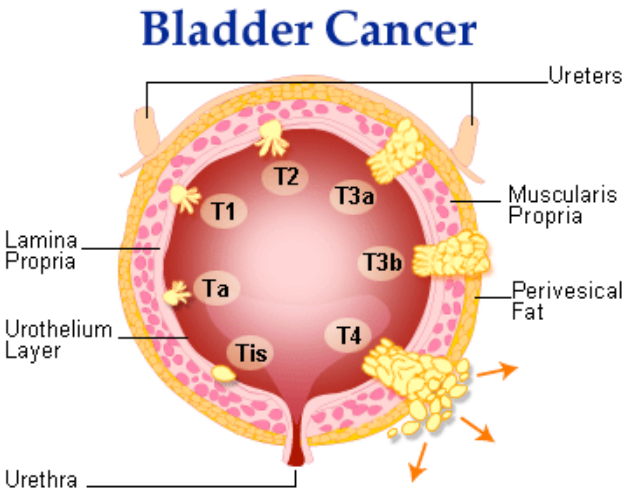
Once a bladder abnormality is diagnosed, it needs to be removed and sent for pathological evaluation. This is performed under anesthesia using the cystoscope and an electric loop, which is used to remove the area(s) of concern. This procedure is referred to as a *Trans-Urethral Resection of the Bladder Tumor* (TURBT). Typically, a *catheter* (a small tube that drains urine out of the bladder through the urethra) will need to be placed for a few days after the biopsy to facilitate bladder healing.

The tissue that is removed is carefully examined by the pathologist, who will provide invaluable information regarding *malignancy vs. benignity*, *type* of tumor, *depth* of tumor, and *grade* of tumor. The vast majority of bladder tumors are *transitional cell cancers*, also known as *urothelial cancers*, referring to the cells that line the bladder. A minority of bladder tumors are *squamous cell cancers* or *adenocarcinomas.* Depth refers to the degree that the cancer is growing into the bladder wall. Bladder cancers are broadly categorized into *superficial* and *deep*. Superficial tumors are largely confined to the bladder lining and superficial layers and do not penetrate the muscle layer of the bladder, whereas deep tumors have "roots" that penetrate the muscular wall of the bladder. Tumor grade refers to how much the microscopic appearance of the cancer deviates from the microscopic appearance of healthy bladder cells. Low-grade cancers are similar in cellular appearance to normal bladder cells and generally behave in an indolent (slow) fashion versus high-grade cancers that can often behave aggressively. Other factors of prognostic importance are the number of tumors present, the size of the tumors, and their physical characteristics.
In general, the best prognosis is for a solitary, small, superficial, low-grade papillary tumor and the worst prognosis is for a *multi-focal* (originating from many different areas of the bladder), large, invasive (deep), sessile, high-grade tumor.

The biopsy information will enable the *staging* of the bladder cancer, a means of classifying the cancer according to the *TNM system*. TNM stands for Tumor, Nodes, and Metastases. Essentially, *T* refers to tumor extent, *N* refers to the presence of lymph node involvement, and *M* refers to metastasis, a term for spread beyond the confines of the bladder. It is extraordinarily unlikely for a superficial cancer to cause lymph node or distant spread, these events occurring with muscle-invasive or more deeply invasive cancers.

Staging of bladder cancer is as follows:

- **Ta**: Superficial cancer is found only in polyps (papillary) on the surface of the inner lining of the bladder. Lymph nodes are not involved and cancer has not spread (metastasized).
- **Tis**: Carcinoma-in-situ. High-grade tumor is found only in flat lesions on the surface of the inner lining of the bladder. Lymph nodes are not involved and cancer has not spread (metastasized).
- **T1**: Tumor is found in the connective tissue below the lining of the bladder but has not spread to the bladder muscle. Lymph nodes are not involved and cancer has not spread (metastasized).
- **T2**: Tumor has spread to the muscle layer deep to the lining of the bladder.
- **T3a**: Tumor has spread through the muscular wall of the bladder into the fatty tissue layer.
- **T3b**: Tumor has spread through the muscular wall of the bladder into the fatty tissue layer and a mass is visible to the eye.
- **T4**: Tumor has spread to the prostate in men and to the uterus or vagina in women, or to the pelvic or abdominal wall in either gender.



Superficial cancers are usually managed *endoscopically* (via the cystoscope) with regular surveillance, due to the high predilection for recurrence. **With the exception of skin cancers, bladder cancers are the most frequently recurring cancer, with up to 70% of patients experiencing recurrence**. It is imperative to have frequent check-ups (every 3 months for the first year after initial diagnosis), consisting of periodic urinalyses, urine cytology, imaging, and cystoscopies. If active surveillance does not demonstrate any recurrences, the interval between follow up can gradually be increased (to every 6 months in the 2nd year; if there are no recurrences, to an annual check-up). If a recurrence is found, treatment must be repeated and the surveillance frequency then starts anew with the every 3-month cycle.

To help prevent recurrence, under certain circumstances it is beneficial to use a medication that is instilled in the bladder on a weekly basis—this is especially

useful for multi-focal cancers, in the presence of a high-grade tumor, or cancers that have already recurred. It is particularly useful for *carcinoma-in-situ (CIS)*, a variant of bladder cancer that is very superficial, flat, yet of a high-grade pathological nature. The medication of choice is tuberculosis vaccine—*BCG (bacillus Calmette Guerin)*, which is live but is an attenuated (weakened) form of tuberculosis bacteria!

Muscle-invasive cancers most often need to be treated with a major surgical procedure involving either partial or complete removal of the urinary bladder. In the circumstance that the entire bladder needs to be removed, the ureters (tubes that conduct the urine from the kidneys to the bladder) need to be diverted to a piece of intestine either attached to the skin and out of the body into a collection bag (*ileal conduit*) or attached to the urethra (*neo-bladder* or "reconstructed" bladder). At times, in lieu of surgery, chemo-radiation can be utilized (a combination of radiation therapy provided by the radiation oncologist and chemotherapy provided by the medical oncologist).

It is important to know that bladder cancer is frequently referred to as two separate types of diseases—one that typically presents as multiple, superficial papillary tumors that have a tendency to recur but are not lethal (similar to many skin cancers), versus another, more deadly form characterized by high-grade, non-papillary, muscle-invasive tumors that have a tendency to metastasize. Fortunately, the vast majority of bladder cancers are the superficial type.

Risk of recurrence, progression, and mortality:

Risk	**Recurrence**	**Progression**	**Mortality**
Low (TaG1; single T1G1)	37%	0%	0%
Intermediate (multiple T1G1; TaG2; Single T1G2)	45%	2%	1%
High (multiple T1G2; TaG3; T1G3; CIS)	54%	15%	10%