



What is Bladder Cancer?

The bladder is an expandable, hollow organ in the pelvis that stores urine (the body's liquid waste) before it leaves the body during urination. The urinary tract, made up of the kidneys, ureters, bladder, and urethra, is lined with a layer of transitional cells called the urothelium. This layer of cells is separated from the bladder muscles (called the muscularis propria) by a thin, fibrous band called the lamina propria. The lamina propria separates tumors that have spread into muscle (called invasive cancer) from those that have not (superficial or non-invasive cancers).

Bladder cancers are malignant tumors that begin in the bladder. Different **bladder cancers** are described by how deep they grow and if they grow into the bladder or through the muscles around the bladder (superficial or invasive).

There are three types of bladder cancer:

- transitional cell carcinoma, or TCC (about 90% of bladder cancer cases)
- squamous cell carcinomas (about 8%)
- adenocarcinomas (about 2%)

There are other less common types of cancer that arise in the bladder, including sarcomas (which begin in the muscle layers of the bladder) and small cell anaplastic cancers (a rare type very likely to spread to other parts of the body).

All three types can metastasize beyond the bladder. The tumor can grow into the surrounding organs (uterus and vagina in women; prostate in men), called locally advanced disease. It can also spread to the nearby lymph nodes, and/or into the liver, bones, or lungs; this is called distant metastasis. In some cases, it can spread to other parts of the body.

As we well know, there are many kinds of cancer; unfortunately they all come about because of the out-of-control growth of abnormal cells.

Leading Cancers in Women, Men, & Children

For Women: Breast cancer is the leading cancer for women in the US. Lung cancer is the second most common form of cancer and colorectal cancer is third among white women. The number 2 and 3 cancers are reversed among black and Asian/Pacific Island women. For all women, the fourth leading cancer is cancer of the uterus.

For Men: Prostate cancer is the leading cancer for men in the US. It is followed by lung cancer and then colorectal cancer. The fourth most common cancer is race-dependent. It is bladder cancer for white men, cancer of the mouth and throat for black men; and stomach cancer for Asian/Pacific Island men.

For Children: The most common malignancies in childhood are leukemia, followed by brain tumors, and lymphoma.

Cancer that is confined to the lining of the bladder is called superficial bladder cancer. Cancer that begins in the transitional cells may spread through the lining of the bladder and invade the muscle wall of the bladder or spread to nearby organs and lymph nodes; this is called invasive bladder cancer.

Bladder cancer is a fairly common form of cancer in the United States. Whites contract bladder cancer twice as often as blacks, and men are affected two to three times as often as women. Most bladder cancers occur after the age of 55, but the disease can also develop in younger people.

Each year, more than 50,000 people in the United States find out they have bladder cancer. The outlook for patients with early bladder cancer is very good. The chances of recovery from more advanced bladder cancer are improving as researchers continue to look for better ways to treat this disease.

Smoking, gender, and diet can affect the risk of developing bladder cancer.

Risk factors include the following:

- Smoking.
- Being exposed to certain substances at work, such as rubber, certain dyes and textiles, paint, and hairdressing supplies.
- A diet high in fried meats and fat.
- Being older, male, or white.
- Having an infection caused by a certain parasite.

Possible Signs of Bladder Cancer

These and other symptoms may be caused by bladder cancer or by other conditions. A doctor should be consulted if any of the following problems occur:

- Blood in the urine (slightly rusty to bright red in color).
- Frequent urination, or feeling the need to urinate without being able to do so.
- Pain during urination.
- Lower back pain.

What is Hematuria?

Hematuria means blood in the urine. Microscopic hematuria indicates that the blood is only seen when the urine is examined under a microscope, while gross hematuria means that there is enough blood in the urine so that it can be seen with the naked eye. Despite the quantity of blood in the urine being different, the types of diagnoses that can

cause the problem are the same, and the workup or evaluation that is needed is identical.

Since blood in the urine must come from one of the organs involved in making or transporting the urine, the evaluation of hematuria requires that we consider the entire urinary tract. This organ system includes the kidneys, ureter (the tube that carries the urine from the kidney to the bladder), bladder, prostate, or urethra (tube leading out of the bladder). It must be emphasized that even a single episode of hematuria requires evaluation, even if it resolves spontaneously.

What are the Causes of Hematuria?

There are multiple causes of hematuria. Some are serious, including cancers, trauma, stones, infections, and obstructions of the urinary tract. Others are less important, and may require no treatment. These may include viral infections, nonspecific inflammations of the kidney, medications which thin the blood's clotting ability, and benign prostate enlargement.

How is hematuria evaluated?

The evaluation for hematuria consists of taking a history, performing a physical examination, evaluating the urine under a microscope, and finally, obtaining a culture of the urine. A significant history would include whether or not there was any pain or discomfort associated with the hematuria; whether the blood was in the beginning, end, or throughout the urinary stream; and finally, whether there is a personal history of smoking, kidney stones, injuries to the urinary tract, trouble urinating, or previous urologic evaluation.

No matter how obvious the reason for hematuria appears to be, a complete evaluation is almost always necessary to rule out a serious underlying disease, such as a cancer. There are usually three diagnostic tests necessary to give us a look at the entire urinary tract, and these include the intravenous pyelogram (IVP), cystoscopy, and urine cytology.

The intravenous pyelogram, or IVP, is an x-ray evaluation of the urinary tract. In this procedure, a dye is injected into the veins, and this is filtered by the urinary tract. A series of x-rays are then taken over a thirty-minute period, looking for abnormalities. This study is especially useful for evaluating the kidneys and ureter, but not the bladder, prostate, or urethra. Therefore, a second examination called a cystoscopy is necessary. In this procedure, a small viewing tube, or cystoscope, is used to visually inspect the bladder and the urethra. In most instances, this can be done without discomfort by the use of local anesthetic jelly. The cystoscope is passed up the urethra into the bladder, and the inspection is carried out. The entire examination takes less than ten minutes. The final test is a urine cytology, which involves voiding urine into a cup and having that urine examined by a pathologist to look for cancer cells.

How is hematuria treated?

Management of hematuria depends upon the underlying cause. Many times a cause cannot be found, which is fortunate, because it generally suggests that there is not a

harmful situation present. Remember that the real reason for a hematuria workup is not to prove a specific cause, but to rule out a serious problem. If no cause is found for the hematuria, the urine should be checked on a yearly basis to make certain that no changes are occurring. However, if gross hematuria were to recur, repeat evaluation may be necessary, and a physician should be consulted. A blood test to check kidney function and a blood pressure check should be done as well. Men over fifty should have a yearly PSA, or prostate specific antigen, to screen for prostate cancer.

Further discussion of the treatment for hematuria would depend upon the results of the previously mentioned workup and the exact cause for the hematuria. The urologist who performs this examination would direct any further treatment or workup that would be necessary.

Tests Used to Help Detect and Diagnose Bladder Cancer

The following tests and procedures may be used:

- **CT scan (CAT scan):** A procedure that makes a series of detailed pictures of areas inside the body, taken from different angles. The pictures are made by a computer linked to an x-ray machine. A dye may be injected into a vein or swallowed to help the organs or tissues show up more clearly. This procedure is also called computed tomography, computerized tomography, or computerized axial tomography.
- **Urinalysis:** A test to check the color of urine and its contents, such as sugar, protein, blood, and bacteria.
- **Internal exam:** An exam of the vagina and/or rectum. The doctor inserts gloved fingers into the vagina and/or rectum to feel for lumps.
- **Intravenous pyelogram (IVP):** A series of x-rays of the kidneys, ureters, and bladder to find out if cancer has spread to these organs. A contrast dye is injected into a vein. As the contrast dye moves through the kidneys, ureters, and bladder, x-rays are taken to see if there are any blockages.
- **Cystoscopy:** A procedure to look inside the bladder and urethra to check for abnormal areas. A cystoscope (a thin, lighted tube) is inserted through the urethra into the bladder. Tissue samples may be taken for biopsy.
- **Biopsy:** The removal of cells or tissues so they can be viewed under a microscope to check for signs of cancer. A biopsy for bladder cancer is usually done during cystoscopy. It may be possible to remove the entire tumor during biopsy.
- **Urine cytology:** Examination of urine under a microscope to check for abnormal cells.

Factors Affecting Prognosis and Treatment Options.

The prognosis (chance of recovery) depends on the following:

- The stage of the cancer (whether it is superficial or invasive bladder cancer, and whether it has spread to other places in the body). Bladder cancer in the early stages can often be cured.
- The type of bladder cancer cells and how they look under a microscope.
- The patient's age and general health.

Treatment options depend on the stage of bladder cancer.

Healthy Cells vs. Cancer Cells

Healthy cells are like a cat. They need structure to determine the size of bones and shape of the body, tail and whiskers. The DNA in genes and chromosomes determine this. They need energy to play and prowl and sustain life. This is derived from chemicals in food. Cats need a system to deliver chemicals (food nutrients like amino acids, carbohydrates, fats, vitamins and minerals) to all parts of their body. These are the blood vessels. Growth factors take a kitten into a lazy old cat, all the while helping it to function normally.

The body and its cells are mostly made up of protein. The building blocks of proteins are substances called amino acids that in the form of enzymes and hormones literally control every chemical reaction within the cells. When these are modified, different messages are sent to a complex control system that can alter their function. There are twenty different kinds of amino acids that are essential to life. Twelve of these can be synthesized within the body however; eight must be supplied by the daily diet.

Structure	
Normal Cells	Cancer Cells
DNA in genes and chromosomes go about their business in a normal way.	Cancer cells develop a different DNA or gene structure or acquire abnormal numbers of chromosomes.
Cells divide in an orderly way to produce more cells only when the body needs them.	Cells continue to be created without control or order. If not needed, a mass of tissue is formed which is called a tumor.
Energy	
Normal Cells	Cancer Cells
Cells derive 70% of their energy from a system called the "Krebs Cycle."	Cells have a defective "Krebs Cycle" and derive little or no energy from it.
Cells derive only 20% of their energy from a system called "Glycolosis."	Cancer cells derive almost all their energy from "Glycolosis."
Cells derive most of their energy with the use of oxygen.	Cells derive most of their energy in the absence of oxygen.
Blood Vessels	
Normal Cells	Cancer Cells
Cells have a built-in blood vessel system.	Cells do not have a built-in blood vessel system. They require more of certain amino acids to grow.

Growth Factors	
Normal Cells	Cancer Cells
While similar to cancer cells, the amount of them is more in balance to produce a more normal level of activity.	These cells have over produced, require more chemicals (food) and are over active.
Functions	

Normal Cells	Cancer Cells
The enzymes and hormones go about business in a normal balanced manner.	The enzymes and hormones are either over active or under active.
Tumors are Different	
Benign	Malignant
Benign tumors are not cancerous. They do not invade nearby tissues nor spread to other parts of the body. They can be removed and are not a threat to life.	Malignant tumors are cancerous. They can invade and damage nearby tissues and organs and they can break away and enter the blood stream to form new tumors in other parts of the body. The spread of cancer is called metastasis.

After bladder cancer has been diagnosed, tests are done to find out if cancer cells have spread within the bladder or to other parts of the body.

The process used to find out if cancer has spread within the bladder lining and muscle or to other parts of the body is called staging. The information gathered from the staging process determines the stage of the disease. It is important to know the stage in order to plan treatment. The following tests and procedures may be used in the staging process:

- **Cystoscopy:** A procedure to look inside the bladder and urethra to check for abnormal areas. A cystoscope (a thin, lighted tube) is inserted through the urethra into the bladder. Tissue samples may be taken for biopsy.
- **CT scan (CAT scan):** A procedure that makes a series of detailed pictures of areas inside the body, taken from different angles. The pictures are made by a computer linked to an x-ray machine. A dye may be injected into a vein or swallowed to help the organs or tissues show up more clearly. This procedure is also called computed tomography, computerized tomography, or computerized axial tomography.
- **MRI (magnetic resonance imaging):** A procedure that uses a magnet, radio waves, and a computer to make a series of detailed pictures of areas inside the body. This procedure is also called nuclear magnetic resonance imaging (NMRI).
- **Physical exam and history:** An exam of the body to check general signs of health, including checking for signs of disease, such as lumps or anything else that seems unusual. A history of the patient's health habits and past illnesses and treatments will also be taken.
- **Chest x-ray:** An x-ray of the organs and bones inside the chest. An x-ray is a type of energy beam that can go through the body and onto film, making a picture of areas inside the body.
- **Bone scan:** A procedure to check if there are rapidly dividing cells, such as cancer cells, in the bone. A very small amount of radioactive material is injected into a vein and travels through the bloodstream. The radioactive material collects in the bones and is detected by a scanner.

The Following Stages are Used for Bladder Cancer:

Stage 0

In **stage 0**, the cancer is found on tissue lining the inside of the bladder only. Stage 0 is divided into stage 0a and stage 0is, depending on the type of the **tumor**:

- Stage 0a is also called papillary carcinoma, which may look like tiny mushrooms growing from the lining of the bladder.
- Stage 0is is also called carcinoma in situ, which is a flat tumor on the tissue lining the inside of the bladder.

Stage 0 Bladder Cancer (Carcinoma in Situ)

Treatment of stage 0 bladder cancer may include the following:

- Transurethral resection with fulguration.
- Transurethral resection with fulguration followed by intravesical biologic therapy or chemotherapy.
- Segmental cystectomy.
- Radical cystectomy.
- A clinical trial of photodynamic therapy.
- A clinical trial of biologic therapy.
- A clinical trial of chemoprevention therapy given after treatment to stop cancer from recurring (coming back).

Stage I

In **stage I**, the cancer has spread to the layer below the inner lining of the bladder.

Stage I Bladder Cancer

Treatment of stage I bladder cancer may include the following:

- Transurethral resection with fulguration.
- Transurethral resection with fulguration followed by intravesical biologic therapy or chemotherapy.
- Segmental or radical cystectomy.
- Radiation implants with or without external radiation therapy.
- A clinical trial of chemoprevention therapy given after treatment to stop cancer from recurring (coming back).
- A clinical trial of intravesical therapy.

Stage II

In **stage II**, cancer has spread to either the inner half or outer half of the muscle wall of the bladder.

Stage II Bladder Cancer

Treatment of stage II bladder cancer may include the following:

- Radical cystectomy with or without surgery to remove pelvic lymph nodes.
 - External radiation therapy combined with chemotherapy.
 - Radiation implants before or after external radiation therapy.
 - Transurethral resection with fulguration.
 - Segmental cystectomy.
 - A clinical trial of chemotherapy before or after surgery.
 - A clinical trial of chemotherapy combined with external radiation therapy.

Stage III

In **stage III**, cancer has spread from the bladder to the fatty layer of tissue surrounding it, and may have spread to the **reproductive organs (prostate, uterus, vagina)**.

Stage III Bladder Cancer

Treatment of stage III bladder cancer may include the following:

- Radical cystectomy.
- External radiation therapy with or without radiation implants.
- Segmental cystectomy.
- External radiation therapy combined with chemotherapy.
- A clinical trial of chemotherapy before or after surgery.
- A clinical trial of chemotherapy combined with external radiation therapy.

Stage III Bladder Cancer

Treatment of stage III bladder cancer may include the following:

- Radical cystectomy.
- External radiation therapy with or without radiation implants.
- Segmental cystectomy.
- External radiation therapy combined with chemotherapy.
- A clinical trial of chemotherapy before or after surgery.
- A clinical trial of chemotherapy combined with external radiation therapy.

Stage IV

In **stage IV**, cancer has spread from the bladder to the wall of the **abdomen or pelvis**. Cancer may have spread to one or more **lymph nodes** or to other parts of the body.

Stage IV Bladder Cancer

Treatment of stage IV bladder cancer may include the following:

- Radical cystectomy.

- External radiation therapy (may be as palliative therapy to relieve symptoms and improve quality of life).
- Urinary diversion as palliative therapy to relieve symptoms and improve quality of life.
- Cystectomy as palliative therapy to relieve symptoms and improve quality of life.
- Chemotherapy.
- A clinical trial of chemotherapy before or after surgery.
- A clinical trial of chemotherapy combined with external radiation therapy.

There are different types of treatment for patients with bladder cancer.

Different types of treatment are available for patients with bladder cancer. Some treatments are standard (the currently used treatment), and some are being tested in clinical trials. Before starting treatment, patients may want to think about taking part in a clinical trial. A treatment clinical trial is a research study meant to help improve current treatments or obtain information on new treatments for patients with cancer. When clinical trials show that a new treatment is better than the "standard" treatment, the new treatment may become the standard treatment.

Three types of standard treatment are used:

1. Surgery

One of the following types of surgery may be done:

- **Transurethral resection (TUR) with fulguration**: Surgery in which a cystoscope (a thin lighted tube) is inserted into the bladder through the urethra. A tool with a small wire loop on the end is then used to remove the cancer or to burn the tumor away with high-energy electricity. This is known as fulguration.
- **Radical cystectomy**: Surgery to remove the bladder and any lymph nodes and nearby organs that contain cancer. This surgery may be done when the bladder cancer invades the muscle wall, or when superficial cancer involves a large part of the bladder. In men, the nearby organs that are removed are the prostate and the seminal vesicles. In women, the uterus, the ovaries, and part of the vagina are removed. Sometimes, when the cancer has spread outside the bladder and cannot be completely removed, surgery to remove only the bladder may be done to reduce urinary symptoms caused by the cancer. When the bladder must be removed, the surgeon creates another way for urine to leave the body.
- **Segmental cystectomy**: Surgery to remove part of the bladder. This surgery may be done for patients who have a low-grade tumor that has invaded the wall of the bladder but is limited to one area of the bladder. Because most of the bladder remains intact, a patient is able to urinate normally after recovering from this surgery.
- **Urinary diversion**: Surgery to make a new way for the body to store and pass urine.

Even if the doctor removes all the cancer that can be seen at the time of the surgery, some patients may be given chemotherapy after surgery to kill any cancer cells that are left. Treatment given after surgery, to increase the chances of a cure, is called adjuvant therapy.

2. Radiation therapy

Radiation therapy is a cancer treatment that uses high-energy x-rays or other types of radiation to kill cancer cells. There are two types of radiation therapy. External radiation therapy uses a machine outside the body to send radiation toward the cancer. Internal radiation therapy uses a radioactive substance sealed in needles, seeds, wires, or catheters that are placed directly into or near the cancer. The way the radiation therapy is given depends on the type and stage of the cancer being treated.

3. Chemotherapy

Chemotherapy is a cancer treatment that uses drugs to stop the growth of cancer cells, either by killing the cells or by stopping the cells from dividing. When chemotherapy is taken by mouth or injected into a vein or muscle, the drugs enter the bloodstream and can reach cancer cells throughout the body (systemic chemotherapy). When chemotherapy is placed directly into the spinal column, a body cavity such as the abdomen, or an organ, the drugs mainly affect cancer cells in those areas. Bladder cancer may be treated with intravesical (into the bladder through a tube inserted into the urethra) chemotherapy. The way the chemotherapy is given depends on the type and stage of the cancer being treated.

What are the Side Effects of Bladder Cancer Treatment?

The methods used to treat bladder cancer are very powerful. It is hard to limit the effects of treatment so that only cancer cells are destroyed; healthy tissue may also be damaged. That is why treatment can cause unpleasant side effects. Side effects depend on the type of treatment used and on the part of the body being treated.

When the bladder is removed, the patient needs a new way to store and pass urine. Various methods are used. In one, the surgeon uses a piece of the person's small intestine to form a new pipeline. The ureters are attached to one end, and the other end is brought out through an opening in the wall of the abdomen. This new opening is called a stoma. (It is also called an ostomy or urostomy.) A flat bag fits over the stoma to collect urine, and it is held in place with a special adhesive. A specially trained nurse or enterostomal therapist will show the patient how to care for the ostomy.

A newer method uses part of the small intestine to make a new storage pouch (called a continent reservoir) inside the body. The urine collects there and does not empty into a bag. Instead, the patient learns to use a tube (catheter) to drain the urine through a stoma. Other methods are being developed that connect a pouch made from the small intestine to a remaining part of the urethra. When this procedure is possible, a stoma and bag are not necessary because urine leaves the body through the urethra.

Radical cystectomy causes infertility in both men and women. This operation can also lead to sexual problems. In the past, nearly all men were impotent following this

procedure, but improvements in surgery have made it possible to prevent this in many men. In women, the vagina may be narrower or shallower, and intercourse may be difficult.

During radiation therapy, patients may become very tired as the treatment continues. Resting as much as possible is important. Radiation treatment to the lower abdomen may cause nausea, vomiting, or diarrhea. Usually, certain foods or medications can ease these problems. Radiation therapy can also cause problems with fertility and can make sexual intercourse uncomfortable.

Chemotherapy also causes side effects because it damages not only cancer cells but other rapidly growing cells as well. The side effects of chemotherapy depend on the specific drugs that are given. In addition, each patient reacts differently. Chemotherapy commonly affects blood-forming cells and cells that line the digestive tract. As a result, patients may have side effects such as a lowered resistance to infection, loss of appetite, loss of hair, nausea and vomiting, less energy, and mouth sores. These are short-term side effects that usually end after treatment stops. When drugs are put directly into the bladder, these side effects may be limited. However, it is common for the bladder to be irritated.

Loss of appetite can be a serious problem for patients during therapy. Patients who eat well may be better able to withstand the side effects of their treatment, so good nutrition is an important part of the treatment plan. Eating well means getting enough calories to prevent weight loss and having enough protein to build and repair muscles, organs, skin, and hair. Many patients find that eating several small meals and snacks during the day is easier than trying to eat three large meals.

Side effects during cancer treatment vary for each patient. They may even be different from one treatment to the next in the same person. Attempts are made to plan treatment to minimize problems. Fortunately, most side effects are temporary. Doctors, nurses, and dietitians can explain the side effects of cancer treatment and can suggest ways to deal with them.

What Happens After Treatment for Bladder Cancer?

Regular follow-up exams are very important after treatment for bladder cancer. The bladder needs to be checked with a cystoscope, any superficial tumors that may have recurred are removed. The urine is checked for cancerous cells and a chest x-ray, an IVP, or other tests may be performed.

A patient who has had bladder cancer should be closely monitored for several years, because bladder tumors can come back. If the cancer does recur, early detection is important so that additional treatment can be started.

Bladder Cancer At a Glance

- While the exact cause(s) of bladder cancer is not known, risk factors have been identified.
- The most common warning sign of bladder cancer is blood in the urine.

- The diagnosis of bladder cancer is supported by findings of the medical history and examination, blood, urine, and x-ray tests, and confirmed with a biopsy (usually during a cystoscope exam).
- Treatment of bladder cancer depends on the growth, size, and location of the tumor as well as the age and health of the patient.

Source: A.P. John Institute for Cancer Research