# Bladder & Urothelial Cancer

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# What is bladder cancer?

Bladder cancer is a disease in which malignant (cancer) cells form in the tissues of the bladder. The bladder is a hollow organ in the lower part of the abdomen. It is shaped like a small balloon and has a muscular wall that allows it to get larger or smaller to store urine made by the kidneys. There are two kidneys, one on each side of the backbone, above the waist. Tiny tubules in the kidneys filter and clean the blood. They take out waste products and make urine. The urine passes from each kidney through a long tube called a ureter into the bladder. The bladder holds the urine until it passes through the urethra and leaves the body.

There are three types of bladder cancer that begin in cells in the lining of the bladder. These cancers are named for the type of cells that become malignant (cancerous):

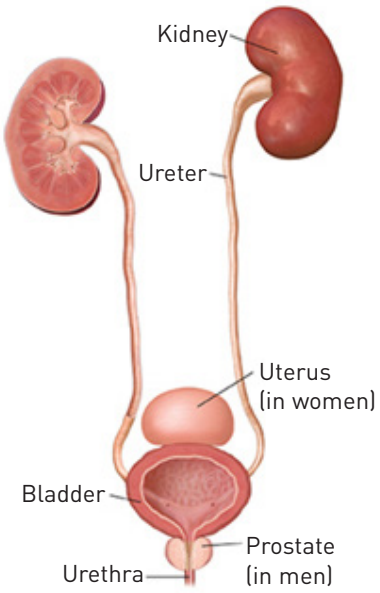
- **Urothelial (Transitional cell carcinoma):** The urothelium is the lining that extends from the renal (kidney) pelvis down the ureters, along the bladder, and out to the tip of the urethra. Urothelial (transitional cell) carcinoma can develop anywhere along this lining. These cells are able to stretch when the bladder is full and shrink when it is emptied. Most bladder cancers begin in the transitional cells. Transitional cell carcinoma can be low-grade or high-grade:
  - Low-grade transitional cell carcinoma often recurs (comes back) after treatment, but rarely spreads into the muscle layer of the bladder or to other parts of the body.

  - High-grade transitional cell carcinoma often recurs (comes back) after treatment and often spreads into the muscle layer of the bladder, to other parts of the body, and to lymph nodes. Almost all deaths from bladder cancer are due to high-grade disease.

- **Squamous cell carcinoma:** Cancer that begins in squamous cells (thin, flat cells lining the inside of the bladder). Cancer may form after long-term infection or irritation.

- **Adenocarcinoma:** Cancer that begins in glandular cells that are found in the lining of the bladder. Glandular cells in the bladder make substances such as mucus. This is a very rare type of bladder cancer.

Cancer that is in the lining of the bladder is called superficial bladder cancer. Cancer that has spread through the lining of the bladder and invades the muscle wall of the bladder or has spread to nearby organs and lymph nodes is called invasive bladder cancer.



## What is urothelial (transitional cell cancer) of the renal pelvis and ureter?

Cancer that starts in the ureters or the renal pelvis (the part of the kidney that collects urine and drains it to the ureters) is different from renal cell cancer.

Urine collects in the middle of each kidney in the renal pelvis. The renal pelvis is the top part of the ureter. The urothelium is the lining that extends from the renal (kidney) pelvis down the ureters, along the bladder, and out to the tip of the urethra. These cells can change shape and stretch without breaking apart. Transitional cell cancer starts in these cells. Transitional cell cancer can form in the renal pelvis, the ureter, or both.

**Risk factors for urothelial cancer** of the renal pelvis and ureter include the following:

- Having a personal history of bladder cancer
- Smoking cigarettes
- Taking a lot of certain pain medicines, such as phenacetin
- Being exposed to certain dyes and chemicals used in making leather goods, textiles, plastics, and rubber

## What are signs of urothelial cancer of the renal pelvis and ureter?

These and other signs and symptoms may be caused by transitional cell cancer of the renal pelvis and ureter or by other conditions. There may be no signs or symptoms in the early stages. Signs and symptoms may appear as the tumor grows.

Check with your doctor if you have any of the following:

- Blood in the urine
- A pain in the back that does not go away
- Extreme tiredness
- Weight loss with no known reason
- Painful or frequent urination

## The following stages are used for urothelial cancer of the renal pelvis and/or ureter:

### Stage 0 (Noninvasive Papillary Carcinoma and Carcinoma in Situ)

In stage 0, abnormal cells are found in tissue lining the inside of the renal pelvis or ureter. These abnormal cells may become cancer and spread into nearby normal tissue.

## Stage I-III (1-3)

Stages I-III, describes the spread of cancer within the layers of the tissue.

## Stage IV

In stage IV, cancer has spread to at least one of the following:

- A nearby organ
- The layer of fat around the kidney
- Lymph nodes
- Other parts of the body, such as the lung, liver, or bone

## Recurrent Urothelial Cancer of the Renal Pelvis and Ureter

Recurrent transitional cell cancer of the renal pelvis and ureter is cancer that has recurred (come back) after it has been treated. The cancer may come back in the renal pelvis, ureter, or other parts of the body.

## Urothelial cancer of the renal pelvis and ureter is also described as localized, regional, or metastatic:

- **Localized:** The cancer is found only in the kidney.
- **Regional:** The cancer has spread to tissues around the kidney and to nearby lymph nodes and blood vessels in the pelvis.
- **Metastatic:** The cancer has spread to other parts of the body.

## Treatment for urothelial cancer of the renal pelvis and ureter:

One of the following surgical procedures may be used to treat transitional cell cancer of the renal pelvis and ureter:

- **Nephroureterectomy:** Surgery to remove the entire kidney, the ureter, and the bladder cuff (tissue that connects the ureter to the bladder).
- **Segmental resection of the ureter:** A surgical procedure to remove the part of the ureter that contains cancer and some of the healthy tissue around it. The ends of the ureter are then reattached. This treatment is used when the cancer is superficial and in the lower third of the ureter only, near the bladder.

# What are risk factors for bladder cancer?

Anything that increases your chance of getting a disease is called a risk factor. Having a risk factor does not mean that you will get cancer; not having risk factors does not mean that you will not get cancer.

Risk factors for bladder cancer include the following:

- Using tobacco, especially smoking cigarettes
- Having a family history of bladder cancer
- Having certain changes in the genes that are linked to bladder cancer

- Being exposed to paints, dyes, metals, or petroleum products in the workplace
- Past treatment with radiation therapy to the pelvis or with certain anticancer drugs, such as cyclophosphamide or ifosfamide
- Taking Aristolochia fangchi, a Chinese herb
- Drinking water from a well that has high levels of arsenic
- Drinking water that has been treated with chlorine
- Having a history of bladder infections, including bladder infections caused by certain bacteria
- Using urinary catheters for a long time

## What are signs of bladder cancer?

These and other signs and symptoms may be caused by bladder cancer or by other conditions. Check with your doctor if you have any of the following:

- Blood in the urine (slightly rusty to bright red in color)
- Frequent need to pass urine
- Pain when passing urine
- Lower back pain

## What tests are done to find out if there is cancer?

The following tests and procedures may be used:

- **Physical exam and history**
- **Internal exam:** An exam of the vagina and/or rectum. The doctor inserts lubricated, gloved fingers into the vagina and/or rectum to feel for lumps.
- **Urinalysis:** A test to check the color of urine and its contents, such as sugar, protein, red blood cells, and white blood cells.
- **Urine cytology:** A laboratory test in which a sample of urine is checked under a microscope for abnormal cells.
- **Cystoscopy:** A procedure to look inside the bladder and urethra to check for abnormal areas. A cystoscope is inserted through the urethra into the bladder. A cystoscope is a thin, tube-like instrument with a light and a lens for viewing. It may also have a tool to remove tissue samples, which are checked under a microscope for signs of cancer.
- **Intravenous pyelogram (IVP):** A series of x-rays of the kidneys, ureters, and bladder to find out if cancer is present in 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.
- **Biopsy:** The removal of cells or tissues so they can be viewed under a microscope by a pathologist 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.

## After cancer has been diagnosed, tests are done to find out if cancer cells have spread.

The process used to find out if cancer has spread is called staging. It is important to know the stage in order to plan treatment. The following tests and procedures may be used in the staging process:

- **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, such as the brain.
- **PET scan (positron emission tomography scan):** A procedure to find malignant tumor cells in the body. A small amount of radioactive glucose (sugar) is injected into a vein. The PET scanner rotates around the body and makes a picture of where glucose is being used in the body. Malignant tumor cells show up brighter in the picture because they are more active and take up more glucose than normal cells do. This procedure is done to check whether there are malignant tumor cells in the lymph nodes.

- **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, 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 with cancer and is detected by a scanner.

## Cancer may spread from where it began to other parts of the body.

When cancer spreads to another part of the body, it is called metastasis. Cancer cells break away from where they began (the primary tumor) and travel through the lymph system or blood.

- **Lymph system:** The cancer gets into the lymph system, travels through the lymph vessels, and forms a tumor (metastatic tumor) in another part of the body.
- **Blood:** The cancer gets into the blood, travels through the blood vessels, and forms a tumor (metastatic tumor) in another part of the body.

The metastatic tumor is the same type of cancer as the primary tumor. For example, if bladder cancer spreads to the bone, the cancer cells in the bone are actually bladder cancer cells. The disease is metastatic bladder cancer, not bone cancer.

## Stages 0-IV (4) are used for bladder cancer:

**In stage 0**, abnormal cells are found in tissue lining the inside of the bladder. These abnormal cells may become cancer and spread into nearby normal tissue. Stage 0 is divided into stages 0a and 0is, depending on the type of the tumor:

- Stage 0a is also called noninvasive papillary carcinoma, which may look like long, thin growths 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.

**In stage I (1)**, cancer has formed and spread to the layer of connective tissue next to the inner lining of the bladder.

**In stage II (2)**, cancer has spread to the layers of muscle tissue of the bladder.

**Stage III (3)** is divided into stages IIIA and IIIB.

- In stage IIIA:
  - Cancer has spread from the bladder to the layer of fat surrounding the bladder and may have spread to the reproductive organs (prostate, seminal vesicles, uterus, or vagina) and cancer has not spread to lymph nodes; or
  - Cancer has spread from the bladder to one lymph node in the pelvis that is not near the common iliac arteries (major arteries in the pelvis).

- In stage IIIB, cancer has spread from the bladder to more than one lymph node in the pelvis that is not near the common iliac arteries or to at least one lymph node that is near the common iliac arteries.

**Stage IV (4)** is divided into stages IVA and IVB.

- In stage IVA:
  - Cancer has spread from the bladder to the wall of the abdomen or pelvis; or
  - Cancer has spread to lymph nodes that are above the common iliac arteries (major arteries in the pelvis).
- In stage IVB, cancer has spread to other parts of the body, such as the lung, bone, or liver.

Recurrent bladder cancer is cancer that has recurred (come back) after it has been treated. The cancer may come back in the bladder or in other parts of the body.

## How is bladder cancer treated?

Different types of treatment are available for people with bladder cancer. Some treatments are standard (the currently used treatment), and some are being tested in clinical trials.

# Four types of standard treatment are used:

## 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.

**Partial cystectomy:** Surgery to remove part of the bladder. This surgery may be done for those who have a low-grade tumor that has invaded the wall of the bladder but is limited to one area of the bladder. Because only a part of the bladder is removed, you

are able to urinate normally after recovering from this surgery. This is also called segmental cystectomy.

**Urinary diversion:** Surgery to make a new way for the body to store and pass urine.

After the doctor removes all the cancer that can be seen at the time of the surgery, some people may be given chemotherapy after surgery to kill any cancer cells that are left. Treatment given after surgery, to lower the risk that the cancer will come back, is called adjuvant therapy.

## Radiation Therapy

Radiation therapy is a cancer treatment that uses high-energy x-rays or other types of radiation to kill cancer cells or keep them from growing. The way the radiation therapy is given depends on the type and stage of the cancer being treated. External radiation therapy is used to treat bladder cancer.

## Chemotherapy

Chemotherapy is a cancer treatment that uses drugs to stop the growth of cancer cells, either by killing the cells or by stopping them 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). For bladder cancer, regional chemotherapy may be intravesical (put into the bladder through a tube inserted into the urethra). The way the chemotherapy is given depends on the type and stage of the cancer being treated. Combination chemotherapy is treatment using more than one anticancer drug.

## Immunotherapy

Immunotherapy is a treatment that uses your immune system to fight cancer. Substances are used to boost, direct, or restore the body's natural defenses against cancer. This type of cancer treatment is also called biotherapy or biologic therapy.

Bladder cancer may be treated with an intravesical immunotherapy called BCG (bacillus Calmette-Guérin). The BCG is given in a solution that is placed directly into the bladder using a catheter (thin tube).

## Follow-up tests may be needed

Some of the tests that were done to diagnose the cancer or to find out the stage of the cancer may be repeated. Some tests will be repeated in order to see how well the treatment is working. Decisions about whether to continue, change, or stop treatment may be based on the results of these tests.

Support is available for coping with changes that may have happened as a result of cancer treatment. Your healthcare team can offer ideas as well as a plan of care for long-term follow-up.

# What are Clinical trials?

Clinical trials are done to find out if new cancer treatments are safe and effective or better than the standard treatment.

- The standard treatment alone or
- The standard treatment plus the new treatment being studied

Taking part in a clinical trial helps improve the way cancer will be treated in the future. Even when clinical trials do not lead to effective new treatments, they often answer important questions and help move research forward.

Many of today's standard treatments for cancer are based on earlier clinical trials.

**Ask if there is a clinical trial right for you.**

Some clinical trials only include people who have not yet received treatment. Other trials test treatments for those whose cancer has not gotten better. There are also clinical trials that test new ways to stop cancer from coming back or reduce the side effects of cancer treatment.

## To learn more about bladder and urothelial cancer

- **American Cancer Society**
  https://www.cancer.org/
- **National Cancer Institute**
  https://www.cancer.gov/
- **National Comprehensive Cancer Network Guidelines for Patients**
  https://www.nccn.org/patients/guidelines/cancers.aspx
- **MedlinePlus**
  https://medlineplus.gov/

## Common questions

What does the pathology report say?

What is the stage of my cancer?

What are my goals for treatment?

What are my treatment choices?

What kind of support services are available for me about finances, emotions, spiritual questions, etc.?

| My Health Care Team | Contact Information |
|---|---|
| Urologist: | |
| Radiation Oncologist: | |
| Primary Care Doctor: | |
| Medical Oncologist: | |
| Navigator: | |
| Nurse: | |
| Registered Dietitian Nutritionist: | |
| Other: | |
| Other: | |
| Other: | |
| Other: | |

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