# Table of Contents

- Symptoms ................................................................................................................. 3
- Causes ........................................................................................................................ 3
- Risk Factors ................................................................................................................. 3
- Types of Bladder Cancer ............................................................................................. 4
- Diagnosis ...................................................................................................................... 4
- Surgery ......................................................................................................................... 5
  - Cystectomy .............................................................................................................. 5
  - Transurethral Resection (TUR) ................................................................................ 6
  - Bladder Reconstruction Surgery ............................................................................ 6
- Chemotherapy .............................................................................................................. 6
  - Methotrexate, Vinblastine, Adriamycin and Cisplatin ............................................ 7
  - Gemcitabine with Cisplatin ..................................................................................... 7
  - Chemotherapy Side Effects .................................................................................... 8
- Radiation Therapy ....................................................................................................... 8
- Immunotherapy ........................................................................................................... 9
- Clinical Trials ............................................................................................................. 10
  - Clinical Trials for Bladder Cancer Patients ............................................................ 10
  - Types of Clinical Trials .......................................................................................... 11
  - MD Anderson Clinical Trials .................................................................................. 11
- Support ......................................................................................................................... 12
- Treatment Maps ......................................................................................................... Appendix 1
Bladder cancer is the fifth most common cancer in the United States. Over 70,000 cases are diagnosed each year, and almost 15,000 people die from the disease every year. Men, Caucasians and people who smoke have two to four times the risk of bladder cancer compared to the general population. When diagnosed and treated before the tumor has spread, bladder cancer is very treatable. When treated early, the survival rate is near 95 percent.

Smoking is the greatest risk factor for bladder cancer. The incidence increases in people 50 years of age and older. Chronic bladder problems such as infections and bladder stones may also be risk factors, although research has not shown a direct link.

**Symptoms**

The most common bladder cancer symptom is blood in the urine (called hematuria), which causes the urine to appear rusty or deep red in color. However, hematuria cannot always be seen by the naked eye, and can also be a symptom of other conditions such as kidney stones and urinary tract infection. If you have hematuria or any of the other bladder cancer symptoms listed below, tell your doctor.

- Painful urination
- Frequent urination
- Having the urge to urinate, but unable to pass urine

**Causes**

Although bladder cancer may not be preventable, not smoking is the best way to lower your risk. People who are exposed to aromatic amines in their work environment are advised to always follow safe work habits. Other healthy practices, such as drinking plenty of fluids (mainly water) and eating a diet high in fruits and vegetables have been shown to protect against bladder cancer.

**Risk Factors**

Although the exact cause of bladder cancer is unknown, studies have found the following to be risk factors for developing the disease:

**Age:** The chance of getting bladder cancer increases with age, and is uncommon in people under the age of 40.

**Tobacco:** Tobacco use is a major risk factor for bladder cancer. People who smoke, cigarettes, pipes and cigars, are four times more likely than nonsmokers to get the disease.

**Race:** Bladder cancer occurs twice as often in Caucasians as it does in African-Americans and Hispanics. Asians have the lowest rate of developing the disease.

**Gender:** Males are two to three times more likely than females to get bladder cancer.
Family history: People with a family history of bladder cancer are more likely than those with no family history of it to get the disease. Studies are underway to determine whether certain genes increase the risk of getting the disease.

Personal history of bladder cancer: Bladder cancer has a 50-80 percent recurrence rate, the highest of any cancer, including skin cancer. Therefore, bladder cancer survivors have an increased chance of getting the disease again.

Occupation: Workers exposed to elevated amounts of carcinogens in the workplace are more at risk. This includes the rubber, chemical, and leather industries, along with hairstylists, machinists, metal workers, printers, painters, textile workers and truck drivers.

Infections: People infected with certain parasites have an increased risk of bladder cancer. These parasites tend to be common in tropical climates (particularly in Egypt).

Treatment with cyclophosphamide or arsenic: These drugs are sometimes used in the treatment of cancer and other conditions and raise the risk of developing bladder cancer.

People at high risk for bladder cancer are:
- At least age 50 with microscopic hematuria (blood seen under a microscope)
- Under age 50 with gross hematuria (blood seen by the naked eye)

Types of Bladder Cancer

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):

Transitional cell bladder cancer – About 90 percent of bladder cancers are transitional cell carcinomas. These cancers begin in the cells lining the bladder. Cancer that has not spread beyond the lining of the bladder is referred to as non-invasive or superficial bladder cancer.

Squamous cell bladder cancer – Bladder cancers that begin in squamous cells, which are thin flat cells, may form in the bladder after long-term infection or irritation.

Adenocarcinoma – Bladder cancer that develops in the inner lining of the bladder including the part of the bladder closest to the belly button or along the urethra.

Diagnosis

Cystoscopy is the most common and reliable test for bladder cancer. It is 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. The cystoscope can also be used to treat non-invasive tumors without surgery.
However, cystoscopy is not perfect. Flat lesions (called carcinoma in situ) and small papillary tumors can be missed. MD Anderson recommends combining cystoscopy with the tests listed below for the most accurate diagnosis. Your doctor will determine which tests are best suited for your specific situation.

**Imaging studies** such as a computerized tomography (CT) scan, ultrasound or intravenous pyelogram (IVP) can provide the doctor with additional information. IVP involves injecting a dye that shows up on an X-ray as it travels through the urinary system.

**Urine-based tests** use a urine sample. Scientists often use a test called cytology to look for abnormal cells in a urine sample under a microscope. There are several types of urine tests available that focus on specific bladder cancer "markers." The urologist will choose the most appropriate urine test for each patient.

Different types of treatment are available for bladder cancer. Some treatments are standard and some are being tested in clinical trials. The next sections will describe different types of treatment for bladder cancer:

- Surgery
- Chemotherapy
- Radiation Therapy
- Immunotherapy

Before starting treatment, patients may want to think about taking part in a clinical trial. See Page 8 for more information on clinical trials.

**Surgery**

This section will help you learn more about the different types of surgeries for bladder cancer.

**Surgeons in the Bladder Cancer Treatment Group**

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**Cystectomy**

Surgery to remove the bladder is called a cystectomy. Most all cystectomies are radical, meaning that the bladder and attached structures (such as the prostate) are removed. Partial cystectomies (where part of the bladder is removed) and simple cystectomies (where only the bladder is removed) are rarely indicated for people with cancer, but may be right for certain patients. Minimally invasive surgeries, such as laparoscopy and robotic surgery are not usually indicated at this time but might be appropriate in selected patients.

In men, the bladder, prostate and lymph nodes are removed in a cystectomy. Surgeons can often spare the nerve bundles responsible for erection if the cancer is not advanced.
In women, the bladder, uterus and part of the vaginal wall are removed. In some cases, the vagina can be spared.

**TUR**

For some early-stage or superficial bladder cancers, your doctor may recommend a procedure called transurethral resection (TUR). The surgeon threads a resectoscope, a thin tool with a wire loop on the end, through the urethra to remove the tumor from the bladder wall. The surgeon may also use the tool to burn the tumor away.

If either surgery is recommended, your doctor will talk with you in detail.

**Bladder Reconstruction Surgery**

A urinary diversion is a procedure to restore urinary function after the bladder is removed. Urinary diversions are done at the same time as a cystectomy. There are three types of urinary diversions:

**Ileal neobladder:** In this procedure a part of the ileum (small intestine) is used to make a new bladder. With the new bladder, most patients can urinate relatively normally. It provides good daytime urinary control, but nighttime incontinence can be a problem. Some patients (especially women) may have trouble completely emptying the neobladder and may need to use a catheter.

**Ileal conduit:** A piece of small intestine is used to create a “pipe” that connects the ureters to the skin on the belly. The urine flows into a plastic bag, called a urostomy bag, which is worn on the outside of the body.

- **Recovery:** Patients usually have a short recovery time after an ileal conduit. Surgeons need less time to create an ileal conduit than a neobladder or a continent reservoir. This is an important consideration for patients who require minimal surgery time.
- **Complications:** Though rare, complications of ileal conduits include narrowing of the conduit opening and weakening of the tissue around the conduit.
- **Outcomes:** It is a simple and quick procedure, but some patients may have problems wearing a urostomy bag.

** Continent reservoir:** Tissue from the intestines is used to create an internal pouch that is connected to the belly button. The pouch is drained with a catheter. This procedure is done less often than the other two because of higher potential for complications.

**Chemotherapy**

Chemotherapy plays a major role in treating bladder cancer that has spread to the lymph nodes, lungs, liver and other parts of the body. After cancer has spread it is called metastatic cancer. Chemotherapy is the frontline treatment for patients who have metastatic cancer when they are diagnosed. This section will help you learn more about treatment with chemotherapy.

**Medical Oncologists in the Bladder Cancer Treatment Group**

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**Methotrexate, Vinblastine, Adriamycin and Cisplatin**

The “gold standard” chemotherapy for metastatic bladder cancer is a combination of four drugs known as MVAC: methotrexate, vinblastine, adriamycin and cisplatin. MVAC has provided good response rates since the 1980s. Approximately 50-70 percent of patients respond to this chemotherapy. In patients receiving chemotherapy before surgery, MVAC has been shown to decrease the likelihood of the cancer recurring.

In recent years, MVAC treatment has been decreased from four weeks to two weeks. Some patients on this treatment schedule experience fewer side effects and improved response rates. MD Anderson treats patients using this two-week schedule of MVAC.

**Gemcitabine with Cisplatin**

Gemcitabine with cisplatin (GC) is another combination treatment that has been shown to improve survival in patients with metastatic bladder cancer. Patient response rates are similar to those who take MVAC every two weeks. While GC has not been studied as extensively in patients preparing for surgery, it is beneficial for patients who are not able to take MVAC.

There are many other treatment combinations for bladder cancer that use chemotherapy drugs. Many of these were developed to help patients whose kidneys may not be working well and for those with pre-existing nerve damage (peripheral neuropathy), hearing loss or other medical conditions. Your doctor will discuss with you the risks, benefits, and alternatives of these combinations to find the best combination treatment for you.

Patients who are at high risk for metastasis may have chemotherapy before surgery (called neoadjuvant therapy). Research shows that this combination treats tumors that have invaded the muscle wall and tumors that may spread to other organs.

MD Anderson researchers are continuing to study different chemotherapy combinations and dosages to improve response rates, slow tumor re-growth and decrease treatment side effects.

Doctors at MD Anderson are highly experienced in treating rare bladder tumors, including:
- small cell,
- squamous cell,
- sarcomatoid/carcinosarcomas,
- micropapillary,
- plasmacytoid,
- lymphoepitheliomas, and
- adenocarcinomas of the bladder like urachal cancer.

We have done several of the first (and only) clinical trials for rare tumors and have developed chemotherapy treatments for these specific cancers. Clinical trials using chemotherapy are
Chemotherapy Side Effects
Side effects that often happen after taking chemotherapy are:
- appetite loss,
- constipation,
- nausea and/or vomiting,
- diarrhea and
- mouth sores.

Other side effects can include:
- sensitivity to sunlight,
- low white blood cell count,
- low red blood cell count,
- low platelet count and
- kidney function or liver function changes, and
- nerve damage including hearing loss.

Certain drugs may cause numbness, pain or tingling in your hands, feet, arms and legs.

Your doctor will monitor you closely for side effects from the chemotherapy you are taking. It is important to tell your doctor or nurse if you have any side effects of treatment. They want to help you manage your side effects so you can feel your best.

Radiation Therapy
For certain cases, radiation therapy may be advised instead of surgery. Cure and survival rates for patients receiving radiation therapy are similar to rates for patients who have surgery. In this section you will learn how radiation therapy is used to treat bladder cancer.

Radiation Oncologists in the Bladder Cancer Treatment Group
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Patients who have radiation therapy will receive more than one type of treatment. A treatment plan may include:

1. Cystoscopy - the doctor inserts a cystoscope into the bladder to remove as much of the tumor
as possible.

2. Radiation therapy and chemotherapy – approximately five weeks of radiation therapy to the pelvis with chemotherapy (usually the drug cisplatin).

3. Cystoscopy – to check how the tumor has responded to treatment. If the tumor has not grown, the patient will receive two additional weeks of radiation therapy with chemotherapy. If the cancer has recurred, doctors usually advise the patient to have surgery to remove the bladder.

**Patients who usually respond well to radiation therapy:**

- have tumors that can be removed by surgery;
- have only one tumor site;
- have good bladder function;
- can tolerate chemotherapy and seven weeks of daily radiation therapy; and
- must be able to follow an involved follow-up plan after treatment.

**Side effects during radiation therapy may include:**

- fatigue (a feeling of tiredness that is not relieved by rest);
- skin reaction (redness, irritation);
- burning with urination;
- increased urgency and frequency of urination; and
- diarrhea and/or loose bowel movements.

Most of these symptoms should get better within two to three months after the end of the radiation therapy.

**Follow-up**

Patients who are treated with radiation therapy and chemotherapy will have a follow-up plan after treatment. Follow-up usually includes CT scans of the abdomen and pelvis and cystoscopy procedures.

**Immunotherapy**

Immunotherapy is treatment that uses the body's own immune system to fight cancer and other diseases.

All cells in the body have protein markers, called antigens, on their surfaces that identify them as either "normal" or "foreign." The presence of foreign antigens (such as cancer cells) provokes a reaction involving lymphocytes, the cells that defend the body against disease. Some of these defender cells produce antibodies. The antibodies can seek out and destroy specific antigens, such as cancer cells.

Immunotherapies are a type of treatment designed to control the antigen/antibody immune response by targeting the antigens on specific types of tumor cells. As researchers identify more of these tumor-specific antigens, they are working to develop therapies that target only those cells.
Two types of immunotherapy:

- Antibody therapy – Antibodies are made in the laboratory and can locate and bind to substances in the body, including cancer cells. Rituximab is a therapy that treats certain types of lymphoma. Herceptin is a therapy that treats certain types of breast cancer.

- Cancer vaccines – Researchers are developing vaccines that may encourage the patient's immune system to recognize cancer cells. Cancer vaccines are designed to treat existing cancers or to prevent the development of cancer. The Food and Drug Administration has not approved cancer vaccines, but several are being tested in clinical trials.

Immunotherapy and Bladder Cancer

For bladder cancer that has not spread, intravesical immunotherapy (meaning inside the bladder) is the standard of care.

Intravesical immunotherapy involves filling the bladder with a solution containing Bacillus Calmette-Guérin (buh-SIH-lus KAL-met-gay-rin) (called BCG), a bacterial organism that is used to vaccinate against tuberculosis but is also used to treat certain bladder cancers. The BCG is put into the bladder through a catheter. It stimulates an immune response within the bladder to destroy any remaining cancer cells. Intravesical immunotherapy is performed after any remaining tumor cells have been removed from the bladder. Six BCG treatments over six weeks is then given with an additional course of treatments for maintenance. This usually is for at least one year but might be for longer if your doctor thinks that is the best course of treatment for you. The treatment success rate with intravesical BCG is 70-80 percent when used as recommended.

Clinical Trials

A treatment clinical trial is a research study meant to help improve current cancer treatments or obtain information on new cancer treatments. When clinical trials show that a new treatment is better than the standard treatment, the new treatment may become the standard treatment.

Clinical Trials for Bladder Cancer Patients

This section explains what clinical trials are and describes several clinical trials that are available at MD Anderson Cancer Center to treat bladder cancer.

Clinical trials are research studies that involve people. The main purpose of a cancer clinical trial is to find a better way to treat cancer and/or reduce complications. All patients who participate in clinical trials are volunteers who can choose to stop participating at any time.

Clinical trials are important to develop new treatments for cancer. Many of today’s standard cancer treatments – treatments that are accepted and widely used by medical experts – are based on the results of previous clinical trials. In some instances, patients may not personally benefit from participating in a clinical trial but by participating, new knowledge will be gained that may help future patients.
Patient Selection
Patients are selected for bladder cancer clinical trials based on factors related to the tumor. Some factors are:

- the stage of the cancer and
- the way the cancer looks under a microscope.

Your doctor may recommend a clinical trial to you based on your particular case. General types of clinical trials and those currently available at MD Anderson are listed below. Although this list is updated frequently, recently opened trials may not be listed. Your doctor will provide you with the most up-to-date and detailed information.

Types of Clinical Trials

Neoadjuvant Trial – In this type of trial, the patient will receive treatment before the bladder is surgically removed or treated with radiation. The “pre-treatment” may include a new bladder cancer fighting-drug.

Adjuvant Trial – The patient will receive treatment after bladder surgery or radiation.

MD Anderson Clinical Trials

Intravesical Administration for Patients Who Have Not Responded to Prior Treatment
SWOGS0337 – The goal of this study is to learn if the drug gemcitabine (when given directly into the bladder within 3 hours after the tumor is removed from the bladder) can help to prevent bladder tumors from returning. To participate, the patient must have a TURBT (bladder surgery) after enrolling in the trial, have had no prior bladder cancer for more than nine months before the TURBT and no more than two recurrences in the past three years.

2009-0938 – A study to evaluate intravesical administration of SCH 721015 (the compound under investigation) in patients with transitional cell carcinoma of the bladder who do not want cystectomy. Patients in this study must have not responded to at least two prior courses of BCG and more than three months has elapsed since the last intravesical treatment.

Recurrent or Extensive Disease Requiring Cystectomy
2007-0704 – A study to learn if the drug Tarceva™ (erlotinib) can help to shrink the tumor or slow its growth, before surgery, in patients with transitional cell carcinoma.

Muscle Invasive Disease after Neoadjuvant Therapy
SWOGS1011 – A surgical trial to compare the side effects of performing a standard lymph node removal to performing an extended lymph node removal. Surgery with extended lymph node removal will remove additional lymph nodes that are farther away from the bladder than those removed during standard lymph node surgery.

MD Anderson Clinical Trials Involving Chemotherapy
2006-0014 – A study to find the highest tolerable dose of Gemzar® (gemcitabine) and Adriamycin® (doxorubicin) that can be given together with Velcade® (bortezomib) in patients with urothelial cancer or other solid tumors. Eligible patients must have had at least one prior
therapy.

A number of new chemotherapy treatments plans are also being studied in clinical trials for their effectiveness for bladder cancer that has spread. These treatment plans include three developed at MD Anderson:

- A three-week regimen of the drugs ifosphamide, adriamycin and gemcitabine
- A two-week regimen of the drugs cisplatinum, gemcitabine and ifosphamide
- A two-week regimen of gemcitabine, paclitaxel, and doxorubicin for patients with poor kidney function.

**Support**

The Bladder Cancer Support Team serves patients who are diagnosed with bladder cancer, as well as their families. It is funded by a generous U.S. Government grant. The Support Team organizes patient and caregiver meetings, events and lecture series to help educate patients about bladder cancer. The Support Team provides information about risk factors and the relationship of bladder cancer to occupational and lifestyle exposures. Patients and families learn about bladder cancer and become more involved in their treatment plan. These efforts improve the overall quality of care for patients and promote patient involvement through education.

The Bladder Cancer Support Team also works to improve public awareness of bladder cancer and its causes. The Support Team is involved in the community. Their goal is to assist individuals with work-related exposure to bladder-cancer causing chemicals and help individuals with nicotine dependence.

**Members of the Support Team:**
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