Bladder Cancer Basics for the Newly Diagnosed



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Many thanks to the doctors, nurses and BCAN volunteers who con-

Many thanks to the doctors, nurses and BCAN volunteers who contributed to the content of this booklet: Marianne Borch, R.N., Dale Heffler, Cheryl Lee, M.D., Edward Messing, M.D., Staci Mitchell, R.N., Michael O'Donnell, M.D., Mark Soloway, M.D., Cindy Soloway,

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GE Healthcare



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way, and Walter Stadler, M.D.

You Are Not Alone

"You have bladder cancer." Words you most likely never expected to hear. As a newly diagnosed bladder cancer patient, the most important thing you should know is that you are not alone. There are people and resources to help you and the thousands of others living with this disease.

Right now, you may be overwhelmed, frightened and perhaps angry. As you begin this journey, it is important to know the facts. This handbook is intended to ease your fears and help you understand the basics about bladder cancer to enable you to take charge of your treatment and your life.

You may be surprised to learn that bladder cancer is one of the most commonly diagnosed cancers, with more than 65,000 new cases each year. In the United States, bladder cancer is the fourth most common cancer in men and ninth in women. With proper diagnosis, bladder cancer is a treatable disease, and there are more than 500,000 bladder cancer survivors in the United States today.

Learn as much about your diagnosis and treatment options as you can—from your medical team, from our website, **www.bcan.org**, and from the additional resources listed in this booklet. Choose a urologist who is experienced in treating bladder cancer, someone you can trust and who will answer your questions. Go for a second and even a third opinion, if you are so inclined. By understanding your options, you can make informed decisions, take control of your disease and learn to live with bladder cancer.

Many people have made this journey and there are sources of support available to you for comfort, hope and healing. Allow this to be your time to heal, to live fully and to love. You are stronger than your disease. You cannot change your diagnosis, but you can change your perception of your situation.

— Larry, diagnosed in 2002

ABOUT BCAN

BCAN—the Bladder Cancer Advocacy Network—is the first national advocacy organization dedicated to improving public awareness of bladder cancer and increasing research directed towards the diagnosis, treatment and cure of the disease.

BCAN was founded in 2005 by Diane Zipursky Quale and her husband, John Quale, who was diagnosed with bladder cancer in 2000. When the Quales began dealing with the disease, they discovered that there was little knowledge among the general public and general medical community about the causes, symptoms and treatment of bladder cancer, and that there was only a limited amount of information available to those suffering from it. Despite the fact that bladder cancer is the 5th most commonly-diagnosed cancer in the U.S., it has been treated like the "elephant in the room," the disease no one wants to talk about in public. Unfortunately, this lack of public recognition results in less funds allocated to research devoted to the diagnosis, treatment and cure of bladder cancer.

While numerous organizations are devoted to other forms of cancer, bladder cancer was by far the most prevalent cancer without a single national advocacy voice. Diane and John thought that it was time to give a voice to bladder cancer and the hundreds of thousands of survivors of this disease. BCAN, a non-profit organization supported by public contributions, is a cooperative effort among bladder cancer survivors, their families and caregivers, and the medical community. More than 35 prominent urologists, oncologists, radiologists and pathologists, representing many of the major cancer centers in the United States and Canada, serve on BCAN's Scientific Advisory Board.

BCAN offers services, information and resources to bladder cancer survivors and caregivers. Our interactive website includes an online community. We sponsor many educational programs each year.

We encourage you to join us in our efforts to raise awareness of this prevalent disease and to work towards finding a cure for bladder cancer.

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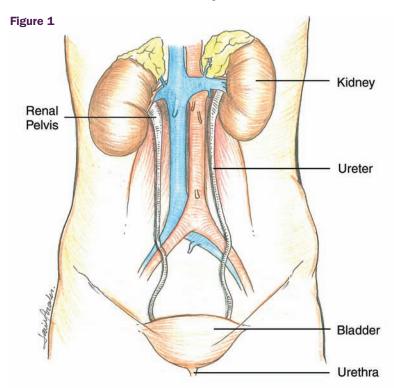
Understanding Bladder Cancer

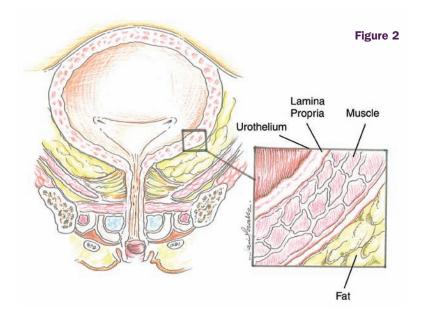
The Bladder and its Function

You generally don't think about your bladder—where it is located or what it does—until you see blood in your urine or have pain or irritation when you urinate. Even then you may not be concerned, thinking it is simply a urinary tract infection (UTI) that can easily be treated with antibiotics. Following weeks of failed treatment, your family doctor, internist or OB-GYN may suggest you see a urologist. It is then that your education about the bladder—where it is located and what it does—begins.

The bladder is part of our urinary system which filters waste products from our blood and then, once produced, transports the waste products or **urine** out of our bodies. The diagram below illustrates the organs of the urinary system (Figure 1).

The primary "machines" in our human filtering system are our two **kidneys**, located close to the spinal cord and protected by our ribs. The kidneys, working independently, have the significant task of filtering approximately 20% of our total blood volume each minute, getting rid of the by-products of digestion and of other body functions. Once produced, the urine (the filtered waste product) is stored in the central part of the kidney called the **renal pelvis**. At regular intervals, the renal pelvis contracts and propels the urine through the **ureters**, a narrow, thin-walled tube that extends from inside the renal pelvis to the **bladder**.





The bladder is a thick-walled structure, consisting of a thick muscle covering and a relatively thin inner layer (Figure 2). This inner layer (urothelium) consists of several layers of cells, called transitional or urothelial cells. The lamina propria is a specialized layer, composed primarily of blood vessels and cells, that separates the lining from the actual muscle wall of the bladder.

For most people, the bladder can hold as much as one pint (16 ounces) of urine at a time and contracts or expands depending on how much fluid is in it. When the bladder contracts following a series of neurological "messages" to the brain and spinal cord, the urine moves through the **urethra** outside the body.

Description of Bladder Cancer

Bladder cancer occurs when cells in the bladder start to grow out of control. Almost all bladder cancers develop in the transitional cells of the inner layer of the bladder which is in contact with urine. Some can grow into the deeper bladder layers. As cancer grows through these layers into the wall of the bladder, it becomes harder to treat. The transitional cells lining the bladder are also found in the inner layers of the renal pelvis, ureters and urethra. Similar cancers can occur in these areas, though much less frequently.

Risk Factors for Bladder Cancer

Cigarette smoking is the most common risk for bladder cancer. Approximately 50% of the men who are diagnosed with bladder cancer have a history of smoking, while 30% of women diagnosed are or have been smokers.

You may also be surprised to learn that there are certain occupations that place a person at a higher risk for bladder cancer. Workers in industries that use chemicals derived from a compound called arylamines have been shown to be at greater risk for cancer, e.g. dye, textile, tire, rubber and petroleum workers as well as painters and hairdressers.

Common Signs and Symptoms of Bladder Cancer

Without question, the most common clinical sign of bladder cancer is painless gross **hematuria**, blood in the urine that can be seen by the patient (Figure 3). The bleeding is often occasional and short-lived rather than consistently present. It may be that the tumors do not produce enough blood for a patient to see (**microscopic hematuria**) and are only detected with the help of special chemicals and/or a microscope after a urine test is done by a physician.

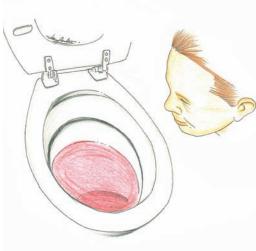


Figure 3

However, blood in the urine does not necessarily mean a diagnosis of bladder cancer. Infections, kidney stones, as well as aspirin and other blood-thinning medications may cause bleeding.

Irritation when urinating, urgency, frequency and a constant need to urinate may be symptoms of bladder cancer. Oftentimes, though, these are merely symptoms of a urinary tract infection and antibiotics become the first line of treatment. To make the necessary distinction between an infection and something more serious, it is critical that a urine culture be done to detect any bacteria in the urine. If the culture is negative for bacteria, patients should be referred to a urologist for further testing.

Types of Tests Used to Diagnose Bladder Cancer

Radiological Tests

One of two radiological tests is prescribed by the urologist to explore possible reasons for the patient's hematuria or irritative symptoms. Historically, the **IVP** or **intravenous pylegram**, using dye, or contrast, with conventional x-ray technology to evaluate the urinary tract system has been the principal test prescribed. Before the IVP, a complete medical history is taken to determine if there are any medical conditions (such as allergy to contrast material or "dye," asthma, or kidney disease) which might alter the way the procedure is performed.

However, in many hospitals, the **CT urogram**, a CT scan using contrast to examine the kidneys, ureters, and bladder is the recommended procedure. Because the CT urogram provides a three dimensional view of the kidneys and urinary system, the urologist is able to use this to also rule out any kidney tumors. In addition, other organs in the abdomen, such as the liver or lymph nodes, can be viewed to ensure that a tumor from the bladder has not spread to those areas. Similar to the IVP, a complete medical history must be performed prior to the procedure.

The most common clinical sign of bladder cancer is blood in the urine that can seen by the patient.

Cystoscopy: The Gold Standard

Although the radiological tests provide important information about the kidneys and the ureters, **cystoscopy** is still the best method of evaluating the bladder and the urethra. The **cystoscope**, a long thin tube, is inserted through the urethra. Today, with the widespread use of the flexible cystoscope (Figure 4), most of these diagnostic procedures are done in the outpatient setting with little or no discomfort.

As the urologist looks through the cystoscope, the locations where there appears to be abnormal features are noted and recorded.

During the cystoscopy, the urologist may choose to take a small piece of

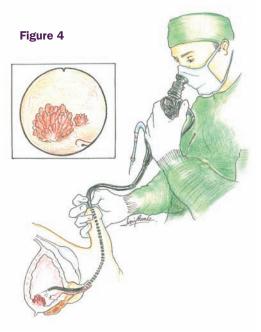
what appears to be abnormal tissue (**biopsy**) and send it to the pathologist to read and analyze. In addition, a sample of the urine from the bladder is frequently sent for analysis (**cytology**) to determine if there are any cancer cells. The biopsy specimen as well as the urine sample will help the urologist make recommendations about your future care.

Patients will go home after the cystoscopy if it is done in the doctor's office. Patients should expect that there may be some bleeding and possible irritative bladder symptoms following the cystoscopy for a day or two. Although seeing blood in the urine may be very troubling for the patient, the urologist, understanding that even small amounts of blood can affect the color of the urine dramatically, may not be concerned.

Staging and Grading of Bladder Cancer

Ninety-five percent of bladder tumors arise from the bladder lining surface (epithelium). Those that arise from that surface are either papillary (tumors that grow out from the surface) or sessile tumors (which are low and flat). While occasionally a benign tumor can arise in the bladder, the overwhelming majority of bladder tumors are malignant, or cancers. A biopsy can distinguish the benign from the malignant cancers.

Grade and Stage describe the bladder tumor, helping to provide guidance for the urologist in choosing the best treatment option(s). **Staging** is a careful attempt to find out the extent of the cancer. Staging will define whether the cancer has invaded into or through the bladder wall, whether the disease has spread, and if so, to what parts of the body. The higher the stage the further the cancer has grown away from its original site on the surface of the bladder. **Grade** refers to what the cancer cells look like, and how many cells are multiplying. The higher the grade, the more uneven the cells are and the more the cells are multiplying. Grade is expressed as a number between 1 (low) and 3 (high, i.e. G3); the higher the number the



Cystoscopy is the gold standard for diagnosing bladder cancer.

less the tumor resembles a normal cell. In lieu of numbers to grade a bladder cancer tumor, your doctor may refer to the tumor simply as low or high grade. Knowing the grade can help your doctor predict how fast the cancer will grow and spread.

The following are the stages for bladder tumors: (Figure 5)

T0: No tumor

Ta: Papillary tumor involves the urothelium without invasion

into the bladder wall

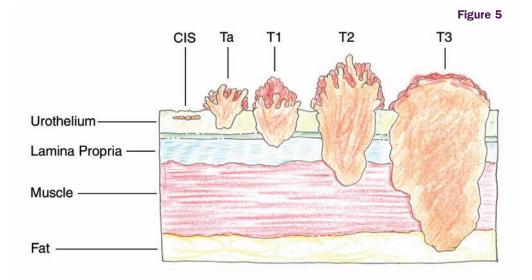
TIS (CIS): Carcinoma in situ (non-invasive flat high grade cancer)

 T_1 : Tumor invades the lamina propria T_2 : Tumor invades the muscle layer

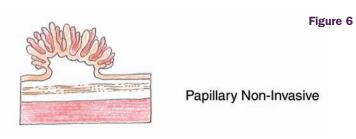
T₃: Tumor grows through the bladder wall into the

surrounding fat layer

Tumor invades other organs near the bladder (i.e., prostate, uterus, vagina, pelvic wall)



Ta papillary tumors are usually low grade (most closely resembling normal cells) and, even though a large majority will recur multiple times after the initial diagnosis and removal, 85-90% will never invade the bladder wall and become life-threatening (Figure 6).



Although CIS is also noninvasive, as the tumor has not grown into the **lamina propria** (the layer of blood vessels and cells that is situated between the bladder lining and the muscle wall), it is more aggressive than Ta noninvasive tumors and will probably be treated with more aggressive therapies.

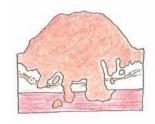


Figure 7

Flat Muscle Invasive

Once the tumor has invaded the lamina propria, it is considered an **invasive tumor** with the potential of spreading through the muscle wall and possibly spreading to those organs that border the bladder (Figure 7).

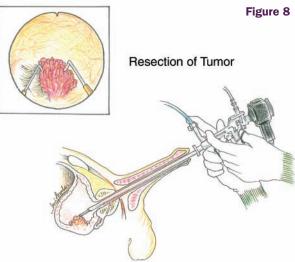
Cancer cells from invasive bladder tumors may also appear in the lymph nodes near the bladder or even in areas further away. Lymph nodes are small glands that store the white blood cells that help fight disease throughout the body. Although they can often only be seen with a microscope, cancer cells in the lymph nodes indicate that the tumor has spread and will influence the management of the bladder cancer patient. Chemotherapy may be suggested.

Treatments for Bladder Cancer

TURBT: Transurethral Resection of a Bladder Tumor

Generally after a diagnosis of a bladder tumor the urologist will suggest that the patient have an outpatient procedure in the hospital to examine the bladder more completely under anesthesia (general or spinal) and to remove, if possible, those tumors which are suitable for resection. The doctor may refer to this procedure as a **TURBT** (**transurethral resection of a bladder tumor**).

The TURBT is "incision-less" surgery usually performed in the hospital as an outpatient procedure. It is the first-line surgical treatment for bladder tumors. Like the cystoscope, the resectoscope or the instrument used to remove the tumor is introduced through the urethra into the bladder. Attached to this scope is a small, electrified loop of wire which is moved back and forth through the tumor to cut and remove the tissue (Figure 8).



The TURBT is

"incisionless"

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surgery usually

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Bladder cancer involves a lifelong monitoring process that requires diligence and compliance on the part of the patient. Electricity is also used to seal off bleeding vessels. This is sometimes called **electrocauterization** or **fulguration**. One of the advantages of this procedure is that it can be performed repeatedly with minimal risk to the patient and with excellent results. There is less than a 10% risk of infection or injury to the bladder, and both are easily correctable.

The most common risks of the TURBT are bleeding, pain, and burning when urinating and all three are temporary. If the bladder tumor is large, the urologist may choose to leave a catheter in the patient's bladder for a day or two to minimize problems occurring from bleeding, clot formation in the bladder or expansion of the bladder due to possible storage of excess urine or blood. Even if the tumor is small, a catheter may be inserted to rinse the bladder out if the bleeding persists.

All the specimens from the TURBT will be sent to the pathologist for review. Whether further treatment is necessary will depend on the pathologist's findings. If the tumor is low-grade, solitary or non-invasive, the urologist will often choose to follow the patient with cystoscopy and/or cytology (urinalysis) on a regular basis. There will be life-long monitoring that will require diligence and compliance on the part of the patient. If you are diligent with this surveillance, and a tumor does recur, it will be caught early, greatly reducing the risk of developing invasive disease.

Intravesical or Immunotherapy: Local Treatments for Non-Invasive Tumors

The procedure of instilling the drug into the bladder is called **intravesical chemotherapy or immunotherapy**. Whether the instillation into the bladder is done in the recovery room immediately following the TURBT or 2-3 weeks following the TURBT will depend on the size, number or stage of the tumors and the drug being instilled.

There are two principal drugs that are used as intravesical chemotherapy or immunotherapy.

- Mitomycin C is an intravesical chemotherapy drug that has been shown to be effective after the TURBT in reducing the number of recurrences of bladder tumors by as much as 50%. An advantage of Mitomycin C is that it is not easily absorbed through the lining of the bladder and into the blood and, thus is less risky than chemotherapy given intravenously (into the veins). Side effects from the drug can be painful urination and/or "chemical cystitis," an irritation of the lining of the bladder which can feel like a urinary tract infection. Both of these side effects are temporary and will disappear when the therapy is stopped.
- Bacille Calmette-Guerin or BCG is intravesical immunotherapy which
 causes an immune or allergic reaction that has been shown to kill cancer
 cells on the lining of the bladder. BCG is often preferred for patients
 who have high grade tumors or who have CIS or T₁ disease.

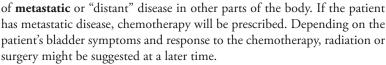
The urologist may also suggest maintenance therapy using BCG, the rationale being that the initial therapy plus intermittent therapy for

2 to 3 years may provide a decreased likelihood that the tumors will recur. The disadvantage to maintenance therapy is prolonged bladder irritation, fever, and bleeding which may force the patient to discontinue the therapy.

Both Mitomycin C and BCG are administered through a catheter which is placed in the bladder through the urethra. The drug is then introduced into the bladder (Figure 9).

Bladder Removal and Reconstruction

If a bladder tumor invades the muscle wall or if CIS or a T₁ tumor still persists after intravesical therapy, the urologist may suggest removal of the bladder or a **radical cystectomy**. Before any radical surgery is performed, a series of CT scans and other tests will be ordered to exclude the possibility



The two types of surgery performed for muscle-invasive or other high risk bladder cancer are **partial or complete radical cystectomy**.

Partial cystectomy is fairly uncommon and is generally only performed:

- if the muscle-invasive bladder tumor is the first and only bladder tumor the patient has had.
- if the tumor is in a location where it is easily accessible for surgery and, if removed, will leave the bladder with enough capacity for the patient to have normal bladder function.

A complete radical cystectomy requires complete bladder removal, and in men, almost always involves removal of the prostate as well. For women, in addition to removing the bladder, the surgeon may also remove the uterus, fallopian tubes, ovaries and cervix. Removal of the bladder also requires the surgeon to create a passage for the urine to go from the kidney to outside the body. Even though the bladder is removed, the kidneys, ureters and urethra are still in place. The types of urinary reconstruction are described in detail below.

Types of Urinary Reconstruction

An Ileal Conduit is the easiest and most common reconstruction
performed by the urologist. A small portion of the ileum or small
intestine is disconnected. One side of the piece of ileum is attached to
a skin opening on the right side and a small stoma or mouth is created.



A plastic appliance or **ostomy bag** is placed over the stoma to collect the urine. The ureters are sewn or re-implanted near the other end of the ileum. Because the nerves and the blood supply are preserved, the conduit is able to propel the urine into the appliance (Figure 10).

Figure 10

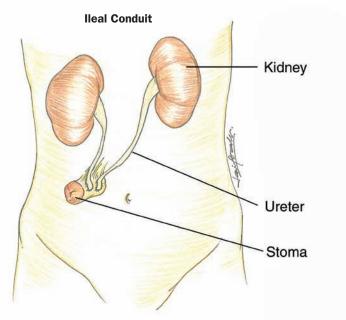
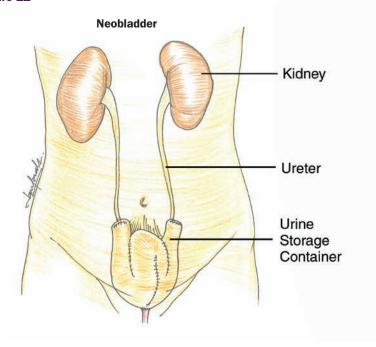


Figure 11



- A **continent cutaneous pouch** is an internal storage "container" for urine. Using a combination of small and large intestine, the urologist reconstructs the tubular shape of the intestine and creates a sphere or pouch. This pouch is connected to the skin on the abdomen by a small stoma creating a type of continent urinary reservoir; no external bag is necessary. The patient drains the pouch periodically by inserting a catheter (a thin tube) through the small stoma and then removing the catheter and, in some cases, covering the stoma with a bandage.
- A **neobladder** creates an internal storage "container" for urine. Using a portion of small intestine, the urologist reconstructs the tubular shape of the intestine and creates a sphere. The ureters are connected at the top of the sphere, while the urethra is attached at the bottom (Figure 11). By tensing the abdominal muscles, relaxing the sphincter muscle, the patient is able to push the urine through the urethra.

A radical cystectomy is considered major surgery and, as in many surgeries, patients may have complications as a result of the operation. The choice of which type of reconstruction to utilize is a highly individualized decision between the patient and the doctor, and depends on a variety of factors, including the patient's overall health, age, and extent of disease. There are advantages and disadvantages to each type of reconstruction. Be sure to discuss each option with your physician so that you can agree on which option will work best for you.

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The choice of

Chemotherapy

Chemotherapy refers to drugs used to treat cancer systemically. These drugs are administered by injection directly into the patient's veins, and attack cancer cells anywhere in the body (Figure 12).

Neoadjuvant chemotherapy is the term used for chemotherapy prior to surgery. Several important clinical trials have shown that the use of intravenous chemotherapy before radical cystectomy improves survival for patients with invasive bladder cancer. It appears that this type of initial chemotherapy shrinks the tumor within the bladder and may also kill small metastatic deposits of disease that have spread beyond the bladder.

Adjuvant chemotherapy is the term used for chemotherapy following surgery. Typically, removal of the bladder also involves removal of a number of lymph nodes surrounding the bladder, which are then sent to the pathology lab for analysis. If the pathology results indicate that the cancer has spread to the lymph nodes or to other organs near the bladder, the doctor may recommend chemotherapy to help prevent any cancer recurrence.



If bladder cancer is found to have spread to other sites, systemic chemotherapy is recommended. It is very difficult to permanently cure metastatic bladder cancer in most people. In most cases, the goal of treatment is to slow the spread of cancer, achieving shrinkage of tumor (temporary remission), relieving symptoms, and extending life as long as possible. With advances in treatment, most patients with advanced bladder cancer can expect to live longer than they could just a few years ago.

Bladder Preservation Therapy

In recent years, chemotherapy and radiation have been combined to provide a bladder preservation therapy in cases where removal of the bladder has been recommended. In the past, radiation therapy alone was used because it effectively shrunk tumors. Bladder cancers react to chemotherapy (chemosensitive) and therefore adding combined chemotherapy (multiple chemotherapeutic agents given together) to radiation has improved results. To ensure the success of bladder preservation therapy, there are at least three requirements which should be met: 1) a "complete" resection of the tumor(s) by TURBT; 2) no obstruction of one or both kidneys as a result of the bladder tumor; 3) no T₄ bladder tumors, and no large fields of CIS.

If the tumors do not respond to an initial course of chemotherapy and radiation, it may be reasonable to perform, if medically possible, a cystectomy, a complete removal of the bladder.

Becoming a Proactive Patient

You are the most important part of your healthcare team. As the team leader, make certain you have a medical team in whom you have a strong sense of trust and with whom you can easily communicate. Share information with your medical team, and do not hesitate to ask questions. If your questions aren't answered completely, ask them again. If possible, bring a family member or friend to each appointment, so they can ask questions and hear the answers—often it takes more than one set of ears to get all the necessary information. Write down your questions in advance, and bring along extra paper to write down the answers.

Questions to Ask Your Doctor

What kind of bladder cancer do I have?
How often do you treat patients in my situation?
What is the stage of the disease? Has the cancer spread?
What is the grade of the tumor?
What are my treatment choices? Which do you recommend
for me? Why?
What are the expected benefits of each kind of treatment?
What are the risks and possible side effects of each treatment
What is the treatment likely to cost? Is this treatment covered
by my insurance plan?
How will treatment affect my normal activities?
Can I speak with a patient who has gone through
this type of treatment?

Research and Clinical Trials

Clinical trials are essential parts of cancer research. A cancer clinical trial is a study conducted with cancer patients, usually to evaluate a new treatment. Clinical trials for bladder cancer may provide possible treatment alternatives to patients who have not had success with standard and approved therapies. You may want to discuss clinical trial options with your physician prior to beginning therapy.

To find information about current clinical trials in bladder cancer:

BCAN's Clinical Trial Matching Service www.bcan.org 800-504-7442

National Cancer Institute www.cancer.gov/clinicaltrials

Coalition of Cancer Cooperative Groups www.cancertrialshelp.org

Additional Resources

So, what comes next? Take some time now to digest and reflect on the information you've just read. You are not alone in this journey, but you are the most important member of your medical team. By reaching out to other survivors, learning as much as you can about your treatment options, and taking advantage of the resources available to cancer survivors, you will gain the tools you need to fight this disease. We encourage you to visit our website, **www.bcan.org**, which provides a listing of current bladder cancer support groups. In addition, you can join our online community which will connect you with other bladder cancer survivors and caregivers. If you want to find cancer support groups in your community, check with your local urologist or cancer center. Additionally, other organizations and resources that may be helpful to you are listed below:

Information about Bladder Cancer, Symptoms and Treatment Options

American Cancer Society

1-800-ACS-2345 www.cancer.org

American Society for Clinical Oncology

1-888-651-3038 www.cancer.net

American Urological Association Foundation

1-866-746-4282 www.auafoundation.org

Bladder Cancer Webcafe

www.blcwebcafe.org

National Cancer Institute

1-888-4-CANCER www.cancer.gov

National Comprehensive Cancer Network (NCCN)

1-215-690-0300 www.nccn.org

Support Services for Cancer Survivors:

CancerCare

1-800-813-HOPE www.cancercare.org

Gilda's Club

1-888-GILDA-4-U www.gildasclub.org

Lance Armstrong Foundation

1-866-467-7205 www.livestrong.org

National Coalition for Cancer Survivorship (NCCS)

1-888-650-9127 www.canceradvocacy.org

United Ostomy Associations of America, Inc.

1-800-826-0826 www.uoaa.org

The Wellness Community

1-888-793-WELL www.thewellnesscommunity.org

www.bcan.org



Visit us online at www.bcan.org and register your e-mail address to receive our regular newsletter, *BCAN Outlook*. It will provide you with updates on our activities, advances in the treatment and cure of bladder cancer, and other helpful information. We are a patient-based 501(c)(3) organization. Tax deductible donations may be made online at www.bcan.org or by check to:

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