

## 2

## Diagnosis and classification

The underlined terms are listed in the glossary.

### Signs and symptoms

Blood in the urine is the most common symptom when a bladder tumour is present. Tumours in the bladder lining (non-muscle-invasive) do not cause bladder pain and rarely present with lower urinary tract symptoms (need to urinate, irritation).

If you have urinary tract symptoms such as blood in the urine, painful urination or need to urinate more often, a malignant tumour might be suspected, particularly if treatment does not reduce the symptoms. Muscle-invasive bladder cancer can cause symptoms as it grows into the muscle of the bladder and spreads into the surrounding muscles.

If you have a more advanced tumour, you may experience additional symptoms like pelvic pain, pain in the flank, and weight loss, or you might be able to feel a mass in the lower abdomen.

More information on muscle-invasive and non-muscle-invasive bladder cancer is available in Leaflet 01, "What Is Bladder Cancer?".

### Diagnosis

Your doctor will take a detailed medical history and ask questions about your symptoms. You can help your doctor by preparing for the consultation.

- Make a list of your previous surgical procedures.
- Make a list of the medications that you take.
- Mention other diseases and allergies that you have.
- Describe your lifestyle, including exercise, smoking, alcohol, and diet.
- Describe your current symptoms.
- Note how long you have had the current symptoms.

### Diagnostic tools

Because blood in the urine is the most common symptom when a bladder tumour is present, your doctor will test your urine to look for cancer cells and to exclude other possibilities like urinary tract infections. Your doctor may refer to this test as 'urinary cytology'.

Physical examination does not reveal non-muscle-invasive bladder cancer, but you might be able to feel a mass if cancer has advanced to the muscle-invasive

stage. If muscle-invasive bladder cancer is suspected, your doctor should perform rectal and, for women, vaginal examinations by hand (bimanual palpation).

In addition, your doctor will do a series of tests to make the diagnosis. Advanced diagnostic tools are described in the next section.

## CT urography

Computed tomography (CT scan) urography gives your doctor information about the lymph nodes and abdominal organs. The scan takes approximately 10 minutes and uses x-rays. It is the most accurate imaging technique for diagnosing cancer in the urinary tract.

CT urography is noninvasive, so no instruments are inserted into your body. A contrast agent is injected into the body through a vein to improve the visibility of certain internal body parts and pathways during the CT scan. For this examination, your kidneys must function normally. Be aware that the contrast agent can cause an allergic reaction, so please let your doctor know if you have had any allergic reactions in the past. The staff will also ask you about allergies. If you are taking any antidiabetic medications, your doctor might ask you to stop taking them for a few days.

If CT urography detects a tumour in the urinary tract, your doctor will recommend a biopsy to confirm the

diagnosis. The biopsy is a surgical procedure to remove small piece of tissue for further examination. Bladder biopsy is usually performed through an endoscope, with the patient under general anaesthesia (combination of intravenous drugs and inhaled gasses; you are 'asleep').

CT urography cannot detect small or superficial tumours (CIS).

## Intravenous urography

Intravenous urography (IVU) is another imaging technique for examining the urinary tract. CT urography provides more information for diagnosis but is not widely available in some countries. IVU provides an alternative means of assessing the lymph nodes and abdominal organs. It cannot detect small or superficial tumours (CIS).

In IVU, a contrast agent (dye) is injected into the body through a vein, and then an x-ray of the abdomen is taken. The kidneys excrete the contrast agent into the urinary tract, which improves its visibility in the x-ray.

Because the intravenous contrast agent can cause an allergic reaction, your doctor will ask you about any allergies. Your kidneys must function normally for this examination. If you are taking antidiabetic medications, your doctor might ask you to stop taking them for a few days.

### The terms your doctor may use:

**Carcinoma in situ (CIS)** CIS is a type of non-muscle-invasive or superficial bladder cancer. The cancer cells are only in the lining of the bladder, but it has a high risk of growing into the deeper layers of the bladder muscle tissue and spreading to other organs or lymph nodes (metastatic disease).

**Urinary cytology** The examination of voided urine or bladder-washing specimens for exfoliated cancer cells

**Cystoscopy** A test that allows your doctor to look at the inside of your bladder and urethra using a thin, lighted tube called a cystoscope

## Transabdominal ultrasound

Ultrasound is a noninvasive diagnostic tool that can visualize large masses in a full bladder. It cannot detect small or superficial tumours (CIS). This study does not require intravenous contrast; however, ultrasound cannot replace CT urography or cystoscopy.

## Cystoscopy

The detection of bladder tumours depends on endoscopic examination of the bladder, called cystoscopy. Cystoscopy is a test that allows your doctor to look at the inside of your bladder and urethra using a thin, lighted tube called a cystoscope.

After the urethra is anaesthetised, the cystoscope—a flexible camera and instrument—is inserted into the urethra and the bladder. If a tumour can be seen or if a probe of fluid from the bladder (irrigation cytology) contains malignant cells, further diagnostic tests are needed.

Small biopsies can be taken immediately with the cystoscope. Larger biopsies or removal of tumours, called transurethral resection of bladder tumour (TURBT), must be done under general anaesthesia.

CIS is diagnosed by combination of cystoscopy, irrigation cytology, and evaluation of multiple bladder biopsies.

After the examination, you might have some blood in your urine for a few days. Drinking an additional 500 mL per day (eg, two extra glasses of water) will help dilute the urine and flush out the blood. You might also have painful urination or have to urinate more often or more urgently. These short-term effects will pass. If they persist for more than 2 days, you might have a urinary tract infection and should contact your doctor.

## Transurethral resection of bladder tumour

TURBT is the surgical removal (resection) of bladder tumours. This procedure is both diagnostic and therapeutic. It is diagnostic because the surgeon removes the tumour and all additional tissue necessary for examination under a microscope (histological assessment). TURBT is also therapeutic because complete removal of all visible tumours is the treatment for this cancer. Complete and correct TURBT is essential for good prognosis. In some cases, a second surgery is required after several weeks.

TURBT is performed by the insertion of a rigid endoscope through the urethra into the bladder, with the patient under general anaesthesia. TURBT usually takes no longer than 1 hour and requires a short hospital stay. After the operation, in some cases, a transurethral catheter is placed for a few days.

As in any surgical procedure, bleeding and infections may occur after the surgery. Symptomatic infections are treated with antibiotics and rarely require longer hospitalization. Perforation of the bladder during the operation is not very common but can occur if the removal procedure goes too deep. Perforations usually resolve with catheterization for a few days; however, some cases require open surgery and suturing of the bladder.

## Photodynamic diagnosis

Photodynamic diagnosis (PDD) is another diagnostic method available at some centres and is performed during TURBT. PDD makes cancer cells visible under violet light to improve detection and removal of tumours and reduce the risk of recurrence.

An hour before the operation, a nurse inserts a catheter and irrigates the bladder with a solution of 5-aminolaevulinic acid or hexaminolaevulinic acid. The catheter is removed immediately after irrigation. Cancer cells in the bladder process the active compound in the solution and become fluorescent under violet light. No side effects or complications have been reported for PDD.

## Narrow-band imaging

Narrow-band imaging (NBI) is the application of light at specific blue and green wavelengths during normal cystoscopy. This enhances the visual contrast between healthy tissue and cancer tissue and improves the detection of tumours in the bladder (studies have not shown that NBI reduces recurrence). This method does not require any bladder instillation.

## Classification

Bladder tumours are classified by tumour stage and subtype and by grade of aggressiveness of the tumour cells. Staging is a standard way to describe the extent of cancer spread. The kind of treatment you receive will depend on these elements.

## Stage and subtype

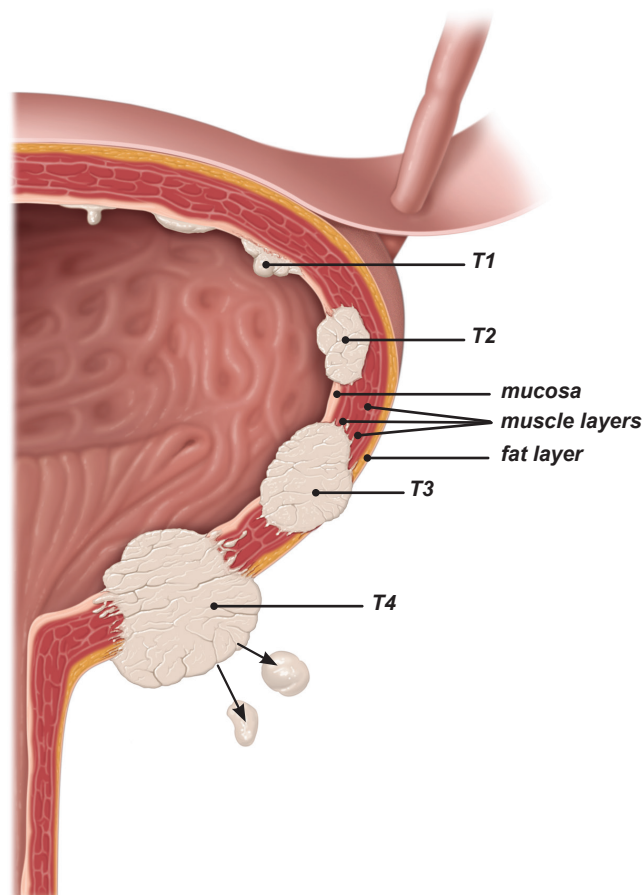
Tumour stage and subtype are based on whether or not the cancer is limited to the bladder (localisation)

and the degree to which the tumour has invaded the bladder wall (**Fig. 1**). This information is important for determining the risk of recurrence (risk stratification) of the disease.

Stages Ta, T1, and Tis indicate non-muscle invasive bladder cancer (**Fig. 1**):

- Ta tumours are confined to the bladder lining (shown as 'mucosa').
- T1 tumours have invaded the connective tissue under the bladder lining but have not grown into the muscle of the bladder wall.
- Tis tumours are flat velvet-like tumours (CIS) that are confined to the bladder wall.

Stages T2, T3, and T4 indicate muscle-invasive bladder cancer, with tumours that have grown into the bladder wall (**Fig. 1**). Imaging is used for staging of this type of bladder cancer.



**Fig. 1** Tumour stage (T) and subtypes

## Imaging for staging invasive bladder cancer

CT and magnetic resonance imaging (MRI scan) are the techniques used for staging invasive bladder cancer. A combination of positron emission tomography (PET scan; uses a radioactive tracer) and CT is increasingly being used at many centres in Europe to enhance the ability of detecting the spread of bladder cancer to the lymph nodes or other organs, mainly in difficult sites like bone.

Imaging is used for staging invasive bladder cancer to determine prognosis and to provide information for treatment selection. Tumour staging must be accurate to ensure the correct choice of treatment.

In staging of muscle-invasive bladder cancer, imaging determines:

- How far the tumour has grown into the bladder wall (extent of local tumour invasion) (**Fig. 1**)
- Whether cancer has spread to the lymph nodes
- Whether cancer has spread to the upper urinary tract and other distant organs

## Grading

During examination of tissue under a microscope (histological analysis), the pathologist will grade the tumours according to their potential to grow (aggressiveness). High-grade tumours are more aggressive, and tissue is greatly altered in appearance. Low-grade tumours are less aggressive, and tissue is mildly altered in appearance.

## Stratification into risk groups

Risk stratification is used to provide more precise treatment recommendations. Your doctor does this based on personal characteristics, disease stage and grade, and study-based data from bladder cancer risk tables.

You will be assigned to one of three groups (low, intermediate, or high risk) based on your risk of recurrence and progression. This stratification is used to determine the treatment options that can be offered and the follow-up that will be needed.

- Low risk: Patients have a single small (<3 cm) tumour that is stage Ta (**Fig. 1**) and that is not likely to grow (low grade). Low-risk patients do not have CIS (stage Tis), which has a high risk of growing into the deeper layers of the bladder muscle tissue and spreading to other organs or lymph nodes.
- High risk: Patients are at high risk if their tumour is stage Tis (CIS) or T1 or is aggressive (high grade). Multiple large (>3 cm) and recurrent tumours of any stage are also high risk.
- Intermediate risk: Patients with tumours that are not clearly either low or high risk are considered to have an intermediate risk of recurrence and progression.

This information was last updated in March 2016 and is subject to change following review by the European Cancer Patient Coalition (ECPC) and EAU Guidelines Office.

This leaflet is part of a series of EAU Patient Information on Bladder Cancer. It contains general information about bladder cancer. If you have any specific questions about your individual medical situation you should consult your doctor or other professional healthcare provider.

This information was produced by the European Association of Urology (EAU) in collaboration with the EAU Section of Oncological Urology (ESOU), the Young Academic Urologists (YAU) the European Society of Residents in Urology (ESRU), and the European Association of Urology Nurses (EAUN).

The content of this leaflet is in line with the EAU Guidelines.

**Contributors:**

Dr. Mark Behrendt – author Basel, Switzerland  
Dr. Juan Luís Vasquez – author Herlev, Denmark  
Ms. Sharon Holroyd Halifax, United Kingdom  
Dr. Andrea Necchi Milan, Italy  
Dr. Evangelos Xylinas Paris, France

Illustrations by: Mark Miller Art  
Missouri, United States of America

Edited by: Jeni Crockett-Holme  
Virginia, United States of America