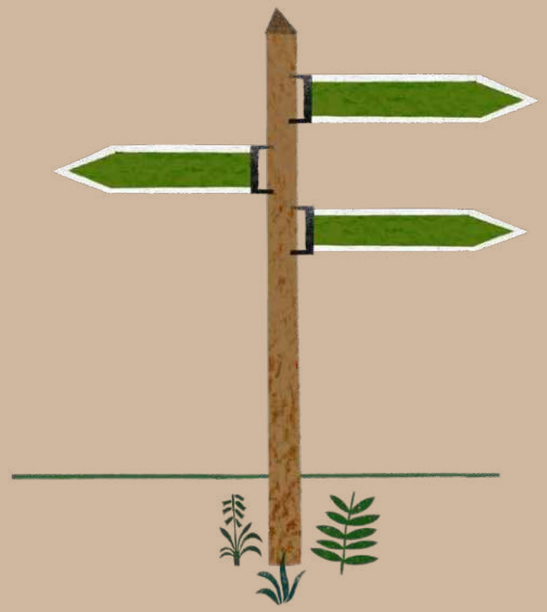
UNDERSTANDING BLADDER CANCER

THE PATIENT PATHWAY
FROM DIAGNOSIS TO TREATMENT



This brochure contains a brief overview about the origin, diagnosis and treatment options for bladder cancer.
This brochure does not replace the discussion with your doctor. Speak to your doctor if you have further questions.

For better readability of personal designations and person-related words, the masculine form is used. These terms apply to all genders.

CONTENTS

THE BLADDER

THE BLADDER AND ITS FUNCTION

The bladder lies in the centre of the pelvis behind the pubic bone. It is part of the lower urinary tract. This consists of the renal pelvis, ureters, urinary bladder and urethra. The bladder wall is made up of several layers.

The inside is lined with a mucous membrane called the urothelium, followed by a connective tissue layer, the muscle layer and finally a fat layer. The bladder is an expandable hollow organ with a volume between 500 and 1000 ml. It is divided into the bladder crown (apex), bladder body (corpus) and bladder floor (fundus).

The ureters (through which urine is transported from the kidneys into the bladder) open into the apex of the bladder in a slit-shaped and oblique manner. This prevents the backflow of urine that is continuously produced by the kidneys.

From 200–500 ml, stretch sensors are activated in the bladder wall and the person feels an urge to urinate. At the base of the bladder, at the transition to the urethra, there are two sphincters. The inner sphincter is opened by a reflex and the outer sphincter can be controlled voluntarily. After opening of the sphincter, emptying of the bladder occurs through the urethra.

WHAT IS BLADDER CANCER?

Changes in the genetic material of cells occur frequently in the course of life. These are normally either corrected by their own repair mechanisms or the cell is sorted out by the immune system. Some factors such as smoking, chronic urinary tract infections and certain chemicals seem to favour such changes in the mucous membrane of the bladder. Changes that are passed on from one generation to another have also been described in bladder cancer. In these families, bladder tumours occur more frequently.

When cells multiply uncontrollably due to changes in their genetic material, cancer has developed. In the bladder, this happens most often to cells in the mucous membrane: the urothelium.

As long as the tumour is limited to the mucous membrane, it is called a non-muscle-invasive carcinoma. If the tumour grows into the muscle layer, this is a muscle-invasive carcinoma. When carcinoma cells are deposited into other organs via blood or lymph channels, secondary tumours, so-called metastases, develop.

Bladder cancer is more common at older ages, over 70 years, and men are three times more likely to be affected than women. In terms of tumour incidence, bladder cancer ranks 7th in Switzerland.

BLADDER CANCER SYMPTOMS

Bladder cancer does not always cause symptoms. Complaints are often non-specific and can also occur with other diseases of the kidneys and urinary tract.

Indications can be blood in the urine, increased urge to urinate, pain when urinating, or pain in the lower abdomen. In this case, you should see your doctor at an early stage and clarify the cause.

Particularly in the advanced stage, general symptoms can also occur, such as weight loss, increased tiredness (fatigue) or reduced performance. If metastases have already formed, these can also cause symptoms depending on their location, such as pain in the bones or shortness of breath due to offshoots in the lungs.

BLADDER CANCER DIAGNOSIS: WHAT NOW?

Immediately after the diagnosis of bladder cancer, it is time to determine the stage of the disease as well as your general health. This is important because the treatment options depend significantly on the stage of the disease and the state of health of the individual patient.

The stage of the disease depends on the local tumour growth as well as its spread, i.e. whether the cancer is only localised, has reached the bladder muscle or has even formed secondary tumours in lymph nodes or distant organs.

At this point, radiological assessment by CT* scan is indicated. These are procedures that allow your treatment team to visualise cancer cells in your body. Your doctor will also do blood tests to check for abnormalities.

Based on all these results, the disease can be correctly classified and the appropriate treatment chosen.

The optimal therapy goals and treatment options will be discussed and determined with you and in a multidisciplinary tumour board (consisting of specialists from different areas of medicine).

If metastases have already formed, depending on the state of health and kidney function, the preferred initial treatment (the so-called first-line therapy) is chemotherapy, usually followed by immunotherapy. If chemotherapy is contraindicated, immunotherapy is an alternative as a first-line treatment.

* Computer tomography

THE LAND
OF SURGERY

SURGERY FOR BLADDER CANCER

If the tumour is limited to the mucous membrane, it is removed under anaesthesia via the urethra with an electric loop (TURB). The bladder may then be irrigated with a chemotherapy solution. Over the course, TURB is repeated to make sure that no tumour is detectable any longer. Depending on the risk, repeated bladder irrigation is used to try to prevent a recurrence of the disease. Either attenuated bacteria (BCG) or a chemotherapy solution is used for irrigation.

If the muscle layer is affected, the bladder is usually completely or partially removed. There are various possibilities for draining the urine. Which one is chosen depends on various factors such as anatomical conditions, concomitant diseases and your individual desire. Basically, a distinction can be made between continent and non-continent urinary diversion.

With continent urinary diversion, emptying can be controlled voluntarily; with incontinent urinary diversion, the urine flows continuously into a reservoir.

Continent options include the replacement bladder, which is formed from a piece of intestine and releases urine out through the urethra, or a pouch, which allows urine to be drained through a valve in the abdominal wall. The incontinent variants include the urostoma, which directs urine into a bag on the abdominal wall. If your general condition allows it, chemotherapy is usually recommended for a period of about three months prior to the surgery.

WHAT IS RADIOTHERAPY?

Radiotherapy is a treatment that uses high doses of radiation to kill cancer cells in a targeted manner. Radiotherapy can be used for bladder cancer with different goals.

For non-metastatic bladder cancer, it can be combined with a chemotherapy to achieve a cure in certain low-risk patients. This combination is called chemoradiotherapy – where chemotherapy is usually given first to reduce the risk of a relapse.

Chemoradiotherapy is also an option for patients who are too frail for surgery. Radiotherapy alone can also be used in palliative care to relieve symptoms, but without the hope of curing patients.

In advanced disease, radiotherapy may be used to relieve symptoms or to treat a small number of lesions/metastases, the latter in the case of an inadequate response to chemotherapy or immunotherapy.

THE LAND
OF RADIOTHERAPY

SPACE FOR YOUR QUESTIONS: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THE BLADDER
The urinary bladder is a hollow organ that serves to store urine. Urine flows continuously from the kidneys into the bladder, where it is collected.
CANCER
Bladder cancer can occur in different forms. Often, the cancer is only superficial on the bladder lining, but it can also grow into the bladder wall or form secondary tumours (metastases) in other organs.
With bladder cancer, there may be no symptoms initially, or various non-specific symptoms. Talk to your doctor immediately if you notice blood in your urine or feel pain when urinating.
SYMPTOMS
INVESTIGATION
?
WHAT NOW?
At this point, some steps are important to understand the disease and choose the optimal treatment. After the spread of the tumour and your general health have been determined, your doctor will discuss the treatment options with you and you will decide on a strategy together.
Every patient is different. Your treating physician may suggest other therapies or a different sequence than the one presented here.
LAND OF SURGERY
CHEMOTHERAPY PORT
LAND OF RADIOTHERAPY
LAND OF CHEMOTHERAPY
Chemotherapy is a widely used treatment to fight malignant cancer cells. It destroys fast-growing cells in particular.
RELAPSE
IMMUNOTHERAPY PORT
LAND OF IMMUNOTHERAPY
Immunotherapy allows our natural defences (the immune system) to recognise and fight the cancer.
At any time during your treatment, your doctor may suggest that you take part in a clinical trial. This enables the use of new and innovative medicines.
LAND OF STUDIES
PORT OF TARGETED THERAPY
SIDE EFFECTS
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LAND OF TARGETED THERAPY
Many cancer cells have individual identifying features on their surface. These can be attacked with a targeted therapy and in this way, the cancer cell can be destroyed.

SPACE FOR YOUR QUESTIONS:

WHAT IS CHEMOTHERAPY?

For bladder cancer, chemotherapy is a drug that damages the cells and blocks their growth and division. Since it inhibits cell division, cells that grow quickly are affected the most. This explains why tumour cells are much more susceptible to the toxicity of chemotherapy than other cells in the body.

In the case of localised disease affecting only the mucous membrane, local chemotherapy (acting only in the bladder) can be administered as described in the chapter on surgery. In the case of more advanced diseases, a systemic therapy (acting throughout the body) is administered intravenously (via the veins).

For non-metastatic disease, chemotherapy is usually given before surgery (called: neoadjuvant), but if this was not possible, it can also be given after surgery (called: adjuvant).

The aim of systemic chemotherapy is to eliminate cells far away from the tumour that cannot be removed by a local intervention. Ultimately, chemotherapy reduces the risk of relapse and significantly increases the survival rate.

Common side effects include fatigue, immunosuppression and nausea. Hair loss is less frequent. Depending on the drug regimen, tingling in the extremities and hearing loss may also occur.

The same drugs are used to treat metastases, but with the aim of controlling the disease rather than curing it.

RELAPSE – WHAT NOW?

Despite optimal treatment, the disease can relapse after a few months or years.

The frequency of relapse depends on the stage of the disease at diagnosis and the treatment given at the beginning.

Most of the time, the relapse is detected during the scheduled follow-up visits. Occasionally, however, new symptoms indicate a relapse and it is important to report any new symptoms early.

In the event of a relapse, metastases (offshoots/secondary tumours) may occur in distant organs such as lymph nodes, lungs, bones, liver, or the cancer may come back localised at the site of the surgery or radiotherapy.

In the case of a relapse, drug therapies are mainly used as described in the section on chemotherapy, in the section on immunotherapy and in the section on targeted therapy. In this situation, we speak of so-called second-line therapies, the second drug treatment since diagnosis. If the relapse is localised, another operation or radiation may be reasonable.

The best course of action is usually discussed at a joint meeting of all specialists (tumour board) and then determined with the patient.

WHAT IS IMMUNOTHERAPY?

Immunotherapy is a drug that reverses the blockage of the immune system caused by cancer cells and uses the body's own immune cells to fight cancer cells.

The immune system is similar to a police force that protects the body from foreign, but also internal threats (such as malignant cells). This complex system is not only able to recognise and fight viruses and bacteria, but can also defend itself against malignant cells (cancer cells) that could cause great damage. To elude this police force, cancer cells "camouflage" themselves in some manner: tumour cells produce certain molecules that they attach to their surface. These molecules impair the immune system's ability to recognise the tumour cell as a dangerous cancer cell and destroy it.

Immunotherapy removes this camouflage so that certain cells of the immune system can actively attack and destroy the malignant cells. Unfortunately, these immune cells can also mistakenly recognise healthy cells in the body as invaders and attack them, leading to "autoimmune" toxicity. These inappropriate reactions can affect any organ, and the most common immune-related side effects include skin rashes, gastrointestinal and thyroid disorders. Most side effects are mild, but it is important to report them to the oncologist immediately.

In bladder cancer, immunotherapy can be used in three areas. In localised disease, immunotherapy after removal of tumour tissue can reduce the risk of relapse in selected high-risk situations. In advanced disease, it can be administered immediately following first-line chemotherapy, both in the case of disease control, as well as for disease progression, and it prolongs survival in these cases. Finally, it is an option for some patients with advanced disease for whom chemotherapy is not an option.

THE LAND
OF IMMUNOTHERAPY

WHAT ARE TARGETED THERAPIES?

Targeted therapies are a range of newer drugs that specifically target cancer cells. A subgroup of these therapies are the so-called antibody-drug conjugates (abbreviation: ADCs). ADCs consist of two main components. The first is an antibody, i.e. a protein that binds to a specific target molecule in the body. As a rule, the target molecule is ubiquitous on tumour cells, i.e. very present, and occurs less frequently in healthy cells. The second part of an antibody-drug conjugate is a chemotherapy payload.

ADCs function according to the following mechanism: The antibody binds to a target protein on the surface of bladder cancer cells. When this happens, the cell does not recognise the chemotherapy payload (the effective drug) as threatening and takes it up. The chemotherapy is activated in the malignant cell and kills it. So, in essence, an ADC works like a Trojan horse: The antibody is the wooden exterior that gives the drug access to the inside of the city, in this case the cell, and once inside, the antibody unleashes its army (the chemotherapy). This works by stopping cell division and causing the malignant cell to die.

An antibody-drug conjugate has been shown to be effective in advanced bladder cancer after chemotherapy and immunotherapy, while others are still in development and may soon be available. ADCs can have a number of side effects, including low blood cell counts, skin rash, hair loss, tingling in the extremities, gastrointestinal and eye problems.

Current clinical development is not only limited to ADCs. Other targeted therapies are also being investigated at this time that could be used in the future for patients with certain molecular variations.

SIDE EFFECTS OF THERAPY

The side effects of the cancer therapies described here vary greatly. In local treatments using surgery or radiation, the side effects are usually limited to the site of the procedure.

Drug treatments lead to side effects of varying degrees that can affect the entire body. The side effects vary greatly from person to person and are perceived in different ways by those affected.

Modern, targeted therapies have somewhat different side effects than chemotherapy or immunotherapy. They mainly lead to sensory disturbances in the hands and feet (tingling, numbness), itching and skin changes, hair loss and, more rarely, increased blood sugar levels. There may also be increased fatigue, loss of appetite and diarrhoea. In contrast, changes in blood count values are rarer.

The treatment team will inform you about possible side effects at the beginning of the treatment and explain preventive behaviour. In any case, it is very important that you report any disturbing side effects to the treatment team early on so that they can be treated quickly and efficiently.

* This video deals mainly with the side effects of antibody-drug conjugates against bladder cancer.
If you would like to learn more about the side effects of other systemic therapies (chemotherapy and immunotherapy), please scan the QR code of the respective chapter.

*

FEELING BETTER

WHAT CAN I DO TO FEEL BETTER DURING TREATMENT?

Every person affected finds their own way to cope with the disease and the treatment. It is important that you determine for yourself what is important and helpful to you. Listen to your needs and your body and express your wishes to those close to you and to your treatment team.

A regular daily routine with physical activities and rest can be helpful. In any case, you should pay attention to a regular, balanced and sufficient diet. Eat what makes you happy and tastes good. Special diets during cancer therapy are not advised. Sufficient fluid intake (1.5 to 2 litres per day) is also very important. The body needs sufficient fluid to feel and function well.

Many of those affected report that light physical activity improves their well-being. The extent and intensity of the activity depends on your state of health.

If you want to do complementary treatments, it is recommended that you discuss this with your treatment team. They will be happy to give you good advice.

Further helpful resources on cancer treatment can be found on the following pages. If you have any questions, please contact your treating physician or treatment team at any time.

FURTHER REFERENCES ON CANCER TREATMENT

- **“Bladder cancer (cancer of the urinary bladder)”**, Swiss Cancer League 2022, available online at https://www.krebsliga.ch/ueber-krebs/krebsarten/blasenkrebs-krebs-der-harnblase
- **“For Patients”**, Swiss Group for Clinical Cancer Research SAKK, available online at https://www.sakk.ch/en/patients/patients
- **“Living with cancer”** The platform for fewer taboo topics and more well-informed affected persons, available online at https://lebenmitkrebs.ch/

This brochure cannot replace the advice of your doctor. Always speak with your doctor if you have questions about bladder cancer and/or your treatment.

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