

## FACT SHEET

### OVERVIEW OF CYSTITIS/INFLAMMATORY BLADDER DISORDERS

A normal urinary bladder should not cause pain, burning or discomfort with a frequent and urgent need to urinate. Pain in the bladder, with a frequent and often overwhelming need to urinate can have many different causes. The term cystitis simply means inflammation of the urinary bladder. An inflammatory bladder disorder may have many possible causes. Some may be mild and respond well to treatment, while others may have very severe consequences and even be fatal. Many of the different disorders have similar pain and urinary symptoms. All lesions should be carefully investigated since many of the disorders may mimic bladder cancer. All of the disorders need careful differentiation from similar conditions seen in gynaecology and urology since treatment may differ per disorder and the wrong treatment will not lead to improvement. Inflammatory bladder disorders can greatly impact all aspects of a patient's quality of life. This means that every effort is needed to achieve the right diagnosis and treatment.

#### Inflammatory bladder

##### Interstitial cystitis/bladder pain syndrome and Hunner lesion

- Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic bladder disorder of unknown cause, with persistent or recurrent symptoms of pain/hypersensitivity, irritation, or pressure sensation related to the bladder, with pain increasing as the bladder fills, and usually accompanied by a frequent and overwhelming need to urinate day and night. The symptoms may be continuous or occur in flares. It is a diagnosis of exclusion. It is currently subdivided into 1. non-lesion IC/BPS and 2. IC/Hunner lesion. Treatment may be conservative, oral, intravesical or surgical depending on the subtype, with cystectomy (bladder removal) as a final resort.

##### Acute radiation cystitis/chronic radiation cystitis

- Radiation therapy is one of the treatments used for cancer and uses high doses of radiation to destroy cancer cells and shrink tumours. Unfortunately, radiation therapy may also affect healthy cells in nearby tissue or organs, causing inflammatory changes. While acute radiation cystitis may occur during therapy or soon after, delayed symptoms may only appear more than 6 months and even years after completion of treatment and may continue in a chronic form for many years. In chronic radiation cystitis, hypoxia of the mucosal layers plays an important role. This is caused by dysfunctional small blood vessels in the bladder wall due to radiation damage. Symptoms may include bladder pain or irritation, spasms, an urgent and frequent need to urinate day and night and painful urination. Treatments include oral therapy, intravesical hyaluronic acid and chondroitin sulphate and hyperbaric oxygen therapy.

##### Cystitis cystica and cystitis glandularis

- Cystitis cystica is a common benign condition of the bladder with inflammatory changes to the urothelium which may involve lesions, cysts, vesicles or so-called von Brunn's nests and resemble a tumour formation. Cystitis glandularis is a further progression of cystitis cystica with glandular metaplasia of the urothelium. These conditions may occur as a response to chronic irritation of the bladder wall including stones and chronic or frequently recurrent UTIs. They may be asymptomatic but may present with non-specific symptoms and therefore need care to exclude other similar conditions such as malignancy. Symptoms may include pain, haematuria, urgency and frequency. Treatment involves removing the cause of the irritation and/ or removal of lesions.

### Follicular cystitis

- Follicular cystitis (FC) is a rare, chronic, inflammatory bladder condition which primarily affects women and is characterised by small mucosal nodules and lymphoid follicles in the lamina propria of the bladder wall, commonly in the trigone area. Symptoms include increased urinary frequency and painful urination. Treatment, which in some respects may be similar to IC/BPS, may also include antibiotics, systemic corticosteroids, surgical resection and as a last resort cystectomy.

### Eosinophilic cystitis

- Eosinophils, are a type of white blood cell that form part of the immune system and are likely to increase or example in autoimmune diseases, allergies, infections, reactions to certain drugs and can cause inflammation and damage. In eosinophilic cystitis there is a build up of these cells in the urinary bladder. The most common symptoms, which can mimic a UTI, are urgency, frequency, painful urination, haematuria and pelvic or suprapubic pain but there may also be nocturia and urinary retention. Patients have an increased risk of vesico-ureteral reflux and upper urinary tract involvement. Current treatments may include steroids or non-steroidal anti-inflammatory agents and transurethral resection of the bladder lesion. Despite therapy it tends to recur.

### Haemorrhagic cystitis

- Haemorrhagic cystitis occurs when the bladder lining becomes inflamed and bleeds. Causes include viral or bacterial infection, radiation therapy in the pelvic region, types of chemotherapy, exposure to certain chemicals and trauma. Haemorrhagic cystitis is also mentioned under other inflammatory bladder disorders with a clearly defined cause (e.g. BK or CMV induced cystitis, chronic radiation induced cystitis or chemical cystitis). Symptoms include blood or blood clots in the urine, painful urination, fever, frequency inability to urinate, loss of bladder control. Haemorrhagic cystitis can be a very serious condition leading to significant bleeding and/or life-threatening infection. Treatment greatly varies depending on the severity but may include antibiotics, antivirals, clot removal, changes to medication, embolisation and hyperbaric oxygen therapy. Rarely, blood transfusion or cystectomy made be needed.

### Drug/chemical induced cystitis

Many drugs can cause an inflammatory bladder, often damaging the urothelium, causing urgency, frequency pain, bleeding and lesions, similar to IC/BPS. Tiaprofenic acid is well-known, but many other drugs may cause symptoms of cystitis in susceptible people. Treatment involves stopping the drug concerned and then treating similarly to IC/BPS, including intravesical GAG treatment.

### Ketamine cystitis (street ketamine)

- Ketamine is a dissociative anaesthetic used for inducing and maintaining anaesthesia, for analgesia in a variety of pain settings, and as a rapid effect antidepressant. It is also used illicitly as a party drug for its hallucinogenic-like effect. In some users, it can cause chronic bladder inflammation, often severe lesions without malignancy, denuded epithelium, reduced bladder capacity and intense pain. Complete cessation is essential to reduce symptoms. Treatment is similar to interstitial cystitis/bladder pain syndrome (IC/BPS) and may include intravesical sodium hyaluronate or chondroitin sulfate, botulinum toxin injections and intravesical coagulation of ulceration. In some cases, a partial cystectomy with bladder augmentation is needed with a cystectomy with urinary diversion as a last resort.

### Chemotherapy-induced cystitis

- Cystitis may often be caused in cancer patients by treatment with the chemotherapy drugs cyclophosphamide and ifosfamide or administration of cancer treatments directly into the bladder. Symptoms include urgency, frequency, burning or painful urination, inability to empty the bladder completely, incontinence, blood in the urine, pelvic/abdominal pain. Chemotherapy can result in severe haemorrhagic cystitis. Treatment may include continuous bladder irrigation, increasing fluid intake, intravesical treatment with hyaluronic acid and chondroitin sulphate for example. The drug mesnex

may be given with infosfamide and higher doses of cyclophosphamide as this can help to protect the bladder.

### Chemical cystitis

- Some people may be particularly sensitive to chemicals found in certain cosmetic or hygiene products. These might include bubble bath, personal hygiene spray or spermicidal jelly. An allergic-type reaction can occur in the bladder, causing inflammation.

### Infectious cystitis

This section includes bacterial, viral, fungal, parasitic, other than common urinary tract infection (UTI) & sexually transmitted diseases (STD).

### Tuberculous cystitis

- Tuberculous cystitis is caused by *Mycobacterium tuberculosis* bacilli which can affect any part of the genitourinary tract and ravage the bladder. Any bladder lesions present are usually secondary to renal tuberculosis. Tubercles or nodules are sometimes seen on cystoscopy and can form ulcers, which then form scars, resulting in fibrosis. The bladder becomes distorted, contracted, and shrunken. One of the main causes for tuberculous cystitis in the Western world is BCG instillations for bladder cancer treatment. BCG uses a weakened tuberculosis pathogen for immunotherapy. On rare occasions, and mainly in immunocompromised patients, this can cause tuberculous cystitis. Voiding symptoms include frequency and urgency, painful urination, bleeding and low grade fever. Multidrug tubercular treatment is the first-line therapy and is effective in most patients, though surgery in the form of ablation or reconstruction may be necessary. Intravesical Bacillus Calmette-Guérin (BCG) treatment is used but may cause further irritative voiding symptoms.

### Schistosomiasis (bilharzia) of urinary tract

- Schistosomiasis is an acute and chronic parasitic disease caused by blood flukes (trematode worms) of the genus *Schistosom*. Infection occurs when larvae of the parasite, released by freshwater snails, penetrate the skin through contact with infected water. There are 2 major forms: intestinal and urogenital. In the case of infection in the bladder, the parasite matures to the adult form and resides in the bladder wall. The subsequent granulomatous inflammation causes nodules, polypoid lesions and ulcerations in the ureters and bladder, resulting in urinary frequency, painful urination and blood in the urine. Praziquantel is the recommended treatment against all forms of schistosomiasis. This form of cystitis has a high risk of causing bladder cancer.

### BK-virus cystitis

- The BK virus is a polyomavirus particularly known to affect transplant recipients. It is a virus often caught in childhood with symptoms of a common cold, but then lies dormant in the body permanently. It may become reactivated if the immune system becomes compromised for some reason. This can be caused by anti-rejection medicines following a transplant, especially in blood stem cell transplantation recipients. Bladder symptoms include brown or red urine, pain on urination, frequency or difficulty urinating, but it can also cause blurred vision, seizures, fever, muscle pain or weakness, coughs, colds or breathing difficulties. A complication can be haemorrhagic cystitis. Reducing the amount of anti-rejection medication can help to decrease the virus.

### Cytomegalovirus (CMV)-related haemorrhagic cystitis

- The cytomegalovirus or CMV is a member of the herpes virus family and is spread through body fluids such as blood, saliva, urine, semen and breast milk. CMV normally stays inactive in the body for life. In the case of pregnancy or a weakened immune system (immunocompromised patients) including following transplants, CMV infection is a cause for concern. CMV-related haemorrhagic cystitis is extremely rare but can occur when CMV has been reactivated for some reason. Symptoms can include bleeding, frequency, bladder pain and fever. CMV in the bladder may respond to antiviral therapy. Cidofovir may become a useful drug in patients who present with haemorrhagic cystitis after transplantation.

### Emphysematous cystitis

- Emphysematous cystitis (EC) is a rare form of urinary tract infection, characterised by gas within the bladder wall and lumen due to gas-forming bacteria. Symptoms include painful urination, blood in the urine, pelvic pain, an urgent and frequent need to urinate. While some people may have no symptoms at all, others may develop a potentially life-threatening infection with septic shock. Treatment mainly comprises antibiotics.

### Other

#### Bladder endometriosis

- Endometriosis is a painful condition in which tissue similar to the inner lining of the uterus grows outside the uterus. It often affects the ovaries, fallopian tubes and pelvic tissue. Bladder endometriosis occurs when endometrial-like cells grow on or in the urinary bladder walls, causing pain and inflammation in the bladder. Symptoms include painful periods with heavy bleeding, pelvic pain, pain when urinating, pain when the bladder is full, loin pain, a frequent and urgent need to urinate and blood in the urine. The symptoms may be continuous or intermittent, worsening around the time of menstruation. There may be superficial lesions on the outer surface of the bladder and deeper lesions or endometriotic nodules on the bladder lining or in the wall. Surgical options depend on the severity and the location.

#### Bladder leukoplakia

- Bladder leukoplakia, also known as keratinising squamous metaplasia, is a rare benign condition characterised by plaques forming on the bladder mucosal lining caused by chronic irritation and inflammation of the urinary bladder usually by bacteria. Most forms include limited leukoplakia in the trigone area in women which is considered harmless. However, in extensive leukoplakia, it has a high risk of becoming malignant (with high mortality rate), requiring strict follow-up. Symptoms include pain, an urgent and frequent need to urinate, painful urination and blood in the urine. Early diagnosis is important since some cases may become malignant. This means that annual cystoscopic monitoring should be performed to look for any malignant changes. Treatment depends on the stage of the disease and the degree of bladder damage. In most cases, it is treated with medication and intravesical instillations. With persistent painful symptoms, surgical laser ablation may be used to remove the plaques.

#### Bladder localized amyloidosis

- Amyloidosis is either a systemic disease where many organs and systems may be affected or it may be 'localised' which means that just a single organ or part of the body is affected. Bladder localized amyloidosis is a rare, recurrent, non-malignant disorder. However, cystoscopy and biopsy are essential to distinguish it from malignancy. Main symptoms are bleeding and irritative urinary symptoms. The standard treatment is surgical transurethral resection and fulguration of lesions.

#### Carcinogenic cystitis

- Local malignant tumours can infiltrate the bladder wall. Those most commonly occurring are prostate cancer, cervical cancer, rectal cancer, ovary (duct) cancer or lymphoma. Metastasis from non-regional cancers can also occur in the bladder. Since tumour cells can cause local necrosis, haemorrhage and bladder wall barrier problems, inflammation and treatment differs between the type of cancer that infiltrated the bladder wall.

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