# Interstitial Cystitis/Bladder Pain Syndrome and Associated Disorders: A Patient Perspective

Many patients with IC/BPS also have one or more associated diseases or disorders. These are also described as co-existing, concomitant or co-occurring disorders, comorbidities or non-bladder syndromes.

Some IC/BPS patients may even have multiple, complex conditions, including potentially very debilitating rheumatic systemic autoimmune diseases and disabling chronic fatigue. Sometimes these manifest themselves before the IC/BPS and sometimes are diagnosed later.

While the exact relationship between these associated disorders and IC/BPS is still inadequately understood, it is possible that some systemic disorders may play a role in making the bladder more susceptible to the development of IC/BPS.

Since diagnosed IC/BPS patients are generally treated by either a urologist or urogynaecologist, associated disorders may go unrecognised, undiagnosed and untreated. Both the doctors treating IC/BPS patients and the patients themselves should be on the alert for symptoms that may indicate another disorder, since in some cases it might change the approach to treatment of either the bladder condition or the associated disorder.

Associated disorders add greatly to the day-to-day problems and suffering of the IC/BPS patient, make coping more difficult and treatment more complex and challenging since a drug prescribed for one condition can exacerbate another and even cause actual damage. A coordinated multidisciplinary approach to treatment is therefore essential, with a patient's different specialists ideally working in collaboration. In practice, this rarely occurs. This means that the patient (or carer) ideally needs to play an active role in management and coordination of his/her own healthcare, keeping records of previous surgery, infections, symptoms, diagnosed conditions and treatment as well as any adverse reactions to drugs.

## Associated disorders may be grouped into the following categories:

- allergies or intolerances (including multiple chemical and drug intolerance),
- different chronic pain and fatigue syndromes,
- systemic autoimmune diseases ,
- gastrointestinal or gastroesophageal disorders
- neurological disorders.

Diseases and disorders that may occur with IC/BPS include for example:

- allergy/hypersensitivity
- drug & chemical intolerance
- asthma
- sensitive skin
- chronic fatigue (syndrome)
- anxiety
- depression
- fibromyalgia
- low back pain

- migraine/headaches
- temporomandibular joint disorder
- gastro-intestinal and gastro-esophageal disorders (such as irritable bowel syndrome (IBS), Crohn's disease, ulcerative colitis, gastro-esophageal reflux disease (GERD))
- interstitial nephritis (e.g. distal renal tubular acidosis – dRTA)
- rheumatoid arthritis (RA)
- Sjögren's syndrome
- systemic lupus erythematosus (SLE)
- thyroid disorders
- endometriosis
- vulvodynia (vulvovaginal pain)
- other pelvic pain.

## A brief look at a few associated disorders…

### Allergy and Intolerance

Many IC/BPS patients suffer from allergy or intolerance. Allergy occurs when the patient's immune system causes a reaction to substances that are harmless to most other people.

True allergies can be identified by allergy tests. Allergies can affect the skin, airways and sometimes organs. Examples of allergy include asthma, rhinitis, urticaria (nettle-rash), eczema and anaphylaxis. In some cases, patients receiving antihistamines for their allergy find that this treatment also has a beneficial effect on their IC/BPS bladder symptoms.

However, not all reactions are true allergy. Adverse reactions (= side effects) without involvement of the immune system are called intolerance which mainly occurs to food, drugs and chemicals (in the widest sense, including for example perfumed products, additives and tobacco smoke).

The problem with non-allergic intolerance is that it can cause symptoms similar to allergy but is unpredictable and can vary in severity according to the patient's general level of health at any given time.

Non-allergic intolerance is still a relatively unexplored, unresearched field and particularly so in relation to the drug intolerance experienced by some IC/BPS patients. Some IC/BPS patients may also have multiple chemical intolerance and feel dizzy and faint if there are chemicals in the air or if perfumed products or chemicals touch their skin or there are additives in their food and drink. Drug intolerance may affect, for example, cognitive functioning, eyesight and balance and cause dizziness, faintness, headache, general malaise, fatigue, drowsiness or sedation. At present, it is unclear why some IC/BPS patients have these problems and others not. It is, however, perhaps interesting to note that multiple drug and chemical intolerance is also found in patients with fibromyalgia.

Patients with extensive drug intolerance often respond better to intravesical treatment for their IC/BPS where less of the drug is likely to be absorbed into the system. Multiple drug intolerance, often misunderstood, can cause great problems with treatment and is depressing and frustrating for the patient.

### Gastro-intestinal and gastro-oesophageal disorders

**Irritable bowel syndrome** (IBS), a functional bowel disorder, is a very common disorder in IC/BPS patients. Symptoms include abdominal pain or cramp, diarrhoea and/or constipation and a bloated feeling due to gas formation.

**Inflammatory bowel disease (IBD)** comprises Crohn's disease and ulcerative colitis and is also found more commonly in IC/BPS patients than in the general population. IBD is a group of disorders

comprising Crohn's disease and ulcerative colitis, with weight loss, blood in the stools and diarrhoea at night. Commonly suspected to be of autoimmune origin.

**Gastro-oesophageal** disorders (gastro-oesophageal reflux disease (GERD) for example) have also been linked to IC/BPS. The most common symptom of GERD is persistent or recurrent heartburn, also called acid reflux, but it may also include regurgitation of food. GERD occurs when the lower oesophageal sphincter becomes weak and in the case of hiatus hernia. The latter can cause not only heartburn but also chest pain and spasms.

For further information about the digestive system and how it works:
https://www.niddk.nih.gov/health-information/digestive-diseases

## Rheumatic systemic autoimmune diseases

**Rheumatic diseases,** also called **musculoskeletal diseases,** encompass more than 200 diseases and are characterized by pain and a consequent reduction in the function of the musculoskeletal system; in some diseases there are signs of inflammation, some can also affect internal organs and some are autoimmune diseases. In relation to IC/BPS, we are particularly interested in the autoimmune and systemic rheumatic diseases.

In autoimmune diseases, the immune system attacks the patient's own body. Some autoimmune diseases may be "organ specific", i.e. they attack one specific organ in the body (for example thyroid disorders). Others may be "generalized" or "systemic": this means that they attack many different organs and systems throughout the body, including the upper and lower urinary tract. Patients who have both a diagnosed autoimmune disease and IC/BPS should be sure to inform their specialists of this fact, particularly if the autoimmune disease is diagnosed after the IC/BPS has been diagnosed and the urologist is unaware of this, since this may mean taking a different approach to treatment of the IC/BPS. Some patients may have more than one of these rheumatic diseases in addition to the IC/BPS. Symptoms of these diseases may overlap. The impact of these diseases can vary greatly depending on the organ(s) affected but they can potentially be severely debilitating.

A problem with some IC/BPS patients who have symptoms indicative of autoimmune disease is that laboratory tests may reveal few or no abnormalities. This has been shown in the case of Sjögren's syndrome. Some patients do not fulfil all the criteria of any single specific disease. While strict criteria are created for the purpose of research, they are all too frequently applied clinically too. The result is that many sick patients may still be going undiagnosed and untreated. If an autoimmune disease is suspected, patients should be referred to an internist, immunologist or rheumatologist. It may also be necessary to see an ophthalmologist, gastroenterologist or neurologist.

**- Rheumatoid arthritis (RA)** is a chronic, systemic, autoimmune, connective tissue disease that mainly affects the synovial membranes of joints and is characterised by pain, swelling and stiffness of joints, usually symmetrically. As the disease progresses, the ligaments are damaged, there is erosion of the bone, resulting in deformity of the joints. This deformity of the joints is an important difference with other rheumatic diseases such as Sjögren's syndrome. The disease can occur together with systemic lupus erythematosus (SLE) and Sjögren's syndrome and is known to occur with painful or irritable bladder disorders.

*Further information:*
https://www.niams.nih.gov/search?search=rheumatoid%20arthritis&type=All&media=All&f%5B0%5D=diseases_and_conditions%3A195

**- Systemic Lupus Erythematosus (SLE)** is a chronic, inflammatory, autoimmune connective tissue disease, involving many organs, with unpredictable flares and remissions. It may involve joints, skin, lungs, heart, vascular system, gastrointestinal tract, central or peripheral nervous system, kidneys and the bladder. A painful bladder disorder in SLE patients was known in the past as 'Lupus Cystitis' but is now generally referred to as IC/BPS. The symptoms and severity of SLE can greatly vary from patient to patient and may also undergo change in an individual patient over time. As in the case of IC/BPS, there is a high predominance of women patients.

*Further information:*
https://ghr.nlm.nih.gov/condition/systemic-lupus-erythematosus
https://www.niams.nih.gov/search?search=lupus&type=All&media=All

**- Sjögren's syndrome** is a chronic, autoimmune, connective tissue disease in which lachrymal (tear) and salivary glands malfunction and in which there may be systemic, multi-organ manifestations.
Its hallmark symptoms are sore, irritated eyes and dry mouth with a need to drink when eating because dry food otherwise sticks to the mouth and cannot be chewed or swallowed properly (so-called "cracker sign"). It is potentially a systemic disease and may therefore affect many organs and systems of the body in some patients. The majority of patients are women. Although it can affect any age group including children, the average age of onset is the late 40s. This disease is traditionally classified into two types: primary Sjögren's syndrome where the disease occurs alone and secondary Sjögren's syndrome when it occurs in association with another disease such as SLE, systemic sclerosis, rheumatoid arthritis and polymyositis /dermatomyositis. Sjögren's patients also have an increased risk of lymphoma. Neurologic involvement includes damage to peripheral nerves, particularly small fibre nerves in hands and feet. Less common forms of neurologic involvement can lead to poor coordination and can affect the brain and spinal cord, similar to MS.
While some patients may experience only mild symptoms, in others their quality of life is seriously impaired by debilitating symptoms and extreme fatigue. It can often take many years for a patient to get a diagnosis, particularly in patients in whom no autoantibodies can be seen and ESR is normal. In recent years, there has been an increased awareness that IC/BPS and Sjögren's syndrome can occur in association with each other and that Sjögren's syndrome may be being underdiagnosed in IC/BPS patients.

*Further information on Sjögren's syndrome:*
An Overview of Sjögren's syndrome by Dr J.P. van de Merwe. In two languages: English and Dutch.
http://www.painful-bladder.org/pbs_ic_ass_dis.html
https://www.sjogrens.org/

**- Sicca Syndrome** is often used to describe dryness of the exocrine glands, particularly the eyes and mouth when there is no evidence of autoimmune disease present. While sicca symptoms occur in the vast majority of Sjögren's patients, not everyone with these symptoms has Sjögren's syndrome. There are many potential causes of sicca syndrome, including side effects of commonly used medications and inflammatory diseases of the saliva and tear-producing glands.

## Distal Renal Tubular Acidosis (dRTA)

Some Sjögren's patients may have an autoimmune kidney condition of the distal tubules known as distal Renal Tubular Acidosis (dRTA) which is a type of interstitial nephritis and causes a urinary acidification disorder (with increased urinary pH) while the blood becomes more acid with loss of potassium (in severe cases leading to hypokalaemia), accompanied by hyperventilation. Instead of being recirculated in the blood, this potassium ends up in the urine and can cause burning pain, urgency and frequency, particularly at night in the bladder of an IC/BPS patient. While treatment with potassium citrate may correct the acidosis in the blood, the pain caused in the IC/BPS bladder is more difficult but may be helped by bladder instillations. A complication can occur when dRTA flares are

triggered by medication, including even over-the-counter vitamins and supplements, since this can cause even more bladder pain or irritation in IC/BPS patients and consequently be a hindrance to treatment of both the IC/BPS and other disorders.

## Fibromyalgia (FM)

Fibromyalgia is a chronic pain and fatigue condition characterized by widespread musculoskeletal pain and tenderness with so-called tender-points, sleep disorders or non-restorative sleep (patients wake up feeling unrefreshed), often extreme fatigue and what has been described as brain fog or "fibro fog" affecting the memory or clarity of thought, anxiety and depressive disorders. It usually affects more women than men. It is today not considered to be an inflammatory or autoimmune disease but possibly a disease of the nervous system. Since there is as yet no cure, treatment is aimed at symptom relief. It is commonly associated with a painful, irritable or overactive bladder and IC/BPS. Fibromyalgia can vary in severity from person to person. Some patients may have a mild form of discomfort, while others may suffer from a very severe and disabling form of fibromyalgia with extreme fatigue and pain. While not strictly considered a rheumatic disease, it is usually diagnosed and treated by a rheumatologist.

*Further information:*
https://fmaware.net/
https://www.rheumatology.org/Portals/0/Files/Fibromyalgia-Fact-Sheet.pdf
https://www.nhs.uk/conditions/fibromyalgia/

## Fatigue

Many IC/BPS patients suffer from fatigue and lack of energy. Fatigue may have many different causes – some known and some unknown - and can vary from mild, fluctuating tiredness at one end of the scale to completely debilitating chronic fatigue at the other end, with an impact that may virtually paralyse the patient's life. It is possible to have only physical fatigue or a combination of physical and mental fatigue (known as "brain fog").
Causes of fatigue may include for example sleep disruption, stress and anxiety, medication, and autoimmune and other diseases associated with chronic fatigue.
Sleep disruption: Lack of proper sleep is the first aspect that anyone is going to think of in relation to fatigue in an IC/BPS patient. While IC/BPS patients vary greatly in their symptom levels, including night-time voiding, this can fluctuate per patient depending on whether the patient is in a flare or in remission. The most severe IC/BPS patients, or patients in a flare, may be out of bed every 20 minutes or worse, even sitting all night on the toilet, or wrapped up in a blanket on the bathroom floor. But even only 2 or 3 times a night on a regular basis can cause considerable tiredness because some people find it very difficult to get off to sleep again once they have got out of bed.
However, many other aspects can contribute either to being unable to get off to sleep or to frequent wakening in the night, leading to extreme tiredness. Causes of fatigue due to lack of sleep can include:

- Pain, not only in the bladder but also elsewhere; many IC/BPS patients may have one or multiple other pain syndromes which may cause pain at night.
- Restless legs syndrome, itching, burning, tingling: all of these can prevent you from sleeping.
- Medications: all kinds of medication can cause insomnia.
- Patients may be woken up by noise: from a snoring partner, crying babies, noisy traffic etc.
- Too much light inside or outside the home, from streetlights or outside security lights.
- Anxiety, work stress, and the stress, worry and sometimes panic of coping with IC/BPS can all prevent sleep.
- Many diseases and disorders can cause sleeping disorders or insomnia, e.g. fibromyalgia.

Therefore, each patient should carefully think about whether it is purely the bladder pain and need to void that is waking them (or preventing them from sleeping), or whether something else has disturbed their sleep and they then feel their bladder discomfort and get out of bed. It may be purely the IC/BPS bladder in some patients, but in others perhaps a combination. The physical and psychological impact of sleep disruption can be extensive. Therefore, treatment for the bladder pain and the frequency and any other pain should have absolute priority. Any diseases causing chronic pain day in day out are very exhausting.
Patients should cut down night-time voiding as far as possible or advisable by limiting drinking in the evening and avoid consuming any food or drink that you know will irritate the bladder or food and drink that is likely to keep you awake. But make up for this by drinking plenty earlier in the day to avoid concentration of urine.
While some medication can cause insomnia, other drugs can cause drowsiness all day long. Medicine intolerance experienced to varying degrees by some IC/BPS patients can make them react much more strongly to even the lowest dosages. It is therefore important to be aware that any medication could potentially either cause insomnia or daytime drowsiness or exacerbate existing chronic fatigue.

Chronic fatigue: A special role is played here by autoimmune diseases such as systemic lupus erythematosus and Sjögren's syndrome in which true chronic fatigue can be a totally disabling symptom. Chronic fatigue can also occur in fibromyalgia. When no identifiable disease or cause of the fatigue can be found, it is known as chronic fatigue syndrome. Chronic fatigue is different to other forms of tiredness and has no bearing on whether the patient has slept well or not.

## Anxiety and Stress

While anxiety and stress are often described as comorbidities or associated disorders, they may also simply be a consequence of the impact of IC/BPS on the patient and his/her quality of life. A painful bladder condition such as IC/BPS can have huge psycho-social consequences and cause great anxiety and stress due to the continual worry about whether the patient is going to find a toilet in time when away from home, by the stress of sexual intimacy problems, anxiety about their job, financial repercussions and the impact on the whole family or simply due to years of being told that their bladder problem is "all in the mind", resulting in the patient losing self-confidence and feeling utterly helpless. In addition, urogenital disorders are still taboo in today's world and this makes sufferers feel stigmatized and socially isolated, and often too embarrassed to discuss sexual difficulties with their doctors. This is why an IC/BPS patient needs support and empathy. And this support aspect - whether it comes from health providers, the family or the patient support group - may be key to coping.

## Depression

Depression is experienced by many people in the general population, either occasionally or persistently but may particularly occur in patients with chronic disorders such as IC/BPS. Sometimes it is a question of being temporarily "down" or "moody" or "sad" or unable to cope, but sometimes it is more serious and needs treatment and professional counselling. Some patients may not actually realize that they are suffering from depression and this may partly be due to confusing usage of the word "depression". People so often say that something that has occurred has made them "so depressed", when in fact they mean that they are upset or sad or shocked about a specific incident. Under normal circumstances, patients will adjust to the situation and soon recover.
However, in cases of true depression, the sad or down feeling will persist. There may be multiple effects: weight can go up or down, patients may sleep too much or too little, may feel tired all the time and have no energy, have feelings of guilt, feel worthless, experience confusion or forgetfulness, have suicidal thoughts. Depression can make it impossible to work, study and cope with or enjoy

everyday life. While depression may be caused by psychiatric disorders, it may also form part of a syndrome of symptoms in chronic diseases, as has been documented in systemic lupus erythematosus, and may potentially occur in any disease with a neurological component including pain syndromes.

In IC/BPS patients, it may be a question of a temporary inability to cope which can be helped by good support and a sympathetic approach from their doctor, by a patient support group, by support in the home environment. If more serious, it should be treated with medication combined with counselling.

*Further reading:*
The National Institutes of Health has a useful booklet on depression online:
http://www.nimh.nih.gov/health/publications/depression/complete-index.shtml

## Endometriosis

Endometriosis is a chronic disease of adolescents and reproductive-aged women where endometrial tissue that normally grows inside the uterus develops abnormally in other places in the pelvis, including the ovaries and fallopian tubes, the bladder and bowel. The symptoms of endometriosis can vary. Some women are badly affected with devastating pelvic pain, while others might not have any noticeable symptoms. It can also cause painful bladder and bowel conditions due to the development of endometrial cells in the bladder or bowel. Endometriosis may occur together with IC/BPS, but a cystoscopy is essential since bladder endometriosis may be confused with IC/BPS if no cystoscopy has been carried out since the symptoms may be similar.

*Further information:*
https://medlineplus.gov/endometriosis.html
https://www.nhs.uk/conditions/endometriosis/
https://www.pelvicpain.org.uk/

## Vulvodynia (vulvovaginal pain)

The vulva is the female genital area including the delicate skin surrounding the opening of the vagina. Vulvodynia (or vulvovaginal pain) is a distressing, painful condition, difficult to diagnose and difficult to treat. It is a broad collective term used to describe any chronic pain condition of the vulvar area (more than three to six months) and embraces a number of different types of vulvar disorder causing chronic or intermittent pain, burning, stinging, rawness and pain with intercourse. There are two main types of vulvar pain who may sometimes occur together:

- Provoked Vestibulodynia (PVD) (also known as vulvar vestibulitis) is pain or burning sensation caused by something touching the vestibule (entrance to the vagina). Pain is caused by sexual intercourse, insertion of tampons, riding a bicycle, gynaecological examination, tight clothes or any situation where the vestibule is touched. There is usually no pain if the area is not touched. Vestibulodynia is diagnosed by touching the vestibule with a Q-tip. Even light pressure such as this can cause pain.
- Generalized Unprovoked Vulvodynia (GV) (previously known as dysesthetic or essential vulvodynia) is spontaneous pain, burning, stinging or rawness on or around the vulva, labia, vestibule, clitoris or perineum most of the time, whatever they are doing. It is not dependent upon touch or pressure but this can nevertheless exacerbate the symptoms. Urination may cause pain and burning. Generalized unprovoked vulvodynia is diagnosed when there is a history of relatively constant pain – although there may be periods of symptom relief - with no visible cause or other identifiable disorder such as infection.

Vaginal candidiasis (also known as thrush or vaginal yeast infection) can cause intense itching, irritation, inflammation and a thick white discharge. More frequent infection (four or more times a year) is called recurrent vulvovaginal candidiasis (RVVC). Frequent vaginal candida can occur with systemic autoimmune diseases and can eventually lead to chronic vaginal hypersensitivity with pain and irritation.

*Further information*
https://www.nhs.uk/conditions/vulvodynia/
https://www.nva.org/

## Thyroid disorders

The thyroid gland is situated at the front of the neck below the skin and muscle layers. It has the form of a butterfly with the two wings represented by the right and left lobes that wrap around the trachea. The function of the thyroid gland is to make thyroid hormone which regulates the body's metabolism and is essential for mental and physical development. The thyroid gland is prone to two extremes of disorders:

- Hyperthyroidism (it makes too much hormone
- Hypothyroidism (it makes too little hormone).

Chronic thyroiditis is an inflammatory condition of the thyroid caused by an autoimmune disorder in which lymphocytes invade the tissues of the gland. The most common type of thyroiditis is Hashimoto's thyroiditis. It includes swelling of the thyroid gland and partial or complete failure to secrete thyroid hormones. Women are affected more than men.

## Sensitive skin:

Many IC/BPS patients have a problem with dry, itchy, sensitive skin that is easily inflamed. It is advisable to keep the skin well moisturized with cream or lotion for sensitive skin to reduce the dryness and this may also reduce some of the itchiness.
IC/BPS patients with this problem should keep away from chemicals such as household cleaning products (wear protective gloves) and perfume, avoid using (perfumed) soap or any other products around the vulvar/genital area, take care with contraceptive devices containing chemicals such as condoms and spermicidal creams. If possible, clothes should be washed with products specially made for sensitive skin that do not contain perfume, wear cotton underwear and loose clothes, avoid touching garden plants that may cause skin reactions and take care in the sun if they find that their skin is sensitive to sunshine.