HUNNER LESION (HL)
(formerly known as Hunner's ulcer)

At the present time, two main types of Interstitial Cystitis/Bladder Pain Syndrome can be distinguished:

- **the classic type with Hunner Lesion** (formerly known as Hunner's ulcer, also known as Classic IC, ulcerative IC/BPS, and sometimes referred to today as Hunner Disease or Hunner IC).
- **the Non-Hunner Lesion type.**

Most IC/BPS experts today consider that these two types represent separate bladder conditions which differ in diagnosis, treatment and outcome.
It is therefore very important for a patient with Hunner lesions to be identified at the earliest possible stage.

BRIEF HISTORICAL OVERVIEW

Guy Leroy Hunner, a Boston gynaecologist, described this inflammatory bladder disease over a century ago in great detail for the first time in a series of papers, the first being published in 1914 (republished in 1915). In this first paper he writes:

"While cystoscopy usually reveals only one inflammatory spot, there may be two or three granulation areas near together or somewhat separated, and operation usually reveals a more extensive area of inflammation than was appreciated by cystoscopy. The ulcer area may be easily overlooked and the attention may first be arrested by an area of dead white scar tissue. In the neighbourhood of this scar-looking area, one sees one or more areas of hyperemia which, on being touched with a dry cotton pledget, or with the end of the speculum, bleed and first show their character as ulcers. In other cases, or perhaps at subsequent examination on the same case, the ulcer may be well defined as a deeply red area with granulating base and with congested vessels surrounding the area. In none of the cases has an individual ulcer area been more than a half centimetre in diameter, although two or three such ulcers have at times been grouped in a larger inflammatory area."

These "ulcers", described by Hunner as "elusive ulcers", came to be known as "Hunner's ulcers", although it was realized very early on that the term "ulcer" was a misnomer since it did not in fact concern a true ulcer at all but an inflammatory lesion, and was indeed frequently described by Hunner's contemporaries as a lesion. Vision with the still rudimentary cystoscope in those days was relatively poor and this may have been one of the reasons Hunner thought he was seeing ulcers. However, his description of lesions remained the gold standard for many years and the name Hunner's ulcer continued to be used, leading many urologists to believe that ulcers were necessary for a diagnosis.

DIAGNOSIS

Diagnostic procedures may include:
- Medical history
- Physical examination
- Laboratory tests including dipstick urinalysis, routine and special cultures, urine cytology

- Cystoscopy with/without hydrodistension and biopsy.

- Exclude other potential causes

It is essential to exclude other potential causes of the lesions. Since lesions and damage to the urothelium can also be drug-induced, it is important for the patient to provide the urologist with a comprehensive list of medications currently being taken and taken in the recent past. This will particularly apply to patients with other disorders/comorbidities, including rheumatic and systemic autoimmune diseases (check for any prescribed anti-inflammatory drugs and immunosuppressants for example). In addition, a number of infections, radiation or endometriosis can also be a cause. An important exclusion today is street ketamine abuse which can potentially cause severe damage to the bladder.

- Cystoscopy

Hunner lesions can only be diagnosed by cystoscopy with or without hydrodistension under general, epidural or local anaesthesia by an experienced urologist trained to recognise the different features and presentations of lesions in order to arrive at the correct diagnosis..

Cystoscopy allows the urologist to look into the bladder and carry out a number of tests and is a standard investigation in urology when it is felt necessary to take a look around the bladder. A narrow tube is inserted into the bladder via the urethra. It has two or more channels: one carrying an endoscope that allows visual examination of the inside of the bladder, the other channel carries fluid for instillation into the bladder.

There are two main methods of cystoscopy:
- Plain (office) cystoscopy using local anaesthesia but without hydrodistension*

- Cystoscopy under general or spinal anaesthesia with hydrodistension .

* hydrodistension = stretching the bladder by slowly filling with water.

The most experienced urologists can probably detect the majority of lesions with plain (office) cystoscopy, but in order to ensure optimal treatment for the patient, all Hunner lesions need to be identified and at the present time this still requires hydrodistension. Without hydrodistension, certain lesions may remain undetected.
A further role of cystoscopy is to rule out certain confusable diseases.

Professor Magnus Fall from Sweden has described these lesions as follows:
“The Hunner lesion typically presents as a circumscript, reddened mucosal area with small vessels radiating towards a central scar, with a fibrin deposit or coagulum attached to this area. This site ruptures with increasing bladder distension, with petechial oozing of blood from the lesion and the mucosal margins in a waterfall manner. A rather typical, slightly bullous edema develops postdistension with varying peripheral extension.”

- Bladder biopsy

A bladder biopsy may be carried out and involves taking a minimum of three small samples of tissue from different levels in the bladder wall, including from the detrusor muscle, at several different sites in the bladder. The biopsy is important to exclude the possibility of other causes of the symptoms (such as bladder cancer, eosinophilic cystitis and tuberculous cystitis). All lesions or patches identified during cystoscopy should therefore be biopsied. The samples obtained will then be examined microscopically by the pathologist with experience in this specific field.

In the case of Hunner lesions, this histopathological examination shows chronic inflammation, with lymphocytes, plasma cells, macrophages, neutrophilic and eosinophilic granulocytes, and a large number of mast cells.
In contrast, in patients who do not have Hunner lesions, completely normal biopsy results may be found.

FUTURE POSSIBILITIES FOR DIAGNOSIS

- Narrow band imaging
In Japan, studies have been carried out into the use of narrow band imaging to detect Hunner lesion and to assist transurethral electrocoagulation.

- Intravesical nitric oxide: a possible marker
In addition studies have indicated that intravesical nitric oxide (NO) may be a potential marker to diagnose Hunner lesion. It has been shown that patients with Hunner lesions have high NO levels symptoms, while those without Hunner lesions have normal levels. While measurement is a simple procedure, it requires a nitric oxide measuring device that is as yet not generally available in urology departments.

PREVALENCE OF HUNNER LESIONS: NOT SO RARE PERHAPS…

Until recently, lesions were considered to be relatively rare at 5-10% of the patients, but it is possible that these lesions are under-diagnosed, particularly in centres with less experience of these patients. Centres with urologists highly experienced in diagnosing lesions are detecting them in some 50% of their IC/BPS patients. Every effort is now being made to ensure that urologists and urogynaecologists can recognise Hunner lesions in the bladder when they see them.

TREATMENT

Hunner Lesion disease responds well to specific treatment in the bladder since the symptoms tend to be bladder-centric in contrast with Non-Hunner Lesion patients who may have multiple comorbidities.

Treatment specifically for Hunner lesion includes:
Submucosal/intra-lesion injection of steroids, laser ablation, fulguration/electrocoagulation or transurethral resection.
Where necessary, this can be combined with other types of treatment used for IC/BPS including intravesical instillations/GAG replacement therapy which can show good results.

Triamcinolone submucosal injection has recently been studied for the treatment of Hunner lesion with very good results. Under general anaesthesia, triamcinolone (40mg/cc) is injected with an endoscopic needle in volumes ranging from 5-10 cc (depending on the number and size of the lesions) into the submucosal space of the centre and periphery of lesion(s). It appeared to be well-tolerated in 66% of patients with Hunner lesion. This study continues to produce positive results.

Laser ablation, fulguration/electrocoagulation or transurethral resection (TUR)
Pain in the bladder caused by lesions can improve dramatically when treated with fulguration/ electrocoagulation, laser (burning out and sealing the lesion) or resection (surgical removal of the lesion). This treatment needs to be periodically repeated as and when the pain returns. This may be after a few months or after several years. TUR has been shown to lead to considerable improvement in both pain and frequency in many lesion patients.

While good symptom improvement has been seen in studies with neodymium Yag-laser treatment, it is essential for patients to be treated by very experienced surgeons since this therapy carries the risk of complications such as accidental bowel perforation in less experienced hands.

TENS (Transcutaneous Electrical Nerve Stimulation)
TENS is a method of pain relief using a small, battery-operated device with leads connected to adhesive electrode pads. While not a cure, it appears to give much better results in Hunner Lesion patients than in Non-Hunner Lesion.

Cystectomy as final resort
Cystectomy (surgical removal of the bladder with urinary diversion) is a final resort option in the severest cases.

References and further scientific reading:

- Hunner GL. A rare type of bladder ulcer in women; report of 8 cases. Boston Med Surg J 1915; 172: 660–4.
- Hunner GL. A rare type of bladder ulcer: further notes with a report of eighteen cases. *J. Am. Med. Assoc.* 1918; 70: 203–12.
- Fall M, Johansson SL, Aldenborg F. Chronic interstitial cystitis: a heterogeneous syndrome. J Urol. 1987;137:35-8.
- Logadottir YR, Ehren I, Fall M, Wiklund NP, Peeker R, Hanno PM. Intravesical nitric oxide production discriminates between classic and nonulcer interstitial cystitis. J Urol 2004; 171: 1148-1151.
- Braunstein R, Shapiro E, Kaye J, Moldwin R. The role of cystoscopy in the diagnosis of Hunner's ulcer disease. *J. Urol.* 2008; 180: 1383–6.
- Van de Merwe JP, Nordling J, Bouchelouche P, et al. Diagnostic criteria, classification, and nomenclature for painful bladder syndrome/interstitial cystitis: an ESSIC proposal. Eur Urol 2008;53:60-7
- Ueda T, Nakagawa M, Okamura M, Tanoue H, Yoshida H, Yoshimura N. New cystoscopic diagnosis for interstitial cystitis/painful bladder syndrome using narrow-band imaging system.
Int. J. Urol. 2008; 15: 1039–43.
- Cox M, Klutke JJ, Klutke CG. Assessment of patient outcomes following submucosal injection of triamcinolone for treatment of Hunner's ulcer subtype interstitial cystitis. Can J Urol 2009;16:4536-40
- Fall M, Logadottir Y, Peeker R. Interstitial cystitis is bladder pain syndrome with Hunner's lesion. Int J Urol. 2014 Apr;21 Suppl 1:79-82. doi: 10.1111/iju.12325. (Free access to full article)
- Meijlink JM. Interstitial cystitis and the painful bladder: a brief history of nomenclature, definitions and criteria. Int J Urol. 2014 Apr;21 Suppl 1:4-12. doi: 10.1111/iju.12307.(Free access to full article)
- Whitmore KE, Fall M, Sengiku A, Tomoe H, Logadottir Y, Kim YH. Hunner lesion versus non-Hunner lesion interstitial cystitis/bladder pain syndrome. *Int J Urol*. 2019;26 Suppl 1:26-34. doi:10.1111/iju.13971. (Free access to full article).
- Akiyama Y, Lou Y, Hanno PM, et al. Interstitial cystitis/bladder pain syndrome: The evolving landscape, animal models and future perspectives. Int J Urol. 2020:1-13.
- Homma Y, Akiyama Y, Tomoe H, et al. Clinical guidelines for interstitial cystitis/bladder pain syndrome. Int J Urol 2020; Apr 14 [Epub ahead of print].

- Fall M, Nordling J, Cervigni M, et al. Hunner lesion disease differs in diagnosis, treatment and outcome from bladder pain syndrome: an ESSIC working group report. *Scand J Urol*. 2020;54(2):91-98. doi:10.1080/21681805.2020.1730948

Books

- Incontinence 7th Edition (2023). ICI-ICS.
Cardozo, L, Rovner, E, Wagg, A, Wein, A, Abrams, P. (Eds) International Continence Society, Bristol UK, ISBN: 978-0-9569607-4-0. Chapter 18. Interstitial Cystitis / Bladder Pain Syndrome, Committee: Chair - Hanno, Philip, Cervigni M, Choo MS, Clemens JQ, Gold D, Lee MH, Malde S, Meijlink J, Samarinas M, Ueda T. https://www.ics.org/education/icspublications/icibooks
- Bladder Pain Syndrome, A Guide for Clinicians. Edited by J. Nordling, J.J. Wyndaele, J.P. van de Merwe, P. Bouchelouche, M. Cervigni, M. Fall. Published 2013. Springer.
- Urological and gynaecological chronic pelvic pain. Moldwin R (Ed.). Springer 2017.
- Bladder Pain Syndrome – an Evolution. Edited by P.M. Hanno, J. Nordling, D.R. Staskin, A.J. Wein, J.J. Wyndaele. Springer; 2018.

Further articles and editorial comments of interest (open access) can be found in:

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