

CHAPTER 1

INTRODUCTION AND OUTLINE OF THE THESIS

Interstitial cystitis (IC) is thought to be an uncommon lesion of the urinary bladder which was probably first described by Nitze in 1907 and termed cystitis parenchymatosa¹. It was popularised by Hunner in 1914, who called it " a rare type of bladder ulcer", and subsequently, the "elusive" ulcer². The term "elusive" was well-chosen; indeed, eight decades later IC remains a mysterious disease engulfed in a shroud of confusion concerning its diagnosis, etiology, pathogenesis and treatment. Hunner's ulcer has become the typical characteristic of 'classic' interstitial cystitis. Although actually not a true ulcer, only a velvety red patch and only present in a small minority of IC patients.

In 1984, IC patients in the U.S.A. founded the ICA (Interstitial Cystitis Association). According to patient's experience the disease was not-appreciated by medical doctors, rather than uncommon. After just one appearance of the ICA president on national television, ABC's "Good Morning America" (1984), the ICA received over 10.000 letters within 2 weeks. It was the start-off of a boom in publicity, funding and IC research in the U.S.A. Over the period 1991 to 1994 IC research funding ranked third in percent increased federal funding (145%), following breast cancer with a 200% increase and ovarian cancer with a 157% increase. Even higher than the increase in AIDS research funding (30%). Despite these overwhelming efforts we are still far from determining a cause for this illness or syndrome, and we still do not have an effective treatment that provides more than temporary symptomatic relief. A committee convened by the National Institutes of Health (U.S.A.) has arbitrarily proposed a set of characteristics to define the disease³.

A comprehensive overview of literature and a current view of experts on interstitial cystitis is provided in several recent publications⁴⁻⁸.

It can be expected that with time all interstitial cystitis patients will consult a urologist because of the severity of the complaints. In **Chapter 2** we conducted a survey among all urologists in The Netherlands, to provide the prevalence of IC in The Netherlands and the most common diagnostic and therapeutic approaches by Dutch urologists.

With no pathologic findings specific for interstitial cystitis, diagnosis of the condition can be extremely difficult. It remains essentially a diagnosis of exclusion⁹. Numerous attempts have been made to find abnormalities associated with the symptoms of interstitial cystitis which might serve

as objective diagnostic marker or therapeutic parameter. Tamm-Horsfall protein (THP) has been related to interstitial cystitis. Auto-antibodies against THP and bladder deposits of THP were reported in IC patients^{10,11,12}. We attempted to further investigate the role of THP in interstitial cystitis. **Chapter 3** reports on the THP urinary production in interstitial cystitis patients and controls, as well as the presence or absence of THP in bladder tissue biopsies. Implications towards the etiology of interstitial cystitis are discussed.

An auto-immune etiology of interstitial cystitis has been suggested for many years¹³. **Chapter 4** describes a study which was designed to evaluate the presence of tissue-specific auto-antibodies in IC patients using a direct immunostaining technique not reported before in relation with IC patients.

Chapter 5 comprises the first of a series of therapeutical trials, a clinical controlled pilot-study with intravesical pentosanpolysulfate instillations. Afterwards, a placebo-controlled, double-blind, trial with intravesical pentosanpolysulfate was undertaken. The results are discussed in **Chapter 6**. Based on the results of the placebo-controlled study, we aimed to increase the therapeutic efficacy by adding oxybutinin. In **Chapter 7** we report on the study with intravesical pentosanpolysulfate versus the application of pentosanpolysulfate combined with oxybutinin, again in a double-blind setting.

If conservative treatment fails in patients suffering from disabling interstitial cystitis, surgical management is inevitable. A number of surgical alternatives have been proposed. Unfortunately persisting pain, urgency and frequency, similar to the pre-operative symptoms are well-recognised complications^{16,17}. In **Chapter 8** our assessment of the most appropriate surgical technique is discussed, based on the analysis of the records of all interstitial cystitis patients treated at our hospital between 1976 and 1991.

Usually dietary manipulation is part of the treatment of interstitial cystitis patients in the U.S.A.^{14,15}. Our urologist-based questionnaire, conducted in 1994, revealed that only 34% of Dutch urologists occasionally use dietary advice in the treatment of interstitial cystitis. In a prospective study, presented in **Chapter 9**, we evaluated the dietary habits of interstitial cystitis patients and compared them to the average diet of the general population. We also investigated whether there was any spontaneous preference or avoidance of specific foodstuffs and fluids by IC patients. Finally, the results of our studies are summarized in **Chapter 10**.

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