

What is the Role of Covert Infection in Detrusor Overactivity, and Other LUTD? ICI-RS 2013

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A think tank was convened at the fourth ICI-RS meeting, which took place June 5–7, 2013 in Bristol UK, to consider current evidence and controversies surrounding the possible role of covert infection in the pathophysiology of refractory detrusor overactivity (DO) and other lower urinary tract disorders (LUTD). The topic was chosen because several authors from different centers worldwide have recently published evidence which supports this concept. However, to date there is inconsistency regarding terminology and microbiological definitions, which were discussed by the participants. The mechanisms whereby infection/inflammation could actually promote aberrant detrusor contractions in the human remain controversial, and are more fully described in this report. Future requirements for research into this topic were outlined. *Neurol. Urodyn.* 33:606–610, 2014. © 2014 Wiley Periodicals, Inc.

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INTRODUCTION

Classically, bacterial cystitis results in inflammation of the lower urinary tract associated with pain upon micturition (dysuria), urgency, increased frequency, and foul smelling, discolored urine. The fact that bacterial cystitis may also be associated with incontinence is not generally discussed in the infectious diseases literature, although most continence clinicians are aware of this phenomenon. For the last 40 years, overactive bladder (OAB) generally due to detrusor overactivity (DO), and defined as urgency with or without urgency incontinence, usually with frequency and nocturia, has generally been considered a separate and independent condition. However, clinicians have traditionally excluded bacterial cystitis (by dipstick test or urine culture) before commencing urodynamic testing or embarking upon treatment for OAB/DO. Early urological publications proposed a link between “uninhibited neurogenic bladder,”¹ or urge incontinence,² and recurrent urinary infection. The suggested mechanism was either ischemia in the bladder wall^{3,4} or an increased sensory input from the inflamed mucosa.^{3,4} In 2000 and 2004, two large urodynamic studies (n = 862 and 1,017) did show that women with newly diagnosed DO were almost twice as likely to reveal bacterial cystitis (defined as < 10⁵ cfu/ml with pyuria > 10/mm³), compared to those without DO.^{5,6}

Subsequently, continence clinicians have shifted away from the emphasis upon DO, and moved toward the term “overactive bladder” (OAB), which by definition excluded bacterial cystitis. Despite this move away from diagnostic urodynamic testing, clinicians providing a regional subspecialty service became increasingly aware of the problem of refractory OAB.⁷ The notion that at least one third of these refractory women were found to have some degree of bacterial cystitis (as evidenced by bacteriuria with or without pyuria, or histological inflammation about refractory OAB, there has been an increasing awareness of the work of Scott Hultgren’s group at St. Louis, MO showing that bacteria may chronically inhabit the urothelial cells of the bladder with formation of intracellular bacterial communities leading to low count bacterial cystitis (or “covert bacteriuria”).^{19–23} Therefore, the members of the ICI-RS voted to

discuss the question as to whether covert bacteriuria could have a role in the pathophysiology of OAB/DO or other LUTD. A number of controversial issues regarding terminology and scientific constructs were discussed as summarized below.

DEFINITION OF REFRACTORY IDIOPATHIC OAB/DO

The terminology problem was considered by a previous ICI-RS “Think Tank,”⁷ but no firm definition was decided upon. As the present meeting, it was suggested that refractory DO should be defined as proven idiopathic DO (no features of outflow obstruction or neurological disorder) in patients who have failed to respond to at least two anticholinergic drugs with detailed bladder training for at least 12 months, as evidenced by persisting frequency > 8 voids per day, disabling urgency, with or without nocturia and urgency incontinence, as documented on a frequency volume Chart.^{24,25} In patients not having had urodynamic testing, the above requirement for proof of persistent symptomatic OAB related disability should remain. The reason for having an agreed definition of the “refractory” status are (a) to facilitate research into the condition, such as biopsy studies of aberrant neuroepithelial antigens/receptors, or microbiological investigations, (b) to define candidates for invasive therapies such as botulinum toxin injections or sacral nerve implantation, and (c) to define a group of patients in which low count bacteriuria should be specifically sought (as a prelude to antibiotic treatment).

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