Editorial comment to: Shkarupa D, Zaytseva A, Kubin N, Kovalev G, Shapovalova E. Native tissue repair of cardinal/uterosacral ligaments cures overactive bladder and prolapse, but only in pre-menopausal women. Cent European J Urol. 2021; doi: 10.5173/ceju.2021.285.3 [Epub ahead of print] [1].

A watershed paper for surgical cure of overactive bladder and nocturia

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What is now known as 'overactive bladder' (OAB), symptoms of urge, frequency, and nocturia [2] is a major concern for up to 30% of the population. Indeed, nocturia is a major scourge for 80-year-old women- more than 50% have this problem [3] with all its consequences, falls, broken hips, accidents which ultimately may lead to their demise. The cost for the USA alone is estimated at many billions of dollars per annum.

The concept of 'OAB' originated as a definition from the 2003 International Continence Society (ICS) report [2]. Prior to this no such entity existed. Frequency, nocturia, urgency were simply symptoms. The name 'OAB' implies that the cause is actually in the detrusor itself. This definition is highly misleading, as it has the effect of leading researchers to concentrate on depressing detrusor contraction. Most treatments, for example anticholinergics and botulinum toxin, are empirical and seek to prevent the detrusor contracting. Such treatments have their own complications, for example the side effects of anticholinergics such as dry mouth, constipation, and even Alzheimer's Disease [4].

One bothersome and not infrequent complication of botulinum toxin is urinary retention and urinary tract infections [5]. More recent treatments include sacral nerve stimulation, a very expensive and only partly effective treatment (50% improvement in some studies is considered a 'cure'), one which requires patients to have implanted wires in their spine for the rest of their lives. The basis of this treatment is essentially unknown.

Some 35 years after the first report in 1976 [6], experts from the International Consultation for Incontinence continued to state that the cause of 'OAB' was unknown and treatment was still unsatisfactory [7]. In 2019, in an extensive review of OAB causation [8], Peyronnet et al. also stated OAB causation was unknown. They objected to the term 'idiopathic', but, seeking a way forward, proceeded to present several hypotheses 'future phenotypes', which they hoped would serve as possible research directions for future treatments of OAB. Notably absent from [8] was any reference to the 1990 Integral Theory's concept of frequency, nocturia, urgency, 'FNU' as a prematurely activated but otherwise normal micturition [9]. The Theory stated the cause of FNU was outside the bladder, from laxity in the vagina or its supporting ligaments [9]. As such, FNU was potentially curable surgically. This prediction was

confirmed by native ligament repair by Shkarupa et al. in premenopausal women [1], and by others with posterior slings in post-menopausal women [10–19]. The mechanisms for understanding cure of 'OAB' [9] are summarized in Figure 1: three opposite reflex forces contract against PUL and USL to close or open the urethra. If PUL or USL are loose, muscles (arrows, Figure 1) lose contractile force; the vagina cannot be stretched sufficiently to support the stretch receptors 'N'; the hydrostatic pressure of the urine fires off afferent impulses to the micturition centre at a lower bladder volume; at a certain critical mass, the micturition reflex is activated and this is interpreted by the cortex as 'urgency'. If this happens at night and it wakes the woman, it is called 'nocturia'. Repair of damaged ligaments restores anatomy and therefore, function [9].

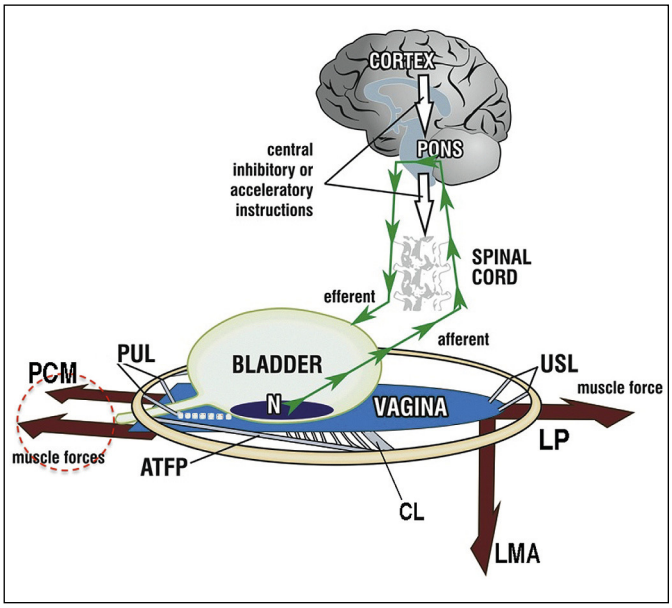

Figure 1. *Binary control of bladder. Schematic 3D sagittal view. System in normal closed mode. Cortical control: afferent impulses from stretch receptors 'N' (green arrows) are reflexly suppressed cortically (large white arrows). When required, the cortex activates the micturition reflex.*

PCM – pubococcygeus muscle; LP – levator plate; LMA – conjoint longitudinal muscle of the anus; US – uterosacral ligaments; PUL – pubourethral ligaments; broken circle signifies relaxation of PCM prior to micturition.

The Shkarupa paper

Very rarely do insights from a scientific work have the capacity to change the direction of medical practice. This work by Shkarupa et al. [1] is, I believe, such a work. It will, I am certain, in time prove to be a 'watershed' paper for female pelvic floor surgery. Their publication makes several important points which will undoubtedly open up new fields of research for years to come.

We live in a world where the population is ageing exponentially. In places where slings are banned, there is no longer anything out there that can safely and expeditiously cure women with OAB with the high rates achieved by posterior slings [10–19]. The surgical methodology is simple [1], easily repeatable by even the most modest surgeon. Shkarupa et al's. first major discovery was that native tissue cardinal/uterosacral (CL/USL) ligament repair was effective for both OAB symptoms and prolapse in premenopausal women at 18 months [1]. However, native repair produced catastrophic results for symptoms and prolapse in women who were post-menopausal [1]. Their results confirmed the conclusions of the PROSPECT TRIAL (mean age 60 years), that vaginal surgery has very high failure rates in post-menopausal women [20]. Shkarupa et al. attributed their own poor results in post-menopausal women to the breakdown in collagen which occurs in the supporting ligaments after menopause [1]. They recommend that tapes be inserted after ligament repair, as they routinely do in their unit [13], so as to create new collagen for a longer-term result. And if posterior sling kits are not available? I recommend addition of an artisan 'tension-free tape' on top of the plicated ligaments as described by Pinango-Luna yet al. [10]. This is a prerogative every surgeon retains for an individual patient. This simple addition, a 1cm wide 10cm tape creates new collagen to reinforce damaged CL/USLs and promises a much longer period of cure for older women, potentially equivalent to the 5year data reported by sophisticated TFS minisling ligament repair kits [19].

The 2nd important discovery [1] was that the failure rate for OAB and nocturia symptoms, proceeded step by step proportionally with the anatomical failure rate at 3,6,12,18 months, proving a key prediction of the Integral Theory [9], that urge symptoms were caused by loose or damaged ligaments.

Shkarupa's paper ends with an important question: how many of the premenopausal women will experience surgical failure after the menopause?

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