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INVITED REVIEW

Overactive bladder (OAB): a failed concept needing revision to accommodate an external anatomical control system

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Abstract

Thesis and aims In 45 years, the definitions and practice of the urodynamically based overactive bladder (OAB)/detrusor overactivity (DO) system have failed to adequately address pathogenesis and cure of urinary urge incontinence, frequency and nocturia.

Methods We analysed the OAB syndrome with reference to the Integral Theory paradigm's (ITS) binary feedback system, where OAB in the female is viewed as a prematurely activated, but otherwise normal micturition caused mainly, but not entirely, by ligament damage/laxity. The ITS Clinical Assessment Pathway which details the relationships between structural damage (prolapse), ligaments and dysfunction (symptoms) is introduced.

Results The ITS was able to "better explain" OAB pathophysiology in anatomical terms with reference to the binary model. The phasic patterns diagnostic of "detrusor overactivity" are explained as a struggle for control by the closure and micturition reflexes. The exponentially determined relationship between urethral diameter and flow explains why obstructive patterns occur, why they do not and why urine may leak with no recorded pressure. Mechanically supporting ligaments ("simulated operations") during urodynamic testing can improve low urethral pressure, negative pressure during coughing with SUI and diminish urge sensation or even DO patterns, transforming urodynamics from non-predictive test to accurate predictor of continence surgery results. High cure rates for OAB by daycare repair of damaged ligaments is a definitive test of the binary system's validity.

Conclusion Conceptual progression of OAB to the Integral Theory paradigms's prematurely activated micturition validates OAB component symptoms as a syndrome, explains pathogenesis, and unlocks a new way of understanding, diagnosing, treating and researching OAB.

Keywords OAB · Urge incontinence · Binary feedback control · Integral theory system · Ligaments · Surgical cure

Abbreviations

AUA	The American Urological Association
DI	Urodynamic detrusor instability
DO	Urodynamic detrusor overactivity
ICI	International Consultation for Incontinence
ICS	International Continence Society
IT	Integral Theory
ITS	Integral Theory System
MUS	Midurethral sling
OAB	Overactive bladder
PUL	Pubourethral ligament
USL	Uterosacral ligaments

Introduction

In 2002, the definition of detrusor instability (DI) was changed to "DO" ("detrusor overactivity"). A new condition, overactive bladder syndrome, "OAB", was created by a specially convened International Continence Society (ICS) committee [1]: urinary urgency, usually with urinary frequency and nocturia, with or without urgency urinary incontinence [1]. The change was justified, not by scientific proof, but because the term "OAB" was considered

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"more intuitive" [1]. However, the question remains, "more intuitive than what?" The previous terms, urgency, urinary frequency, nocturia [2] were well defined, well understood. A further qualification was, "The clinician is expected to exclude other causes for these symptoms, and to treat the patient *on the assumption* that OAB is caused by involuntary detrusor contractions, i.e., detrusor overactivity (DO)" [1]. DO was defined as "a urodynamic observation characterized by involuntary detrusor contractions during the filling phase that may be spontaneous or provoked" [3].

An important part of the OAB system which began in 1976, was the convention [4], which continues to this day, that surgery was contraindicated in women who had urodynamic "DO".

OAB system management was summarized by the American Urological Association (AUA) [5] as: "Treatments are aimed at relieving symptoms and not necessarily at reversing pathophysiologic abnormalities". Learned journals state there is no known pathogenesis and no cure [6]. Yet, the population continues to age. Bladder/bowel incontinence and evacuation problems increase parallel with ageing [7]. Costs to the nation and the community are escalating and range from $61 billion [8], to 14 billion [9]. Current OAB practice has few answers to these escalating problems. Anticholinergics can cause Alzheimer's disease [10]. Desmopressin, when placebo effect is subtracted, has a dismally low success rate for nocturia, as low as 0.22 voids/night [11]. Surgery for OAB is not curative. Sacral nerve stimulation, very expensive, requiring wires in the spine 24/7, is only partially effective [12]. Botox has urinary retention problems [13]. Ileal bladders, a disfiguring, complication-laden major procedure is a last resort [14]. Absent cure, a series of "phenotypes" for "future research" was proposed [6]. In summary, OAB as defined and practised fulfils criteria for a failed system as described in "The Structure of Scientific Revolutions" [15]. In 45 years, it has provided no pathogenesis or cure for urge incontinence, frequency, nocturia, conditions which severely impact quality of life.

Thesis and aims

Our aim is to analyse why OAB has failed and to compare the OAB system with the anatomical system proposed by the Integral Theory paradigm*, Fig. 1, where OAB symptoms are manifestations of a prematurely activated, uncontrolled micturition, a consequence of anatomical damage in its cortical/peripheral control system, but mainly ligament damage due to changed collagen [16]. As such, OAB is potentially curable [17].

* "paradigm" according to Kuhn is a global organizing model or theory with great explanatory power. The prevailing OAB system which is based on urodynamics, cannot be classified as a paradigm, as it offers no anatomical causation or cure for urge, frequency, nocturia—only ever-changing definitions and "guidelines" by "expert committees" which do not help the 20% of women world-wide who suffer from these conditions.

Methodology of this review has been largely inspired by the 2019 AUA statement: "*understanding the pathophysiology and the risk factors for development of OAB is needed both to treat the syndrome as well as to prevent it* [5].

The Integral Theory paradigm—a ligament-based system for managing OAB

The 1990 Integral Theory of Female Urinary Incontinence (IT) comprised five main discoveries [16]. 1st: three reflex muscles act in opposite directions against pubourethral (PUL) and uterosacral (USL) ligaments to close urethra, open it and stretch the vagina in opposite directions to prevent afferent impulses activating the micturition reflex prematurely, cortically perceived as urge, Fig. 1. 2nd: loose ligaments causes BOTH stress and urge incontinence. 3rd: key role of collagen in ligament damage; 4th: a new surgical principle, a precisely implanted tape could create collagenous 'neoligaments' to repair damaged ligaments. 5th: such neoligaments could cure stress and urge incontinence.

By 1997, the IT had evolved into the ITS, Integral Theory System [17], Figs. 2, 3. The three examples below show how the ITS works. Each is compared with management by the ICS inspired OAB urodynamics-based system.

The ITS protocol for SUI, urge, nocturia Fig. 2, was first applied in 1997 [17]: answers from a validated Integral Theory System questionnaire (ITSQ) [18] were transferred to a pictorial algorithm which diagnosed damaged ligaments, Fig. 3; vaginal examination detected prolapse and ligament weakness; "simulated operations" applied mechanical support to PUL https://youtu.be/0UZuJtajCQU) and USL ligaments, Fig. 1, confirming SUI and urge causation and probability of cure with midurethral (PUL) and posterior (USL) slings [17]. Patients were assessed with pre and post-operative urodynamics and 24 h pad tests. Of 85 women, 73 had mixed incontinence, 74 urge incontinence, 12 pure SUI (stress urinary incontinence). At 20 months review, urodynamically diagnosed detrusor instability "DO" was present in 36/85 patients preoperatively (42%) and in 13/61 postoperatively (21%). Of these 13 patients, 12 had no incontinence symptoms whatsoever. Of the five operative failures who were tested postoperatively, four had a stable detrusor, i.e., DO was neither predictive of, nor associated with surgical failure in this study. There was no incidence of de novo symptoms of DO. Following daycare surgery to repair pubourethral and uterosacral ligaments, symptom cure [17] was: SUI 88%

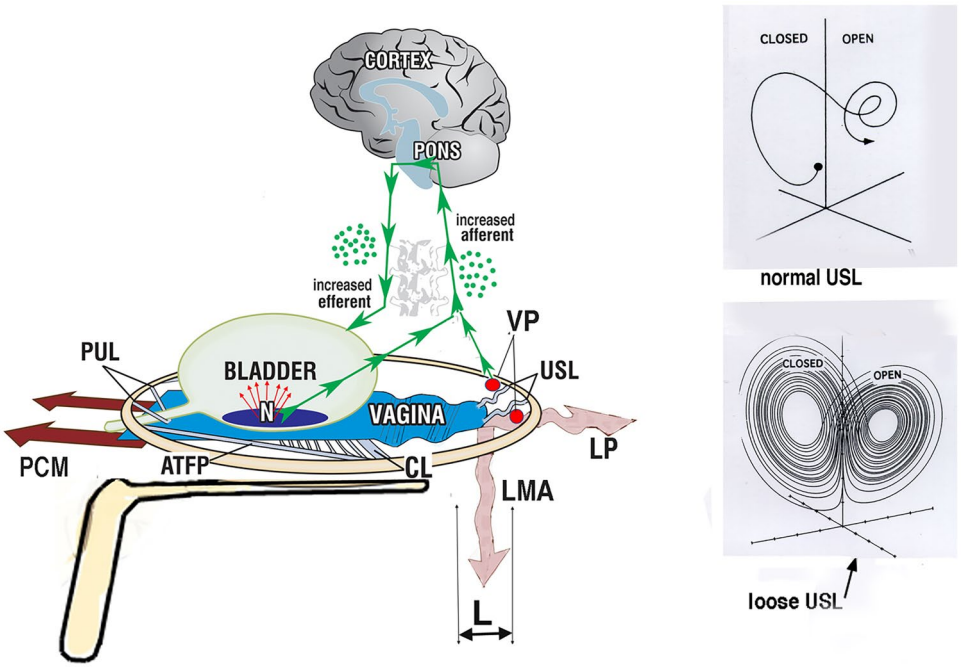

Fig. 1 Binary model of bladder control. System in normal closed mode. Main diagram *Cortical control* Afferent impulses from stretch receptors 'N are reflexly suppressed cortically When required, the cortex activates the micturition reflex. *Peripheral control* is by a musculo-elastic mechanism which responds to cortical efferents (small arrows). The three directional muscles (large arrows), forward, pubococcygeus muscle "PCM", backward, levator plate" LP", and downward, conjoint longitudinal muscle of the anus "LMA" contract against the supporting ligaments, PUL (pubourethral) and USL (uterosacral), to stretch vagina tightly, much like the membrane of a drum. The stretched vagina supports the urine column from below, preventing activation of the stretch receptors "N", decreasing afferent impulses to the cortex. *Micturition* Central control relaxes, as does PCM; this allows the posterior muscles LP and LMA to unrestrictedly open out the posterior wall of urethra (white broken lines) just prior to bladder evacuation by global detrusor muscle contraction. *CX* cervix; *CL* cardinal ligament; ATFP = arcus tendineus fascia pelvis. *Dysfunction* Lax ligaments "L" weaken the muscles LP/LMA which contract against them (wavy arrows). PUL. Muscle weakness affects the ability of the peripheral control mechanism to mechanically close the urethra (incontinence), open it (obstructed micturition) or control micturition by bilateral stretching of vagina by the 3 opposite muscle forces to support "N" (urge incontinence). *Pain control* The visceral plexuses (VP) are supported by USLs. Lax USLs cannot support VPs which act like a relay station for the afferent axons from end organs. If unsupported, the force of gravity or muscle movement stimulates the afferent axons to send impulses to the cortex. These are mistakenly interpreted as coming from the end organ where the pain is experienced. Speculum mechanically supports USLs to prevent VPs firing off and to create a firm anchoring point to restore LP/LMA contractile strength to tension vagina to support "N". Right diagram chaos theory attractors *Upper figure. Normal*. The closed attractor (closure reflex) dominates. Open attractor temporarily dominates when time to evacuate. *Lower figure. Unstable bladder*. Loose ligaments do not allow closed attractor (closure reflex) to dominate. Feedback control swings between open and closed attractors

($n = 85$), frequency 85% ($n = 42$), nocturia 80% ($n = 30$), urge incontinence 86% ($n = 74$), emptying symptoms 50% ($n = 65$) Fig. 4.

Analysis According to the Bates convention [4] (SUI surgery is contraindicated in patients with urge incontinence), only 12 patients would have been allowed surgery for SUI. The other 73 women would be told (even today) that surgery would worsen their incontinence. Yet, even in 1997, at 20 months review [17], these 73 women achieved 88% cure for SUI, 86% for urge, 85% for nocturia. These data have been validated by many other authors and publications [15–36].

ITS cure of posterior fornix syndrome [21] serendipitously cured interstitial cystitis with Hunner ulcer [19] based on the Integral Theory System [17–21].

The aim was to treat a classical posterior fornix syndrome* (rectangle Fig. 3): urgency, half-hourly frequency and nocturia twice/night, a moderate cystocele, entero/rectocele, laxity of the cardinal/uterosacral ligaments (USLs) and pubocervical/rectovaginal fascia. Speculum test, (Fig. 1), relieved urgency and pain. Urodynamics was normal. Cystoscopy: chronic cystitis glomerulations, non-ulcerating Hunner's ulcer confirmed by histology. Cardinal/USL repair with a TFS minisling corrected apical descensus, frequency, urgency, nocturia. Follow-up cystoscopy: complete healing of the Hunner's ulcer, no bleeding, and no glomerulations. Patient still cured at 3-year review.*Posterior Fornix Syndrome (PFS), itself based on the Integral Theory [16], was described in 1993 [21] as predictively co-occurring symptoms urge, frequency, nocturia, chronic pelvic

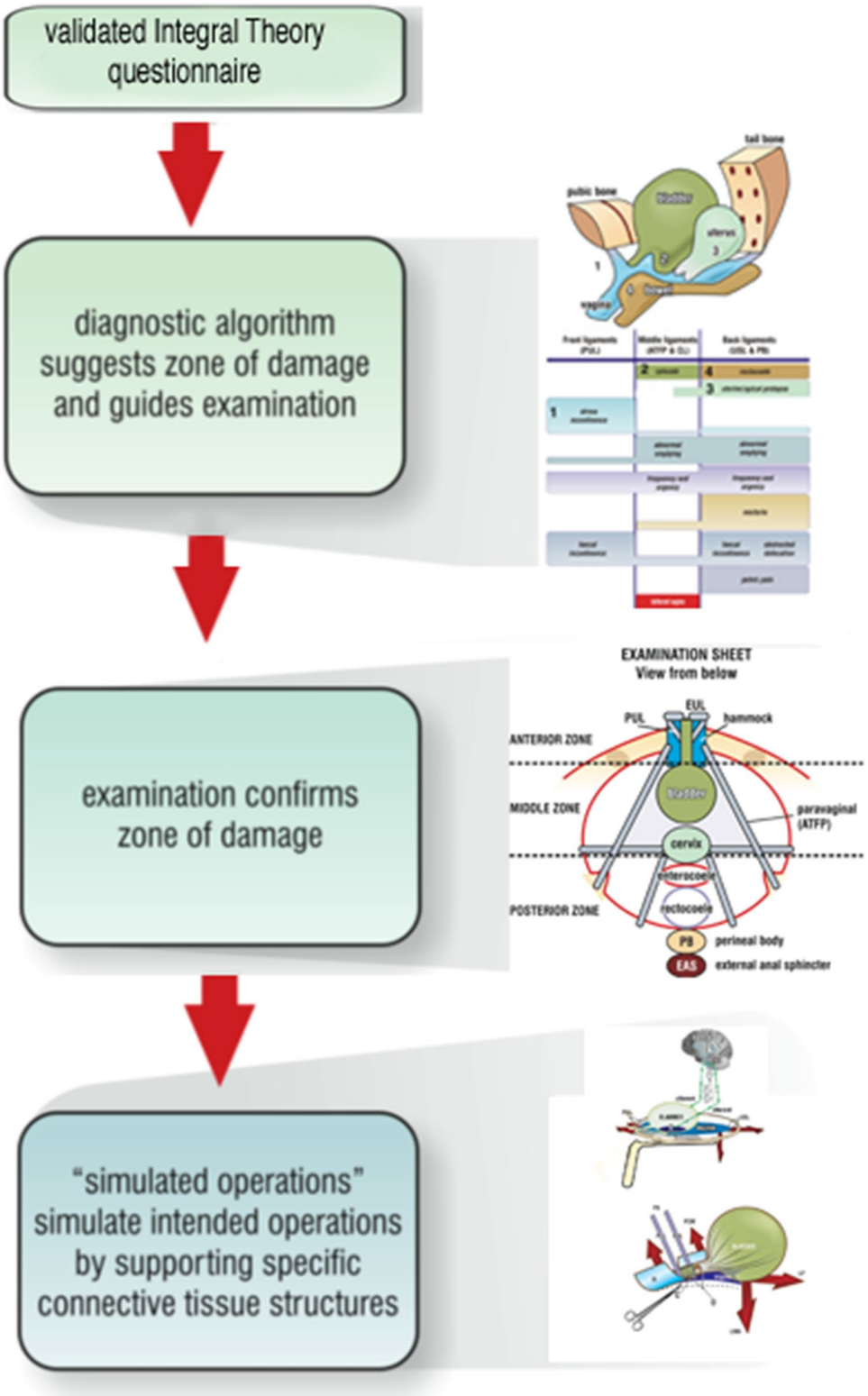

Fig. 2 The Integral Theory System Clinical Assessment Pathway. Answers from the validated ITSQ (Integral Theory System Questionnaire) are transferred to the diagnostic algorithm, Fig. 3. Vaginal examination confirms which ligaments are loose. Next, "simulated operations" mechanically support either pubourethral ligament (PUL) to relieve SUI, or uterosacral ligaments (USL) to relieve urge and pain validate the diagnosis from the algorithm, Fig. 3

pain, abnormal emptying/retention caused by USL laxity and cured by repair thereof.

Analysis Though a singular case, cure of interstitial cystitis (IC) by ITS methodology for the Posterior Fornix Syndrome indicate IC and PFS may be one and the same thing [16]. Assessed by the OAB system, this patient would have been turned away.

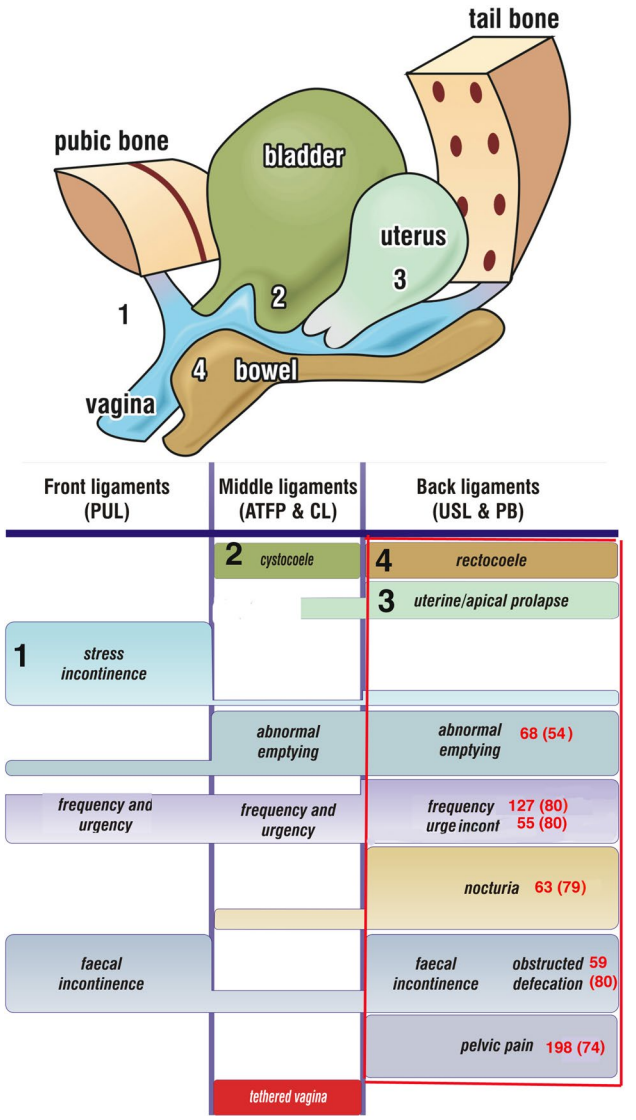

Fig. 3 The Pictorial Diagnostic Algorithm summarizes the relationships between structural damage (prolapse), ligaments in the three zones and function (symptoms). The size of the bar gives an approximate indication of the prevalence (probability) of the symptom. Laxities (red lettering) which can be repaired: pubourethral ligament (PUL); external urethral ligament (EUL); pubocervical fascia (PCF); CL cardinal ligament; arcus tendineus fascia pelvis (ATFP); uterosacral ligament (USL); rectovaginal fascia (RVF); perineal body (PB)

Symptom cure rate (brackets) 198 women with POP after surgery [24]

Native ligament plication cure of urge and nocturia based on the Integral Theory System

Shkarupa's comparative study [39] showed high cure rates at 18 months for premenopausal women, but catastrophically bad results for post-menopausal women (% cure in brackets): for prolapse, 80% (16.7%); urgency, 67.5% (16.7%); nocturia, 87.5% (18.8%); frequency, 60% (14.6%). Shkarupa concluded slings were needed to cure OAB and prolapse

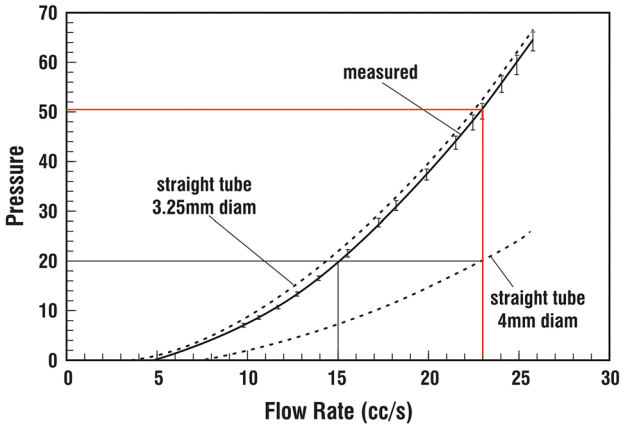

Fig. 4 The exponentially determined pressure/ flow relationship as measured during bench experiments (unbroken lines) and by computer simulation (broken lines). Note1: if the urethra can be opened to 4 mm by the external mechanism, urine can leak out at zero pressure at a flow rate of 7.5 ml/sec. Note2: a 0.75 mm decrease in tube diameter from 4 to 3.25 mm (a 19% decrease) increases the expulsion pressure by 250% (red lines), consistent with the 4th Power Law of Poiseuille

in post-menopausal women, thereby validating the slings inserted in the first example [17].

Analysis None of these women would be offered surgery by followers of the OAB system. They would be given expensive urodynamics (cost up to $1000), 50% would be told they had "DO"; all would be told no cure was possible.

Terminology must be testable and falsifiable according to Merriam-Webster, a definition is "a statement expressing the essential nature of something". Popper [40] stated scientific statements must be stated in a way in which they can be falsified. Popper: *"It is always possible to find some way of evading falsification, for example by introducing* ad hoc *an auxiliary hypothesis, or by changing* ad hoc *a definition*". The original definition of "detrusor instability" specified a detrusor pressure rise to 15 cm H2O ICS (1975). Subsequently, the definition was modified in 1988 and again in 2002 [3].

The 2017 updated Integral Theory of Female Urinary Incontinence (ITS), as now defined, [41] is testable: "*pelvic organ prolapse, chronic pelvic pain, bladder and bowel dysfunction are mainly caused by lax suspensory ligaments as a result of altered collagen/elastin. Repair the structure (ligaments) and you will restore the function*". [41].

The term "OAB" is also testable. If, as frequently happens, its main symptom, urge, is improved by the speculum test, Fig. 1, the cause is clearly not from the bladder, but outside it, probably in the uterosacral ligaments.

Urodynamic DO, however, is not stated in a way which can be falsified [40]. "The definitive diagnosis of an overactive detrusor can only be made by urodynamic studies.

However, the observation of involuntary contractions must be correlated during the urodynamic test and with their presenting symptoms" [1]. Put another way, urodynamic testing is required to diagnose an "overactive bladder" because symptoms are unreliable and symptoms are required because urodynamics are unreliable.

Urodynamics as a diagnostic test fails almost all Sacket's criteria [42] for test validity, a "blind" comparison with:

a. A "gold standard" of diagnosis. DO is only found in 50% of patients with urge incontinence. DO can occur in 60% of asymptomatic patients during ambulatory urodynamics [43].
b. Reproducibility. DO is not reproducible [44].
c. Sensible definition of "normal" (including a range beyond which disease is likely to be present, and therapy harmful). The 15 cm pressure rise was removed in 1988 [2]. Diagnosis became subjective, a "wavy pattern".
d. Utility of the test, especially as concerns the fate of false positive and negative results. DO has 60% false positives [45] and 50% false negatives [45].

All ITS statements are precise and testable: loose ligaments cause prolapse, bladder, bowel and cause pain symptoms. The algorithm, Fig. 2, relates symptoms to causation by lax ligaments, which when repaired, result in improvement in symptoms [17–39]. The ITS Posterior Fornix Syndrome (rectangle, Fig. 2), consists of predictably co-occurring symptoms of urge, frequency, nocturia, chronic pain, emptying problems caused by USL laxity, cured/improved by repair thereof [17–39]. As defined by the ICS [3], both OAB and interstitial cystitis can be considered part of the Posterior Fornix Syndrome, easily testable with the speculum test, Fig. 1, both potentially curable surgically, by native cardinal/USL repair [39], or posterior slings [17–39] or in younger women, by squatting-based exercises [46].Understanding the pathophysiology AUA [5]: "*understanding the pathophysiology and the risk factors for development of OAB is needed both to treat the syndrome as well as to prevent it*.

Pathogenesis of OAB is stated as "unknown" [6], with "no known cure" [6]. "DO" experimentally exhibited [48] exactly the same pattern as observed in normal micturition by Tanagho [47]: fall in proximal urethral pressure, rise in detrusor pressure, evacuation by detrusor contraction, i.e., DO is urodynamically one and the same as normal micturition [48]. The assumption of detrusor muscle pathogenesis inherent in the OAB definition can be immediately disproved by the speculum test, Fig. 1: mechanical support of utero-sacral ligaments diminishes or abolishes urge in 70–80% of cases, as does reported cure of urge and nocturia [17–39].

"OAB" as defined, is indistinguishable from "urge to go" in a normal person. Consciously disregarding a full bladder is common for normal people. At some point, the "urge to go" can no longer be ignored; the micturition (open) reflex, Fig. 1, lower Chaos attractor, dominates temporarily and the person may wet while rushing to the toilet; other examples: putting a key in the door, sudden urge on turning on a tap. All examples fulfil the 2002 ICS definition for "OAB", yet these people are continent. Definition problems disappear if "OAB" and "DO" are considered as uncontrolled, but otherwise normal micturitions under binary control, Fig. 1.

The binary model essential to understanding the Integral Theory paradigm's interpretation of urodynamics, is that the closure and opening (micturition) reflexes act in a binary way, EITHER open or closed. With reference to Fig. 1, as the bladder fills, hydrostatic pressure is exerted on urothelial stretch receptors "N". Afferent impulses to the micturition centre from "N" increase. The closure reflex is activated, and the three opposite muscles contract to close urethra distally and at bladder neck [16, 41] VIDEO of reflex closure. https://www.youtube.com/watch?v=3vJx2OvUYe0. As the bladder fills further, the opening (micturition) reflex is activated, (Fig. 1, upper Chaos attractor), detrusor contracts. If totally controlled by the closure reflex acting cortically and peripherally, Fig. 1, there is no detrusor pressure increase. If only partly controlled, the detrusor may contract tonically and be recorded as "low compliance" [49].

The definition of urodynamic DO, as a phasic pressure curve, or "wave" form is a good expression of the binary control system, inability of either the closure or opening reflex to dominate (Fig. 1, lower Chaos attractor): control switches from "closed" attractor (urethral pressure rise) to "open" attractor (urethral relaxation). The time interval needed for the pons to switch from "closed" to "open" is 4–8 s [49], recorded as a phasic pressure curve, a "wave" pattern. The sound of water, e.g., from handwashing may remove pontine block and allow the afferents from "N" to pass through to activate detrusor contraction and urine loss "incontinence", as demonstrated during an urodynamic experiment [49].

The other standard urodynamic test is flow or pressure/flow measurement. Griffiths [50] and later Bush [51] demonstrated that the detrusor pressure recorded is entirely a function of the resistance within the urethral tube; if there is little or no resistance, the detrusor force is converted to flow and detrusor pressure is low or absent [50, 51]. Not mentioned by Griffiths, is the 1990 IT finding [16], that the backward muscles LP/LMA, Fig. 1, actively open out the posterior urethral wall immediately prior to micturition [16]. This action exponentially decreases urethral resistance to flow inversely by the 4th power of the radius (Poiseuille's Law). VIDEO micturition https://www.youtube.com/watch?v=eiF4G1mk6EA&feature=youtu.be. There is no description by ICS of the anatomical basis for urodynamics [1–3].

OAB pathogenesis as explained by the Integral Theory paradigm

Pathogenesis is binary [16, 49]: anatomical damage somewhere along the binary feedback track of Fig. 1 interferes with the closure reflex, allowing the opening reflex (micturition) to dominate, even if transiently. For example, at "N", infection, cancer, a uterine fibroid or prostate enlargement distending bladder base may increase afferent impulses to the micturition centre. Damage to the brain's inhibitory centres may allow the afferent impulses free passage to activate micturition. Damage to afferent nerve fibres, (e.g., multiple sclerosis, cord transection) may cause retention; damage to efferent inhibitory nerves may facilitate micturition.

A head passing through the hiatus may damage distal attachments of levator muscles to cause prolapse and conditions such as diverted urinary stream [37]. However, collected data from the many surgical studies which show major improvements of OAB symptoms by ligament repair only, indicate ligaments, not muscles, are the major cause of bladder dysfunction [17–39]. Loose or weak PULs or USLs, Fig. 1, weaken the contractile strength of the three muscles which contract against them; the vagina cannot be stretched sufficiently to support the stretch receptors "N" from below; these fire off afferent impulses at lower bladder volumes to activate micturition, albeit, inconveniently.

Urge incontinence ("OAB") as a prematurely activated but otherwise normal micturition is a fundamental pillar of the Integral Theory paradigm: pathogenesis is an inability of the cortical and peripheral control system to control afferent impulses from "N", Fig. 1**.** A 1993 urodynamic experiment [48] demonstrated that the sequence of events in urodynamic DO was identical with Tanagho's observations in normal micturition [47]: sensation of urgency, fall in proximal urethral pressure, rise in detrusor pressure, urine loss.

Feedback control, Fig. 1, is another fundamental pillar of the Integral Theory paradigm [49]. Handwashing provoked sudden urine loss in 13/16 low compliance group with an unstable pattern. This was attributed to interruption of cortical suppression of afferent impulses from "N", Fig. 1, allowing the micturition reflex to dominate. Digital support of bladder base caused sensory urgency to disappear in 18/20 women and in six, detrusor contraction also. These apparently disparate results were reconciled by a neurologically driven feedback control system consistent with a non-linear Chaos Theory feedback equation $X_{NEXT} = cX(1 - X)$. The equation was able to explain each bladder mode UAB, low compliance, normal closed state, and especially, OAB [49]. These modes are dynamically depicted in Fig. 1, upper and lower figures.

Discussion

The analysis to date indicates the OAB/DO system, as defined and practised, conforms with Kuhn's descriptions of a failed system [15]; DO fails criteria for a diagnostic test; both OAB and DO lead nowhere as regards patient care. Meanwhile, OAB problems continue to increase with age [7]: "OAB" affects over 45% of women aged 65 and older [8], is associated with falls, hip fractures, anxiety/depression, social isolation, reduction in quality of life and economic burden of over $14 billion per annum in older women [8]. At present these women are told no cure is possible. Yet, daycare cure for OAB symptoms has been known for 25 years [19–39].

The model, Fig. 1, also holds for the male, at least for male children. A squatting-based RCT based on the Integral Theory [16], gave high cure rates for day/night enuresis for 6–11 year old children, male and female [52]. We have no data for adult males. However, any urothelial cancer, or pressure from an enlarged prostate, or lax bladder base support from puboprostatic ligament dissection could conceivably cause pathogenesis equivalent to that in the female.

Progression of OAB to an anatomical management system

If OAB symptoms are considered as the cortical perception of an activated micturition [48, 49], almost all objections raised in this review disappear, and the Integral Theory paradigm's binary system, Fig. 1, emerges. Figures 2, 3 guide diagnosis of specific ligament damage. Initial treatment is unchanged, drugs. As regards surgery for OAB, midurethral slings and cardinal/USL plications are standard operations. Though posterior slings are banned for now, other options exist, or will materialize. Mechanical support of ligaments during urodynamics ("interventional urodynamics"), alters recorded patterns to become an accurate predictive tool for success of ligament-based surgery [53]. Examples: for SUI, midurethral support of PUL can reverse urethral pressure fall on coughing, stop cough-activated DO, increase maximal urethral closure pressure [53]. For urge, mechanically supporting bladder base "N" or USL, Fig. 1, can diminish sensory urgency and alter DO patterns urodynamically [49].

Conclusions

The proofs presented for OAB symptoms as manifestations of an "uncontrolled micturition" stemming from anatomic damage to the binary control system, removes many

objections hitherto associated with OAB and DO, opens up new directions for diagnosis and treatment not previously recognised, and new research possibilities.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00345-022-03938-z.

Declarations

Conflict of interest No conflicts for any author.

Research involving human participants and/or animals Not applicable.

Informed consent Not applicable.

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