The Integral Theory and Integral System

Table of Contents

List of Figures and Tables

Section 1: Summary

The Integral Theory,[1] discovered in 1990, (which later evolved into the Integral System), defined for the first time how ligaments, muscles and nerves interact inside the pelvic floor to allow retention and voiding of human waste products. The Integral System also demonstrates

how muscles and ligaments, and not full bladders and bowels, work in conjunction to determine the mechanism for retention and voiding.

Originally called the Integral Theory, it later became known as the Integral System, and is disruptive technology. It was the brainchild of Royal Perth Hospital academic surgeon Professor Peter Petros, and Professor Ulf Ulmsten of Uppsala, Sweden. In 1990, they published their theory which revolutionised the understanding of the way in which the pelvic floor functioned; their breakthrough was the discovery of the central role of ligaments and how the reflex pelvic muscles contracted against them for all pelvic functions. Since the early days of anatomy, ligaments had been thought of as little more than strong tissue to support vital organs, but Petros and Ulmsten determined that ligaments played an essential role in working with the musculature of the pelvis to enable body functions.

The Integral System is a method for management of pain and bladder disorders.

The discovery of the importance of muscle-ligament interaction paved the way for the first time, for a cure of chronic pelvic pain, overactive bladder, bedwetting, interstitial cystitis, and many other previously incurable conditions which affect approximately one third of all adult women. Research is also underway to determine how the Integral System can aid in the cure of chronic pelvic pain in men.

Until the discovery of the Integral System, it was assumed by medical science that internal pressure from an over-full bladder and bowel were the mechanisms which triggered waste evacuation. However, the Integral System disproved this long-held supposition, and its discovery introduced a series of operations and surgical procedures which now offer cures, or partial relief, of previously incurable medical problems. For the first time, urinary stress, chronic pelvic floor pain, constipation, prolapse and many more conditions can now be surgically cured or relieved.

The revolution in understanding the way in which the pelvic floor functioned was the centrality of the role of ligaments. Until 1990, they were assumed to do little more than ensure the correct positioning of organs within the pelvic floor. But the Integral System, first explained by Petros, showed that it was the interaction of muscles and ligaments, directed by nerve impulses from the brain, which opened and closed the waste organs. If the ligaments were over-stretched due to a mechanical failure – such as a difficult delivery during the birth of a child - then the muscles were unable to function properly, and leakage and spillage of body waste was the result. A relatively simple operation to tighten the ligaments and create new collagen, generally solved the problems.

The second major Integral System discovery, also in 1990, was that the reason ligaments became weak, was that their main structural component – collagen - became damaged during labour or broke down after the menopause.

The third major discovery, also in 1990, was a new surgical principle, how to repair the collagen in the damaged ligaments, with a day-care operation which worked by creating new collagen. First performed in 1987-8, the prototype the mid-urethral sling for cure of stress urinary incontinence, became famous as the TVT, with more than 10,000,000 operations to date. Over the next 30 years, it was found that these three basic science discoveries inspired further cures into widely varied conditions such as chronic pelvic pain, bladder/bowel urgency and evacuation conditions, interstitial cystitis, bedwetting in children, which many learned societies stated were not curable.

Of special humanitarian interest was how the application of the Integral system was able to solve the scientific dilemma of the 50% of women who had successful closure of their obstetric fistula and who still continued to leak urine afterwards.

A brief background and timeline of the Integral System discoveries follows below.

Section 2. Background to the Integral Theories discoveries

2.1 Two significant observations led to the Integral Theory

1.In 1986, Peter Petros observed that if a woman was coughing and leaking urine and he pressed behind the pubic bone on one side where the ligament was positioned, the leaking stopped. By supporting the ligament with his finger, it returned to normal function which suggested to him that the ligament was weak.

2. From experimental work, he had observed that the key structural components of ligaments was collagen. Petros knew that when a plastic material like a Teflon tape was inserted

anywhere into the body, the Teflon tape created scar tissue which was composed of pure collagen.

These two observations led to the hypothesis that by placing a sling in the precise location of the ligament, new collagen would be created which could support, reinforce and repair the ligament (pubourethral ligament). A special instrument was designed to position the sling so it attached to the ligament, which originated behind the public bone, and then attached to the middle part of the urethra.[1,2]

2.2 1987 The first step - from observation to experiment

In 1987, assisted by Professor John Papadimitriou, a pathologist and world expert in Inflammatory Research, Petros conducted the required animal experiments [2] [Fig.1] to prove that the hypothesis for new ligament creation was correct and that an operation on humans to place a tape where the ligament was located would be both safe and effective.

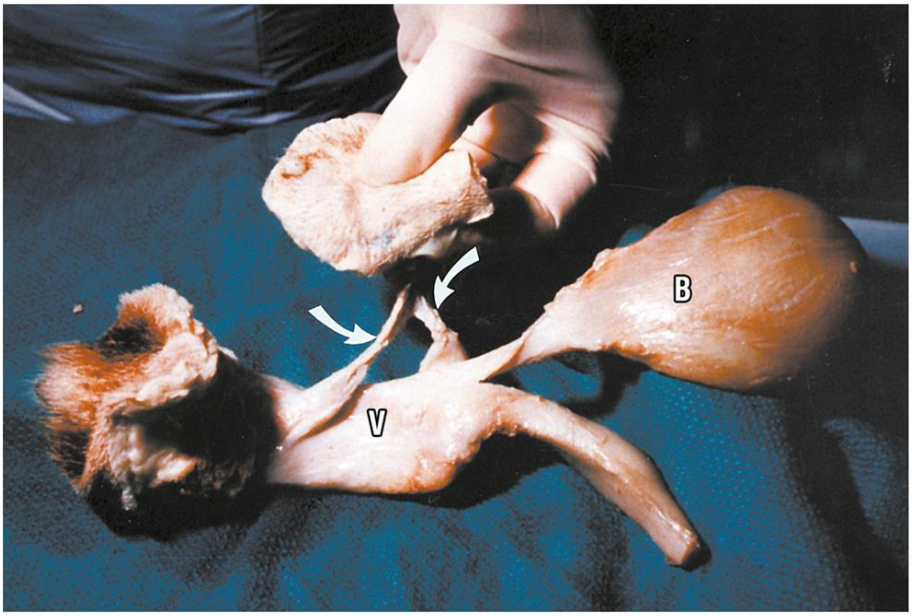

Fig.1 Formation of artificial collagenous neoligaments. Specimen of vagina (V), vulva bladder (B) dissected from a dog 2 weeks after the implanted tape had been removed. Note the significant artificial collagenous neoligament created by tissue reaction against the tape (white arrows).

2.3 The second step – prototype midurethral sling

In 1987, based on these animal studies, the prototype midurethral sling operations [3] to support the front ligaments (pubourethral) to cure stress urinary incontinence were performed [3].

2.4 The first scientific presentation of the prototype sling

In late 1988, at an Incontinence Conference in Melbourne, Australia, Petros presented positive results of his research on patients who had undergone the prototype midurethral sling procedure to cure stress and urge incontinence. Professor Ulf Ulmsten, from Uppsala, a world expert on incontinence and official physician for the female members of the Swedish Royal family, attended the lecture. Later, he sought clarification on some key aspects of the prototype midurethral sling, in particular, its performance as a day-care procedure under local anesthetic and the apparent absence of urinary retention in the post-operative period.

2.5 Collaboration with University of Uppsala, Sweden

When Ulmsten returned to Sweden, he asked to be kept informed of the ongoing research in Perth, Australia. Ulmsten, eager to learn more about this operation, visited Perth in 1989. By then, the essential parts of the Integral Theory had been developed. Over a 5-day period, Ulmsten observed several operations being carried out and assessed a total of 80 patients, many of whom had previously undergone the prototype midurethral sling procedure. After several hours of discussion about the theory, Ulmsten said, " I think your theory is correct, but it needs more work". He had similar thoughts about the prototype sling. He invited Petros to join his academic department at the University of Uppsala in Sweden in order to further progress on the invention and the theory itself.

From 1990 - 1993, Petros, unable to move permanently to Uppsala because he had a young family to support, divided his time between Uppsala and Perth. This was the start of a close collaboration that would last from 1990 to1993. Between 1993 and1997, their collaboration on several research projects continued, with Petros as Associate Professor and Docent at the Department of Obstetrics and Gynecology at the University of Uppsala, Sweden.

Section 3. Evolution of the Integral Theory into the integral system 1990 - 2021

3.1. 1990 The Integral Theory

The Integral Theory [1] of female urinary incontinence was revolutionary because it explained that the cause of bladder problems was not from the bladder, but outside the bladder, mainly in the ligaments. Loose ligaments caused by collagen damage do not allow

the muscles which control the 3 functions of the bladder (which are storage, evacuation and control of urgency to work properly) resulting in stress incontinence, inability to empty and urge incontinence.

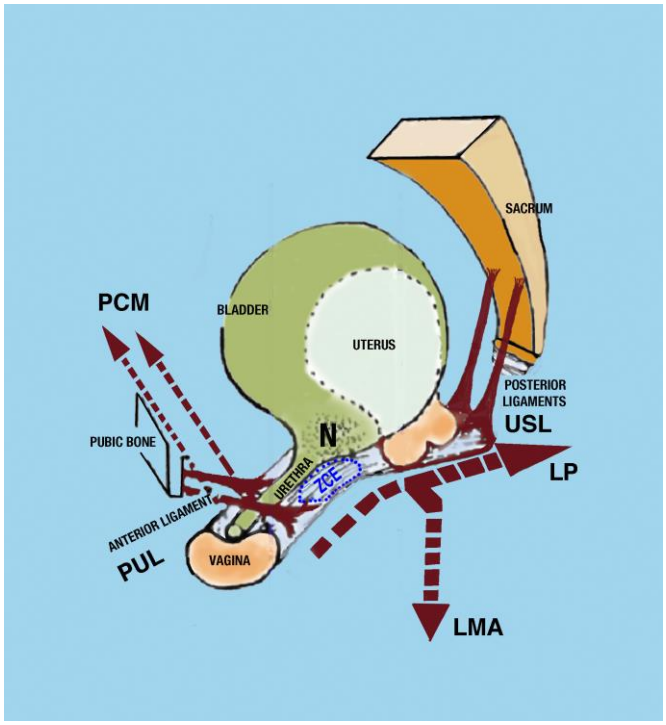

Fig.2 Urethral closure mechanism simplified

The 3 directional forces in the xray work in opposite directions. They require adequate vaginal elasticity at bladder neck called 'Zone of critical elasticity' (ZCE) to operate separately.

Urethral closure The forward muscle forces pull the front wall of vagina forwards against the PUL (pubourethral ligament) to close the distal urethra. The backward muscles LP (levator plate) and LMA (conjoint longitudinal muscle of the anus) backwardly tension the urethra and vagina, which then rotate the bladder around bladder neck to close off bladder neck.

Micturition (bladder emptying) PCM relaxes. The back muscle forces, LP/LMA actively pull back the vagina and posterior wall of the bladder and urethra. The bladder contracts to empty.

Control of urgency The opposite muscle forces (arrows) , stretch the vagina like a trampoline to support the urine in the bladder, lessening the pressure on the stretch receptors "N", preventing them firing off uncontrollably to cause urge.

The methods used to identify loose ligaments and to strengthen or repair them led to a new anatomical method for management of the female pelvic floor, now known as the Integral System.

3.2. 1990 Publication of the prototype midurethral sling

It was in 1987 that the prototype midurethral sling operation [3] was first performed. In the original midurethral sling operation, a specially designed instrument (tunneller) was used to insert a 5mm wide removable Mersilene tape in precise locations to create a sling to reinforce the front (pubourethral) ligaments which structurally support the urethra. This resulted in a cure for stress urinary incontinence "SUI" (urine loss on coughing) and also, urge incontinence "UI" (a compelling desire to pass urine) without any obstruction to passing urine freely. This discovery was objectively evaluated by x-rays and clinical data. It demonstrated that surgery for stress urinary incontinence was possible on a day-care basis, instead of the 10-14 days required for the much more invasive abdominal procedures, then in practice, such as Burch Colposuspension. It also invalidated the common belief, held by doctors that 'urge' incontinence was an incurable condition. However, when the tape was removed 6 weeks later, stress urinary incontinence (SUI) and urgency (UI) to urinate re-occurred in 40% of the women. It took another 6 years of intensive research before the cure rate was able to reach 90%.

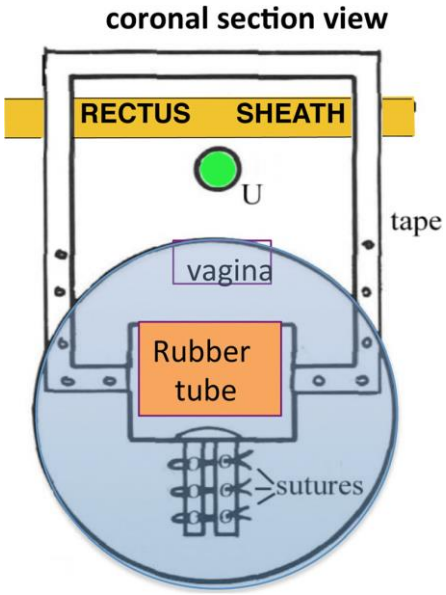

Fig.3 Prototype tension-free vaginal tape. Perspective: coronal section immediately behind the pubic symphysis. The tape was configured around the rectus sheath into the vagina as an inverted "U", through both ends of a rubber tube, exiting at its inferior end, both ends secured with interrupted sutures in holes set 0.5 cm apart to lower the sling if there was retention. The tape was removed at 6 weeks.

3.3. 1990 Discovery that muscles contract against ligaments

The Integral Theory revised the understanding of how pelvic muscles interacted with pelvic ligaments. This discovery demonstrated that there were three pairs of muscles pulling in opposite directions against paired ligaments, fig.2 [1]. The muscles assist the bladder

mechanism to close for continence; also, for evacuation of urine, by pulling open the back wall of the urethra to reduce frictional resistance to flow [4,5]. When the bladder fills up with urine, a message is sent to the brain via 'stretch receptors' in the bladder wall. If it is not convenient to pass urine at that time, the brain sends a signal to the muscles to stretch the vagina to help support the stretch receptors and control the 'urge to go'.

3.4. Why weak ligaments may cause incontinence and emptying problems

The muscle/ligament discovery demonstrated that if either the front or back ligaments are weak or loose, the muscles which contract against them weaken. The 3 pairs of muscles, fig.2, need a firm ligament 'anchoring point'. If the ligaments are weak, the muscles cannot function as they are meant to. This may cause three different bladder problems, 1. Urine loss on coughing or exercise (stress incontinence). 2. The patient cannot "hold on" (urge incontinence). 3. The patient cannot empty the bladder adequately which may lead to urinary retention and repeated bladder infections**.**

3.5. How incontinence and emptying problems can be cured.

In brief, incontinence and emptying problems can be cured by repairing the damaged ligaments. If the collagen in the ligaments is good (e.g., in younger women) and the ligaments are overstretched and loose, then they can be 'plicated', that is, folded and stitched to shorten them. However, if the ligaments are structurally weak because they lack collagen (e.g., in older women) a tape inserted in the position of the weak ligament is required to create new collagen. The effectiveness of this method was proven by the original experimental studies performed in 1987 [2] which preceded the prototype midurethral sling [3].

Section 4. Further Significant Findings in 1990

4.1 Six other significant experimental findings in 1990 [1].

The Integral Theory led to other new ways of understanding pelvic floor problems.

1.In 1988, it was observed that a woman who had a successful prototype sling operation became incontinent when she became pregnant and within 48 hours of delivery her continence was restored. This showed that collagen depolymerizes (breaks down) during pregnancy and repolymerizes (rejoins) immediately afterwards.

2.Microscopic studies showed a very important role of ligaments as being active structures which can contract and relax to assist bladder function. They contain elastin which allows them to stretch and collagen which gives them structural support.

3.Bladder and bowel function was related and sometimes bowel incontinence was also fixed by the prototype sling. Bladder incontinence was fixed in a woman after her external anal sphincter was repaired.

4.Pain could be caused by looseness in the back ligaments.

5. The distal part of the vagina below the urethra, also played a role in continence control and needed to be fixed as part of the midurethral sling surgery.

6. A key missing element in the 1990 Theory was that stretch receptors 'N' at bladder base [fig.2] had never been identified anatomically. Stretch receptors were crucial for the Theory's hypothesis that urge incontinence was a prematurely activated uncontrolled micturition. In fact, the stretch receptors predicted by the Theory were not described until some 14 years later, comprising part of the urothelium, as reported by de Groat [6].

4.2 1990 Tethered Vagina Syndrome and zone of critical elasticity (ZCE).

The Tethered Vagina Syndrome (TVS) was first described in the 1990 Theory: severe urinary incontinence because of loss of elasticity at bladder neck area of vagina from scarring following vaginal repair or excess elevation from Burch Colposuspension. TVS generally requires a skin graft in the vagina. Its ultimate application began in 2011in addressing a major problem after successful Obstetric fistula closure: continued massive urine loss.

Pathogenesis Because the front and back muscles pull the vagina in opposite directions, the middle part of vagina, known as the "Zone of Critical Elasticity"(ZCE) [fig.2] [1] needs to be especially elastic so that the muscles can do their work independently of each other. If the elasticity of ZCE area has been compromised by rigid scar tissue from the implanting of large mesh sheets to cure prolapse or scarred from excess removal of the vagina or destruction of the vagina from obstetric fistula, it can lead to massive urine loss when the brain gives the signal to close the urethra. The reason for this is that the scarring 'tethers' (joins) the more powerful back muscles to the less powerful front muscles, so that when the signal is given to close the urethra (the emptying tube) the urethra is forcibly pulled open and the patient loses urine uncontrollably. This is known as the tethered vagina syndrome. In 1993, this understanding of ZCE led to the use of skin grafts [7-9] to the bladder neck of the vagina to cure these problems by restoring elasticity.

4.3 Repairing ongoing urine loss after successful Obstetric Fistula closure.

The discovery of the Tethered Vagina Syndrome and skin graft in 1993, had major beneficial consequences for women with Obstetric Fistulas as it led to the solution of a significant problem: ongoing massive urine loss in up to 50% of women after successful Obstetric Fistula repair. In 2011, using this knowledge of the Tethered Vagina Syndrome, Professor Gordon Williams, Chief of the Hamlin Hospital, Addis Ababa, and Petros diagnosed Tethered Vagina Syndrome as the cause of this problem and they performed the first successful skin graft operations to cure it. However, the procedure was put on the map by an exceptional young Australian fistula surgeon, Dr Andrew Browning who is revolutionizing Obstetric fistula surgery with his Singapore flap grafts based on the Integral System. The work in this field has restored quality of life to women, who had been marginalized and exiled from their family and village, because of this debilitating condition [10-12].

Section 5. The Integral System

5.1 1992 Integral Theory evolves into the Integral System.

By 1992, it had been observed that specific symptoms indicated damage to specific ligaments, for example, women who lost urine on coughing had weak front (pubourethral) ligaments. Women who complained of pelvic pain or nocturia (getting up at night to pass urine) had weak back (uterosacral) ligaments. From this knowledge, evolved the symptom-based, Integral Theory System Questionnaire (ITSQ) [13]. When the answers were transferred to the pictorial algorithm it provided doctors with a visual diagnostic tool to identify which ligaments were causing symptoms and therefore, needed to be reinforced to restore them to their normal function. The Integral System was born.

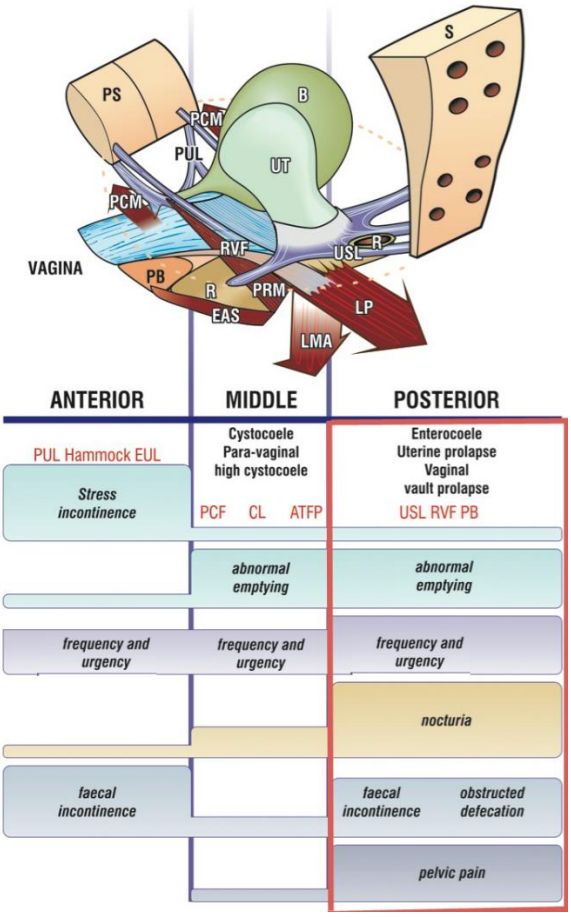

Fig.4 The pictorial diagnostic algorithm. Symptoms indicate which ligaments are damaged.

The numbers in red indicate the number of symptoms co-occurring with the 46 symptoms of chronic pelvic pain to confirm the diagnosis of USL damage. The 3 reflex muscle forces (arrows) tension the organs and the vagina to support urothelial stretch receptors 'N'. The height of the bar indicates probability of association of a symptom with a particular zone. The connective tissue structures causing prolapse and pelvic symptoms fall naturally into 3 zones.

Anterior zone: external meatus to bladder neck PUL=pubourethral ligament; hammock= suburethral vagina;

EUL=external urethral ligament

Middle zone: bladder neck to anterior cervical ring. CL=cardinal ligament; PCF=pubocervical fascia; ATFP=

arcus tendinous fascia pelvis.

Posterior zone posterior cervical ring to perineal body (PB): USL uterosacral ligaments; RVF =rectovaginal

fascia; PB. The rectangle indicates the symptoms associated with USL laxity and the posterior fornix

syndrome. Chronic pelvic pain and nocturia are uniquely caused by uterosacral (USL) ligament laxity.

5.2 1993 -1999 The "posterior fornix syndrome" (PFS)

The "posterior fornix syndrome"(PFS) was described in 1993 [14] and consisted of symptoms of urge incontinence (wetting before arrival at the toilet), frequency (going frequently to urinate) nocturia (getting up many times at night to urinate), chronic pelvic pain of unknown origin and urinary retention. These symptoms occurred in predictable groupings, in different proportions for each patient. The cause was weak uterosacral (USL) ligaments in the back part of the vagina and symptoms were cured by plication of the USLs.

It was found that although this simple operation worked well in younger women, it was not very successful in older woman because of collagen breakdown in the ligaments after the menopause. This problem was solved by applying a sling to the back (uterosacral) ligaments (uterosacral) to create new collagen to strengthen the ligaments. This was a very successful operation and Japanese surgeon, Dr Inoue reported high cure rates for symptoms and prolapse even 5 years after the back ligament sling was inserted.

5.3 1996 Final version of the midurethral sling operation.

The Australian /Swedish collaboration required several more prototypes before the final version of the midurethral sling in 1996. It was found that a permanent tape was needed with polypropylene as the ideal sling material [15]. By 1993, it had also become evident that collagen deficiencies in other ligaments* were causing prolapse, chronic pelvic pain and bladder symptoms such as urgency, nocturia and emptying problems. It was found that the same surgical principle which repaired the front ligaments, could also repair other ligaments to cure these problems.

- According to the Theory, the large failure rates known to occur in post-menopausal women after prolapse surgery was due to collagen breakdown and hydroxyproline excretion. This process caused not only osteoporosis, but also collagen leaching from the ligaments, to cause prolapse and pelvic symptoms.

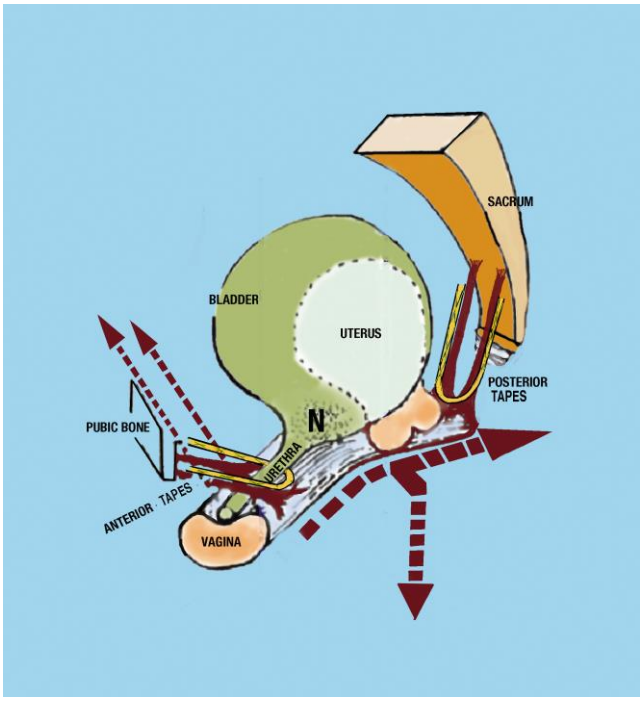

Fig.5 Precise placement of tapes on damaged ligaments. Note (in yellow) precise placement of anterior and posterior polypropylene tapes in the position of weak or loose ligaments. These create new collagen to reinforce, them, pubourethral anteriorly and uterosacral posteriorly. The new collagen creates a firm anchoring point for the three reflex muscle forces (arrows) to perform their autonomic functions, close urethra, open it, and stretch vagina bilaterally to support stretch receptors 'N'.

2021 Routine application of the PFS protocol and algorithm, [fig.3], was to later (2021) lead to the first cure of Interstitial cystitis with Hunner's ulcer in 2020, by Dr Kay Scheffler, urological surgeon from Rostock Germany [16].

5.4 Urge incontinence ("overactive bladder") and urodynamic "detrusor overactivity" (DO)

In 1993, it was demonstrated by urodynamic testing [17] that the Integral Theory's prediction of what is known as **urodynamic "detrusor overactivity" (DO)** was, in fact, no different from the urodynamic events which Tanagho described in the 1970s as occurring during a normal urination: first, a sense of urgency, then, relaxation of the urethra, contraction of the bladder, urine loss [18,19].

The difference was that in women who had OAB and DO, weakness in the muscles and ligaments prevented the mechanism which controlled timely bladder emptying from functioning as it normally should, causing women to wet before reaching the toilet.

"Detrusor overactivity" is urodynamically equivalent to normal micturition, fig6. In 1993, in a urodynamically controlled study, it was demonstrated that the sequence of events in what was then known as "detrusor instability", (now "urodynamic detrusor overactivity"), had exactly the same sequence of events as what Tanagho described for normal micturition in the 1970s [20,21]: first sensory urge, then relaxation of the proximal urethra, detrusor contraction, urine loss [22].

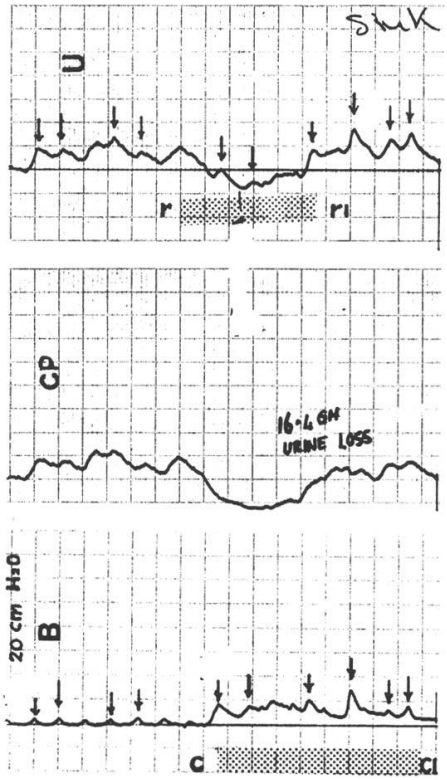

Fig.6 'Bladder instability' is a premature activation of the micturition reflex [19]. This is an actual graph

of a provocative handwashing test. The top graph, U, represents the recorded maximal intraurethral pressure, taken at the midpoint of the urethra. B, the bottom graph, represents the bladder pressure. The middle graph, CP, represents the electronically subtracted closure pressure; ‘‘r” to “rl ”represent the fall in the urethral pressure (U); c to cl represent the phasic contraction of the bladder.

5.5 The ‘Speculum’ Test [22]

This simple, standard test, performed on patients was able to predict whether reinforcing their back ligaments would solve their pain or urge problems. It involves gently inserting the bottom half of a speculum into the vagina to support the back ligaments. If the pain or urge were alleviated, the doctor would have confirmation that the symptoms originated from loose or damaged back ligaments.

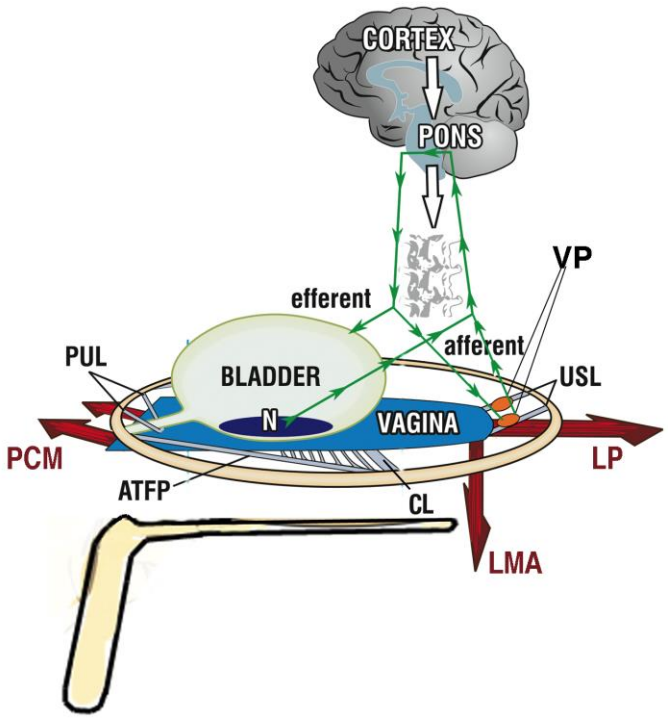

Fig.7 Speculum test. [22]This is a 3D view of the bladder sitting on the anterior vaginal wall. The vagina is suspended from the pelvic brim by ligaments, pubourethral (PUL), cardinal (CL) ATFP and uterosacral USL. A speculum inserted into the posterior fornix mechanically supports lax USLs and the nerve plexuses VP (S2-4, T11-L2) supported by USLs to prevent afferents (small green arrows) to the cortex perceived as pain from the

appropriate end organ whose afferent to the plexus was stimulated. Firm USLs restore the contractile strength of the posterior muscle forces LP and LMA which contract against them. These now tension the vagina like a trampoline to support the stretch receptors 'N', decreasing the afferent impulses which on passing a critical mass, are interpreted as urgency. The VPs also serve as relay stations for efferent impulses to the end organs. LP=levator plate; LMA= conjoint longitudinal muscle of the anus; PCM= pubococcygeus muscle. Large white arrows = reflex cortical suppression.

Section 6. Discoveries from 1996-2000

6.1 Further progress of the midurethral sling [1996-2000]

By 2000 The midurethral sling was on its way to becoming the gold standard operation for stress urinary incontinence. The instrument used to insert the tape for ligament repair was copied and marketed by more than 170 companies under their own brand name. The success of the midurethral sling was demonstrated by many research papers (now more than 2000) claiming 90% or greater cure of stress urinary incontinence. In 2001, Rezapour and Ulmsten demonstrated that as well as cure of SUI, a midurethral sling also cured urge incontinence (OAB) in some 50% of cases [23]. By 2019, it was estimated that a total of 10 million slings had been performed worldwide.

Another important breakthrough was achieved in 2019 by Nakamura et al.who reported 90% cure for Intrinsic Sphincter Defect (ISD) with a TFS midurethral minisling. ISD had previously been considered incurable [24].

6.2 1997 Urinary retention and chronic urinary infections

It is known that women who cannot empty their bladder have repeated bladder infections. In 1990, it was demonstrated that the urethra was opened out by external muscles pulling against the back (uterosacral) ligaments prior to bladder emptying [fig 2] and repair of these with a posterior sling could cure bladder emptying and urinary retention [16]. However, the importance of this external opening of the urethra was not fully appreciated until Bush et al.'s. bench experiments at the University of Western Australia's Engineering School [4,25-26]. They demonstrated the marked effect of the urethral width (diameter) on urine flow. For example, in fig.8, if the diameter was reduced from 4mm to 3.5 mm, really a very tiny amount, the pressure required for the bladder to expel the urine almost doubled, from 100 cm to 180cm.

The consequence of this discovery, was understanding that even minor looseness in the ligament against which the opening muscles contracted, would weaken the muscle forces, ability to actively open the urethra, resulting in incomplete emptying by the bladder, retention of urine and infection. This problem could only be cured by repair of the USLs [16,27].

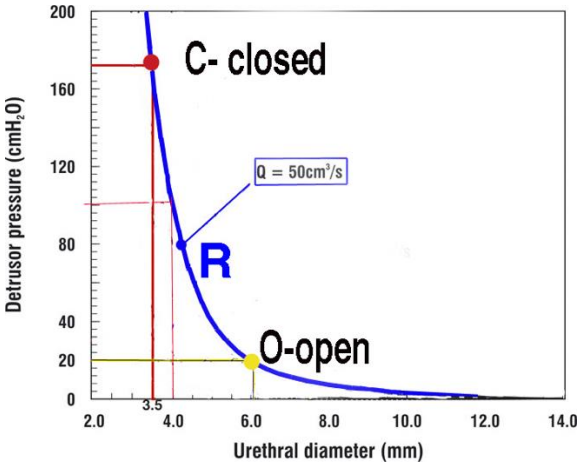

Fig.8 Relationship of urethral diameter to urine flow rate Bush et al. [25,26] demonstrated that urine flow is exponentially determined, simplistically, inversely to the 4^{th} power of the radius.For a flow rate of 50 ml/sec (thick blue line), opening the urethral diameter from 3.5 mm to 4 mm reduces the head of pressure required by the detrusor to expel urine from the bladder from 172 to 100 cm water. Expanding to 6 mm (yellow lines), reduces the head of pressure to 20 cm water. The blue line represents the total urethral resistance to flow, which is composed of dynamic and frictional flow components

6.3 Feedback control of the bladder [28,29].

When the bladder fills and it is not convenient to urinate the pelvic floor muscles reflexly contract in opposite directions to stretch the vagina (like a drum) to support the stretch receptors in the bladder ('N', fig.9) to stop them sending signals to the brain to empty. However, if the ligaments are loose, then the muscles which contract against them weaken and they cannot stretch the vagina to support the stretch receptors in the bladder. This causes signals to be sent when there is a lower volume of urine in the bladder and the person interprets this as urge symptoms to urinate.

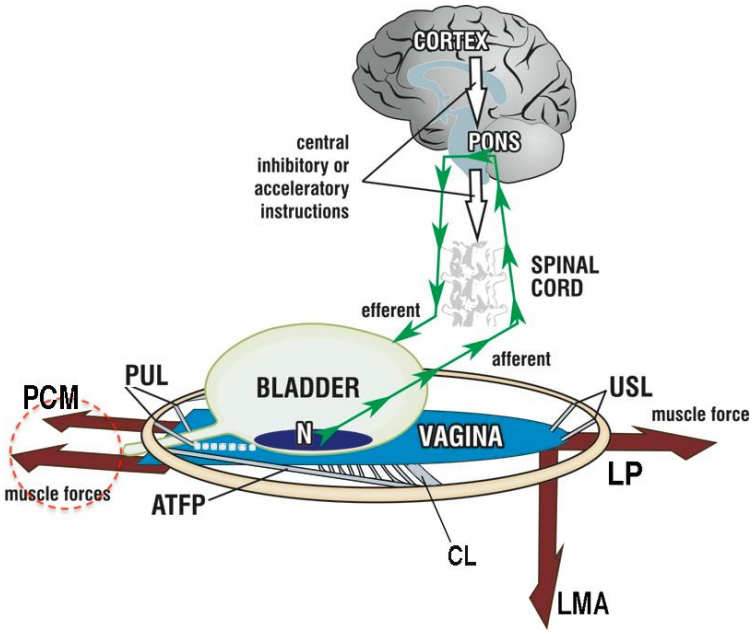

Fig.9 Binary model of function and dysfunction

The Binary model summarizes the Integral Theory System's view on urge (OAB) control. System in normal closed mode. The control of bladder is binary EITHER closed (most of the time) or open (only when the brain deems it appropriate to evacuate)

Cortical control Afferent impulses from stretch receptors 'N are reflexly suppressed cortically (white arrows). 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, preventing activation of the stretch receptors 'N', decreasing afferent impulses to the cortex.

Micturition Central control (white arrows) relaxes, as does PCM (broken circle); 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 Weakness in the muscles PCM, LP, LMA and/or the ligaments they contract against, PUL, USL, will affect the ability of the peripheral control mechanism to mechanically close 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).

6.3.1 Mathematical expression of the feedback control system, fig10.

This feedback control system, [fig.9], can be expressed as a mathematical equation Xnext = Xc (1-X), [fig.10]: X represents the number of signals which the bladder stretch receptors 'N' [fig.9] give and 'c' represents the ability to dampen these signals. Slope 'c' represents all the different phases of the bladder. For example, at the bottom of the slope [fig.10] ('retention') is what normally happens. The X impulses are dampened down by efficient muscles contracting against strong ligaments. As the slope process upwards then the closure reflex 'c' which dampens these impulses is less efficient. Not all signals are suppressed at source but are sufficiently dampened by the closure reflex 'c' for adequate control. As the slope 'c' proceeds upwards more and more impulses fail to be dampened. At the top of the slope the opening (micturition) reflex breaks through, as it cannot be fully controlled by the closure reflex, fig9; the woman gets urgency and may wet until the closure reflex gains control again. This battle for control is represented at the top of the slope as a swing between the closure reflex ("CLOSED unstable) and opening (micturition) reflex (OPEN unstable). At that point the woman cannot fully control their bladder

6.3.2 Fig.10 Modes of the bladder iterated by the Chaos Theory equation

Graph of an iterated Chaos Theory feedback equation $X_{NEXT} = cX(1 - X)$ applied to urodynamic experimental findings. Vertical axis = afferent impulses X_{next}; horizontal axis = Time. 'd' (broken lines) = iteration with one variable (central inhibition) and 'c'(unbroken lines) an inhibitory constant comprising, the sum of two variables, central inhibition plus peripheral suppression as in fig.9. X = fraction of possible nerve impulses in the micturition circuit. The whole spectrum of bladder conditions can be graphically expressed by iteration of the feedback equation varying the constant 'c'.

If vaginal tension is excessive, e.g., Fowler's Syndrome, excessive elevation by Burch colposuspension, peripheral inhibition of stretch receptors is high, 'c' is low. The system goes into retention. In stable closed (normal), micturition is quiescent. Higher up the slope 'c' is in "low compliance", with micturition activated but controlled; at the bifurcation, the micturition reflex overcomes the closure reflex, the system swings between open and closed. This is the symptomatic state of OAB, or that recorded urodynamically as DO [28].

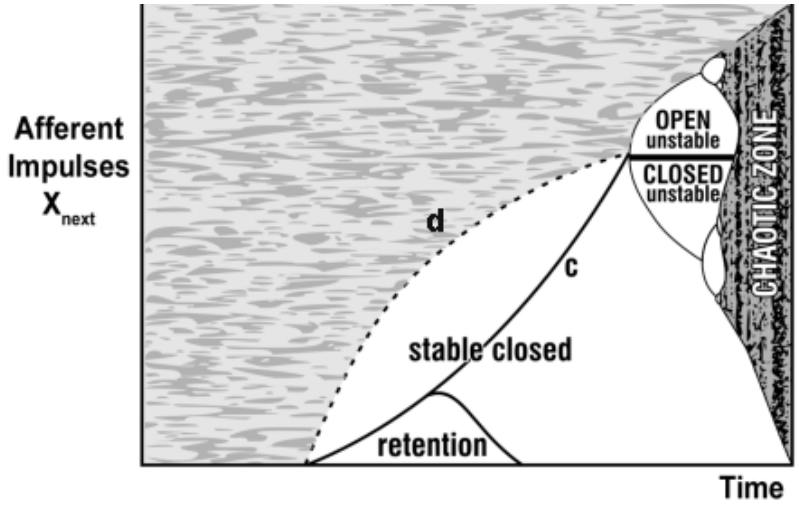

Fig.10 Modes of the bladder iterated by the Chaos Theory equation

Graph of an iterated Chaos Theory feedback equation $X_{NEXT} = cX(1 - X)$ applied to urodynamic experimental findings. Vertical axis = afferent impulses X_{next}; horizontal axis = Time. 'd'(broken lines) = iteration with one variable (central inhibition) and 'c'(unbroken lines) an inhibitory constant comprising, the sum of two variables, central inhibition plus peripheral suppression as in fig.1. X = fraction of possible nerve impulses in the micturition circuit. The whole spectrum of bladder conditions can be graphically expressed by iteration of the feedback equation varying the constant 'c'.

6.4 1995 Final invalidation of the pressure transmission theory

The essence of the Integral Theory is that a competent front (pubourethral) ligament is required for the pelvic muscles to close the urethra. Prior to 1990, the pressure transmission theory stated that the urethra was closed by abdominal pressure acting from above. Though ultrasound studies from the 1990 Integral Theory showed that the urethra was closed from behind, an impossibility according to the pressure transmission theory, this theory continued to have credibility with some experts.

The pressure transmission theory was finally disproved by measuring the pressures directly inside and outside the urethra. It was found the pressures inside the urethra on coughing were vastly higher than the pressures in the corresponding positions outside [29]. This could only be explained by reflex muscle action as stated by the Integral Theory. This could only be explained by reflex muscle action as stated by the Integral Theory.

6.5 1996 the origin and cure of chronic pelvic pain [30].

In 1996, a laparascopic study was performed on women who suffered with chronic pelvic pain from various sites, lower abdomen, vagina, tailbone, deep contact dyspareunia (pain with intercourse) in order to determine the origin of their chronic pelvic pain. No abdominal abnormality was found and their conditions were 85% cured at 3 months by an operation using native tissue to repair the back (uterosacral) ligaments. The operation worked by supporting the nerve plexuses (T11-L2 and S2-4) which were sending aberrant signals to the brain because they (the plexuses) were not supported by the back ligaments (fig.11).

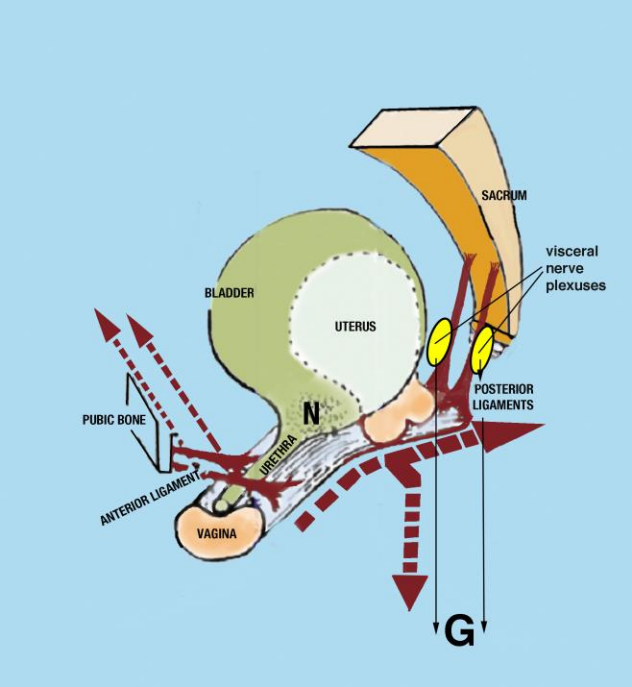

Fig.11 The visceral nerve plexuses (VP) are supported by the uterosacral ligaments. If these are weak or loose, gravity "G" or muscle movement may stimulate afferent visceral nerves as they pass through VP from the end organs to send "de novo" impulses to the brain. The brain falsely interprets these impulses as pain coming from the end organ which may be bladder, bowel, muscle spasm, lower abdomen, tailbone.

Section 7. Discoveries from 2000 onwards

Section 7. Discoveries from 2000 onwards

7.1 2000 Hysterectomy may cause or worsen pelvic problems

A research article in the Lancet,[31] in 2000, confirmed the Integral Theory prediction that women, especially after the menopause who had undergone hysterectomies, suffer more bladder, bowel and pain problems than women who had not. The stated cause was that during a hysterectomy operation, the blood supply to the back (uterosacral) ligaments is cut off when the descending uterine artery is tied. The result is atrophy of the posterior ligaments which caused posterior fornix syndrome symptoms (urge, frequency, nocturia, chronic pelvic pain, abnormal emptying).

7.2 2004-5 Origin of vulvodynia and chronic pelvic pain from lax uterosacral ligaments

Cure of **vulvodynia and other sites of chronic pelvic pain** [32,33] by uterosacral ligament repair led to a hypothesis that the cause was unsupported T11-L2 and S2-4 visceral plexuses. This hypothesis was validated by what is now known as the Bornstein Test [33],[fig 11]. Local anaesthetic was injected into the back ligaments in the site of the nerve plexuses in 10 women. The pain and tenderness of their vulvodynia was relieved for 20 minutes. Later, the Bornstein test was applied to 3 women with interstitial cystitis and several co-occurring chronic pains in different sites of their pelvis [34]. It was found that the pains were fully or partly alleviated. These results with the 'Bornstein Test' raised the question of whether all chronic pelvic pains, whatever their manifestation, mainly arose from the inability of loose uterosacral ligaments to support visceral nerve plexuses. If so, such pains were potentially curable by strengthening the back (uterosacral) ligaments.

7.3 The first minisling for the cure of stress urinary incontinence-

In 2004, the first minisling for cure of urinary stress incontinence [35,] and uterine/apical prolapse [36], was described It required only a single incision and was able to repair pelvic ligaments in a very minimal way. The minisling operations are exactly as represented in fig.3, except there is a small 4-pronged anchor, 11x4mm at the tip of the tape to anchor the tape in the tissues. The "single incision" minisling more safely reinforced the same ligaments than the more traumatic operations such as "TVT", with equal efficiency, achieving up to 90% cure rates for stress urinary incontinence (SUI) at 3-5 years [37,38] and 90% cure for ISD (Intrinsic Sphincter defects) [22].

Later, this minisling and other sling methods were applied to other ligaments in the pelvis, cardinal, uterosacral, arcus tendinous fascia pelvis, perineal body to cure multiple prolapse and symptom conditions, for example, apical prolapse, cystocele, rectocele, descending perineal syndrome, chronic pelvic pain, OAB, fecal incontinence, obstructed defecation [15,16,21,22,25,26,30, 32,35,36,37,38,39-53]. The minisling was less invasive, used less implanted tape, was less likely to damage an organ and was equally effective as the more major operations for prolapse. Long-term results from studies in Japan showed it was effective for at least 5 years [41]. Besides Japan, studies in Germany, Austria, Australia, and Turkey achieved 90% cure of prolapse, and up to 80% cure of pelvic symptoms such as urge incontinence, nocturia, chronic pelvic pain, emptying problems and bowel problems.

14.

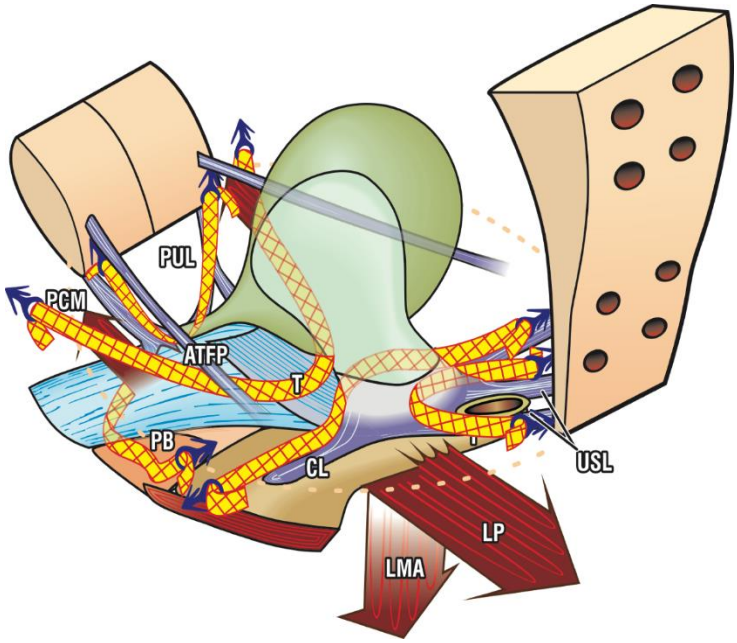

Fig.12 minisling repair of all 5 ligaments CL USL PB PUL ATFP and dislocated PCM (refs)

7.4 (2008) A new theory of anorectal function and dysfunction [54]

Even with the prototype operations in the late 1980's, some patients were reporting that the sling operations they were having for their bladder were also curing their bowel symptoms. This prompted further investigation which resulted in a new theory of how the bowel worked, why it did not and why the same day-care ligament repairs could fix both bladder and bowel problems simultaneusly. The new theory [54], was a collaborative effort based on 12 experimental studies in surgery, neurology, neuropathology, ultrasound and radiology, by several authors including, Abendstein, Richardson, Anderson, Gunnemann, Bush, Hocking, Liedl, Kakulas, Brugger, Furtschegger, Rieger.

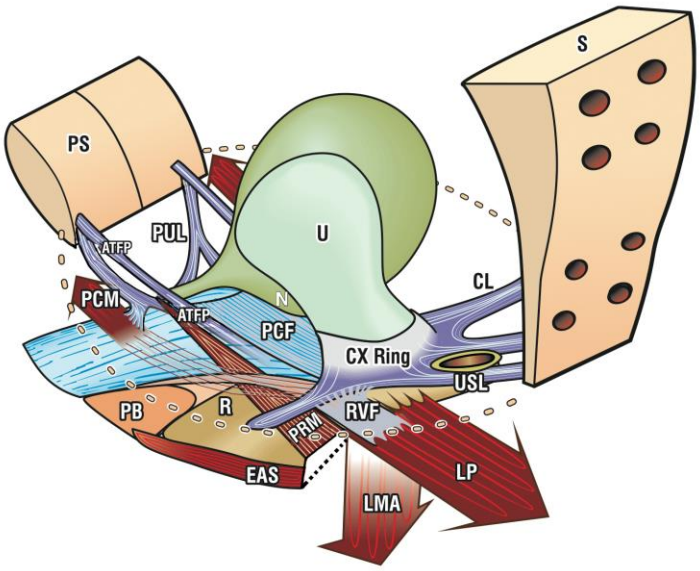

Fig.13 The dynamics of anorectal closure, opening, pathogenesis and surgery. Arrows denote directional muscle forces. Anorectal closure: the rectovaginal fascia (RVF) inserts into perineal body (PB), levator plate (LP) and the uterosacral ligaments (USL). Contraction of LP stiffens RVF and both walls of rectum. Contraction of LMA (conjoint longitudinal muscle of the anus) against USL stretches the rectum around puborectalis muscle (PRM), to create the anorectal angle and closure. Defaecation. PRM relaxes. LMA/LP vectors open out the anorectal angle (broken lines); pubococcygeus (PCM) vector stiffens PB and anterior wall of anus; rectum (R) empties. ATFP = arcus tendineus fascia pelvis; CL = cardinal ligament; circular broken lines = pelvic brim;

Pathogenesis. Damaged ligaments decrease the force of opening and closure vectors for urethra and anus. **Surgery:** Reinforcement of damaged ligaments with implanted polypropylene tapes, [fig.3].

7.5 (2008) Muscle or ligament? Which is the principal cause of incontinence

The question arose, since the muscles and ligaments work together to control the bladder and bowel, which one was the prime cause of incontinence, muscle or ligament? This was solved in a blinded muscle biopsy experiment in women who were having a sling operation for their stress urinary incontinence [55]. The muscle biopsies were examined by Professors Swash and Kakulas, without knowledge of the surgical outcomes. Almost all the 48 biopsies showed evidence of severe muscle damage, yet 89% of the patients reported a cure of incontinence the day after surgery. This demonstrated the most vulnerable structures to birth damage were the ligaments and not the muscles.

7.6 2008 Cure of diverted urinary stream.

Some women after they had given birth, reported that their urine stream did not go in a straight line but “flowed everywhere”. Two German surgeons, Dr Scheffler and Prof Hakenberg [56] proved the problem was a muscle that was torn from the bone. Paired muscles pull equally on the right side and on the left side of the urethra. However, if a muscle is torn on one side after childbirth, the pulling of the other muscle causes the urinary stream flow to deviate to one side. Using the principles of the Integral Theory as a guide, they inserted a sling to reattach the damaged muscle to the ligaments behind the pubic bone. This corrected the urine flow.

7.7 2013 Cure of the bowel emptying problems caused by over distension of the perineum[57, 58].

If at childbirth, there is excess distension (expansion) of the perineum by the baby’s head, some women find that they cannot empty their bowel and need to insert their hand into the rectum or vagina to support the perineum so that they can effectively evacuate their faeces. This is necessary because the perineum has dropped down and has to be manually supported, with faeces sometimes manually removed. By inserting a sling to reattach the perineum to the tissues covering the descending ramus of the pelvic bone, the perineum is kept in position and the women can then empty their bowels normally.

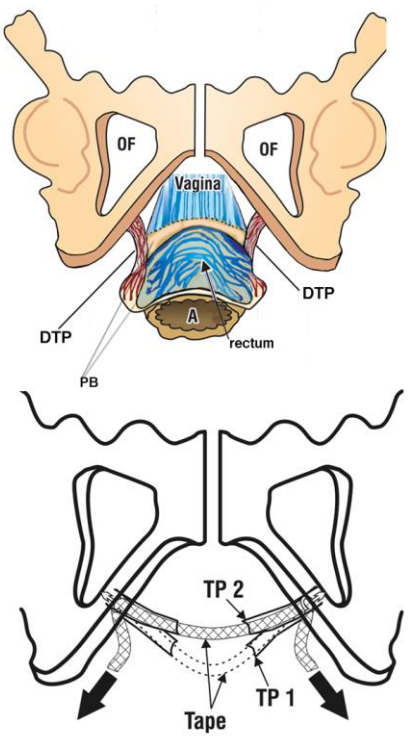

Fig.14 Pathogenesis and cure of descending perineal syndrome (DPS).

Upper figure The perineal body, PB, is suspended by the deep transversus perinei ligaments (DTP). Birth damage has stretched PB laterally and downwards, so it descends as DPS, often below the ischial tuberosity. The thinned or broken PB allows the rectum to prolapse through, to spread laterally and adhere to the vagina and PB itself.

Lower figure The principles of DPS repair by the tensioned TFS mini sling. The rectum is dissected off the vagina and PB and its serosa repaired. The laterally displaced PBs are located and a tunnel is made to the DTP

Section 8. Integral Theory application for "bedwetting"

8.1 **Squatting based exercises for incontinence** [59]

Between 2000-2004, Dr Patricia Skilling, head of pelvic floor rehabilitation at the Kvinno Centre in Perth, Australia, developed a new series of squatting- based exercises for pelvic floor problems which were based on the Integral System; these were the first new exercises since the 1948 Kegel exercises. From research studies of women to evaluate the effectiveness of these new exercises, it was found that pre-menopausal women improved their pelvic floor health much more than post-menopausal women. In fact, it was found that the majority of

pre-menopausal women reported a 50% or more improvement in a varied array of symptoms such as stress incontinence, urge incontinence, frequency, nocturia, chronic pelvic pain and bladder and bowel emptying problems, Table 1. Unfortunately, due to collagen breakdown in the ligaments, results were much poorer in women who had passed the menopause.

[2000-2021]

Table 1 Results from Skilling's squatting bases exercises in premenopausal women [59]

Fate of Individual Symptoms (n=78)	
condition	**>50% improvement**
stress incontinence (n=69)	57 (82%)
urge incontinence (n=44)	33 (68%)
frequency only (n=12)	10 (83%)
nocturia (n=32)	29 (90%)
pelvic pain (n=17)	13 (76%)
residual urine 202ml (n=23)	71 ml

8.2 (2020) Integral theory application for bedwetting [60].

In 2020, Professor Garcia Fernandez, a specialist pediatric surgeon, performed a special trial on children who wet themselves during the day and at night (day/night enuresis). The Skilling exercises were modified to engage the children's interest and involved squatting and bridge exercises twice daily for 4 months. The children were strictly supervised by their parents to ensure that the exercises were performed as required and once a week each child's progress was reviewed by Professor Garcia Fernandez and the staff of his specialist clinic. The children's parents kept a detailed written account of their child's 'wetting' episodes and an independent external assessor validated the results as well. The positive outcomes the children achieved in controlling their incontinent conditions were considered remarkable, 86% cure.

A major unstated conclusion from this study was that bedwetting was not psychological, and was not the child's fault. To emphasize this message to the public at large, Professor Garcia

Fernandez and Dr Skilling wrote a book “End Bedwetting Now”, which was published in both Spanish and English. It described the exercise routine, but more importantly, it emphasized the cause was not psychological. Rather, the cause was immaturity in the muscles and ligaments which were both strengthened by the exercises.

Section 9. The Mesh controversy – not the Integral system

Following on the abdominal hernia analogy, where mesh sheets are used to block descent of the hernia, large meshes were attached to slings. Though results were, in general, superior to those from vaginal excision of the bulge, severe, even crippling complications were reported by some women. These were sufficient to cause the banning of mesh in some countries. [61,62].

The actual structural components of the pelvis are ligaments. The vagina’s role is to transmit muscle forces for opening, closure and control of urgency, so it needs to be elastic [1]. Vaginal meshes placed behind the vagina did not reinforce the ligaments. Rather, they worked by blocking the descent of the prolapse. Mesh created scar tissue in the vagina, which removed the elasticity so important for the 3 functions of the bladder, continence, evacuation and tensioning to control urgency. Furthermore, in some cases, the scar tissue caused pain by entrapping nerves and if there was sufficient fibrosis, creating the tethered vagina syndrome, where the bladder empties massively when it is given the signal to close. [9,11]. Such problems have never been reported with back ligament (posterior) sling surgery [39-53], perhaps because the slings were transversely applied and so had very little contact with the vagina. Any scarring was confined to a small transverse strip. With such slings, the vagina is able to retain its elasticity and correct function.

Undoubtedly, the discoveries that can be ascribed to the Integral Theory and Integral System have over the past decades revolutionized the management of pelvic floor problems. However, it has not been without controversy, as is the case with the introduction of any new paradigm, which challenges the status quo. The evolving nature of the Integral System with its application to the many pelvic floor problems detailed here, many previously considered incurable, has demonstrated that it is an emerging practical and effective system for the treatment of pelvic floor conditions.

REFERENCES

1. Petros PE, Ulmsten U. An Integral Theory of female urinary incontinence. Acta Obstet Gyne Scan. 1990;69 Suppl 153:1-79.

2. Petros PE, Ulmsten U, Papadimitriou J. The Autogenic Neoligament procedure: a technique for planned formation of an artificial neo-ligament. Acta Obstet Gyn Scan. 1990;69 Suppl 153:43-51.

3. Petros PE, Ulmsten U. The combined intravaginal sling and tuck operation:an ambulatory procedure for stress and urge incontinence. Acta Obstet Gyn Scan. 1990;69 Suppl 153:53-59.

4. Bush MB, Petros PEP, Barrett- Lennard BR. On the flow through the human urethra. Biomechanics. 1997;30(9):967-969.

5. Petros PE, Bush MB. A mathematical model of micturition gives new insights into pressure measurement and function. Int Urogynecol J. 1998;9:103-107.

6. de Groat WC. The urothelium in overactive bladder: passive bystander or active participant? Urol. 2004;64:7-11. https://doi.org/10.1016/j.urology.2004.08.063.

7. Petros PE, Ulmsten U. The tethered vagina syndrome, post surgical incontinence and I-plasty operation for cure. Acta Obstet Gyn Scan. 1990;69 Suppl 153:63-67.

8. Petros PE, Ulmsten U. The free graft procedure for cure of the tethered vagina syndrome. Scand J Urol Nephrol. 1993;Suppl 153(Pt 4):85-87.

9. Goeschen K, Müller-Funogea A, Petros P. Tethered vagina syndrome: cure of severe involuntary urinary loss by skin graft to the bladder neck area of vagina. Pelviperineology. 2010;29:100-102.

10. Browning A, Williams G, Petros P. Skin flap vaginal augmentation helps prevent and cure post obstetric fistula repair urine leakage: a critical anatomical analysis. Br J Obstet Gynaecol. 2018 May;125(6):745-749. doi:10.1111/1471-0528.14953. Epub 2017 Nov 17.

11. Williams G, Browning A, Petros PE. The integral theory and its tethered vagina syndrome revisited: vaginal scarring may cause massive urinary incontinence. BJU Int. 2018 Oct;122(4):532-534. doi:10.1111/bju.14218. Epub 2018 Apr 23.

12. Browning A, Williams G, Petros P. Prevention and cure of post vesico-vaginal fistula repair incontinence by insertion of skin graft in the bladder neck area of vagina- update on hypothesis and interim report. Pelviperineology. 2017;36:9-11.

13. Wagenlehner FM, Fröhlich O, Bschleipfer T, Weidner W, Perletti G. The integral theory system questionnaire: an anatomically directed questionnaire to determine pelvic floor dysfunctions in women. World J Urol. 2014;32(3):769–81.

14. Petros PE, Ulmsten U. The posterior fornix syndrome: a multiple symptom complex of pelvic pain and abnormal urinary symptoms deriving from laxity in the posterior fornix. Scand. J. Urol. Nephrol. 1993;27:89-93.

15. Ulmsten U, Petros P. Intravaginal slingplasty (IVS): an ambulatory surgical procedure for treatment of female urinary incontinence. Scand J Urol Nephrol. 1995 Mar;9(1):75-82.

16. Scheffler KU, Oliver W, Hakenberg OW, Petros PE. Cure of interstitial cystitis and non-ulcerating Hunner's Ulcer by cardinal/uterosacral ligament repair. Urol Int. 2021.

17. Petros PE, Ulmsten U. Bladder instability in women:a premature activation of the micturition reflex. Neurourol Urodynam. 1993;12:235-239. F

18. Tanagho EA. The anatomy & physiology of micturition. Clinics in Obstets & Gynecol. 1978;5:1:3-26.

19. Tanagho EA,Miller ER. Initiation of voiding. British Journal of Urology. 1970; 42:175-180.

20. Wu Q, Luo L, Petros P. Mechanical support of the posterior fornix relieved urgency and suburethral tenderness. Pelviperineol. 2013;32:55-56.

21. Rezapour M, Ulmsten,U. Tension-Free Vaginal Tape (TVT) in women with mixed urinary incontinence :a long-term follow-up. Int Urogynecol J. 2001; **12:**S15–S18; https://doi.org/10.1007/s001920170006.

22. Nakamura R, Yao M, Maeda Y, Fujisaki A, Sekiguchi Y. Retropubic tissue fixation system tensioned mini-sling carried out under local anesthesia cures stress urinary incontinence and intrinsic sphincter deficiency: 1-year data. Int J Urol. 2017 Jul;24(7):532-537. doi: 10.1111/iju.13360. Epub 2017 May 14. PMID: 28503734.

23. Petros PE. New ambulatory surgical methods using an anatomical classification of urinary dysfunction improve stress, urge, and abnormal emptying. Int Urogynecol J. 1997;8(5):270-278.

24. Bush M, Wagenlehner F, Liedl B, Petros P. A finite element model validates an external mechanism for opening the urethral tube prior to micturition in the female. World J Urol. 2015;33(8):1151-1157. 2014 Oct 19. [Epub ahead of print] PMID: 25326768.

25. Bush M.B, Moron C, Messner-Pellenc L, Petros PE, Millard R. A mechanical model for the opening of the human female urethra. Proceedings of Biomedical Engineering 2005, Austria, KP. Adlassnig and M. Bracale (eds), Acta Press, 2005:210-213.

26. Goeschen K. Posterior Fornix Syndrome:Comparison of original (2004) and modified (2015) post-PIVS anatomic and symptomatic results: a personal journey. Pelviperineology. 2015;34:85–91.

27. Petros PE. Detrusor instability and low compliance may represent different levels of disturbance in peripheral feedback control of the micturition reflex. Neurourol Urodynam. 1999;18:81-91.

28. Petros PEP, Bush M. A feedback control system explains clinical and urodynamic bladder instability in the female. Pelviperineology. 2016;35:90-93.

29. Petros PE, Ulmsten U. Urethral pressure increase on effort originates from within the urethra, and continence from musculo-vaginal closure. Neurourol Urodynam. 1995;14:337-350.

30. Petros PE. Severe chronic pelvic pain in women may be caused by ligamentous laxity in the posterior fornix of the vagina. Aust NZ J Obstet Gynaecol. 1996;36(3):351-354.

31. Brown JS. Urinary incontinence after hysterectomy. Lancet 2000;356:9246,pp2012,3; DOI:https://doi.org/10.1016/S0140-6736(05)75214-4.

32. Petros PE, Bornstein J. Vulvar vestibulitis may be a referred pain arising from laxity in the uterosacral ligaments: a hypothesis based on 3 prospective case reports. ANZJO&G. 2004;44:483-486.

33. Bornstein J. et al. Causation of vulvar vestibulitis. ANZJOG. 2005;45:538-541.

34. Petros PEP. Interstitial cystitis (painful bladder syndrome) may, in some cases, be a referred pain from the uterosacral ligaments. Pelviperineology. 2010;29:56-59.

35. Petros PEP, Richardson PA. The midurethral TFS sling- a 'micro-method' for cure of stress incontinence- preliminary report. ANZJOG. 2005;45:372-375.

36. Petros PEP, Richardson PA. The TFS posterior sling for repair of uterine/vault prolapse-a preliminary report. ANZJOG. 2005;45:376-379.

37. Nakamura R, Yao M, Maeda Y, Fujisaki A, Sekiguchi Y. Outpatient mid-urethral tissue fixation system sling for urodynamic stress urinary incontinence: 3-year surgical and quality of life results. Int Urogynecol J .2017 doi: 10.1007/s00192-017-3341-4.

38. .Sivaslioglu AA, Eylem U, Serpi A, et al. A prospective randomized controlled trial of the transobturator tape and tissue fixation minisling in patients with stress urinary incontinence: 5-year results. J Urol. 2012;188:194-9.

39. Liedl B, Inoue H, Sekiguchi Y, Haverfield M, Richardson P, Yassourides A, et al. Is overactive bladder in the female surgically curable by ligament repair? Cent European J Urol. 2017;70(1):53-9.

40. Wagenlehner F, Müller-Funogea IA, PerlettiG, et al. Vaginal apical prolapse repair using two different sling techniques improves chronic pelvic pain, urgency and nocturia – a multicentre study of 1420 patients. Pelviperineology. 2016;35:99-104.

41. Inoue H, Kohata Y, Fukuda T, Monma M, Uzawa Y, Kubo Y, et al. Repair of damaged ligaments with tissue fixation system minisling is sufficient to cure major prolapse in all three compartments: 5-year data. J Obstet Gynaecol Res. 2017 Oct;43(10):1570-7.

42. Haverfield M. Tissue Fixation System (TFS) neoligament pelvic organ repair procedures –12 and 24 month results. Pelviperineology. 2015;34:70-74.

43. Richardson P. Surgical cure of nocturia using 4 different methods based on strengthening the structural supports of the vaginal apex: a short review. Pelviperineology. 2015;34:92-93.

44. Inoue H, Kohata Y, Sekiguchi Y, et al. The TFS Minisling restores major pelvic organ Prolapse and symptoms in aged Japanese women by repairing damaged suspensory ligaments– 12–48 month data. Pelviperineology. 2015;34:79-83.

45. Petros P, Richardson PA. TFS posterior sling improves overactive bladder, pelvic pain and abnormal emptying, even with minor prolapse: a prospective urodynamic study. Pelviperineology. 2010;29:52-55.

46. Goeschen K, Gold D. Surgical cure of chronic pelvic pain, associated bladder & bowel symptoms by posterior sling in 198 patients validates the Pescatori Iceberg principle of pelvic symptom co-occurrence. Pelviperineology. 2017;36:84-88.

47. Caliskan A, Goeschen K, Zumrutbas AE. Long term results of modified posterior intravaginal slingplasty (P-IVS) in patients with pelvic organ prolapse. Pelviperineology. 2015;34:94-100.

48. Abendstein B, Brugger BA, Furtschegger A, Rieger M, Petros PE. Role of the uterosacral ligaments in the causation of rectal intussusception, abnormal bowel emptying and fecal incontinence-a prospective study. Pelviperineology. 2008;27: 118-121.

49. Goeschen K. Role of uterosacral ligaments in the causation and cure of chronic pelvic pain syndrome. Pelviperineology. 2015;34:2-20.

50. Liedl B, Goeschen K, Sutherland SE, Roovers JP, Yassouridis A. Can surgical reconstruction of vaginal and ligamentous laxity cure overactive bladder symptoms in women with pelvic organ prolapse? BJU Int. 2019 Mar; 123(3): 493-510.

51. Liedl B, Goeschen K, Durner L. Current treatment of pelvic organ prolapse correlated with chronic pelvic pain, bladder and bowel dysfunction. Curr Opin Urol. 2017 May;27(3):274-81.

52. Müller-Funogea A. Posterior fornix syndrome: a new urogynecologic entity. Ethiopathogenesis and proposal for surgical therapy. Thesis, Romania: Medical University of Bucharest; 2014.

53. Petros P, Richardson PA. TFS posterior sling improves overactive bladder, pelvic pain and abnormal emptying, even with minor prolapse: a prospective urodynamic study. Pelviperineology. 2010;29:52-55.

54. **Petros PE**, **Swash MA**. **Musculoelastic theory** *of* **anorectal function and dysfunction** in the **female**. J Pelviperineol. ***2008***;27:**89-121.**

55. Petros PE, Swash M, Kakulas B. Stress urinary incontinence results from muscle weakness and ligamentous laxity in the pelvic floor. Pelviperineology. 2008;27:107-109.

56. Scheffler KU, Hakenberg OW. A hypothesis for urinary stream divergence in the female: unilateral dislocation of the pubovisceral muscle. Pelviperineology. 2014;33:10-13.

57. Wagenlehner FME, Del Amo EGA, Santoro GA, Petros P. Live anatomy of the perineal body in patients with third- degree rectocele. Colorectal Dis. 2013;15;11;1416-1422.

58. Wagenlehner FM, Del Amo E, Santoro G, Petros P. Perineal body repair in patients with 3rd degree rectocele. A critical analysis of the tissue fixation system. Colorectal Dis. Dec 2013;15(12):e760-e765.

59. Skilling PM, Petros PE. Synergistic non-surgical management of pelvic floor dysfunction: second report. Int Urogyne J. 2004;15:106-110.

60. Garcia-Fernandez A, Petros PE. A four-month squatting-based pelvic exercise regime cures day/night enuresis and bowel dysfunction in children aged 7–11 years. Cent Eur J Urol. 2020;73:307-314.

61. FDA Public Health Notification: Serious complications associated with transvaginal mesh placement and stress urinary incontinence Issued: October 20, 2008.

62. Baroness Cumberlage Press conference speech, 8th July 2020. The Medicines and Medical Devices Safety Review - UK.