CHAPTER 8

Committee 4

Pathophysiology of Urinary Incontinence, Fecal Incontinence and Pelvic Organ Prolpase

Chairman

J. MOSTWIN (USA)

Members

A. BOURCIER (FRANCE),

F. HAAB (FRANCE),

H. KOELBL (GERMANY),

S. RAO (USA),

N. RESNICK (USA),

S. SALVATORE (ITALY),

A. SULTAN (U.K),

O. YAMAGUCHI (JAPAN)

CONTENTS

LIST OF ABBREVIATIONS

ACS	American College of Surgeons
ANS	Autonomic Nervous System
ACh	Acetylcholine
AChE	Acetylcholinesterase
ASR	Anal Sphincter Rupture
ATP	Adenosine Triphosphate
BPH	Benign Prostatic Hyperplasia
BPO	Benign Prostatic Obstruction
CNS	Central Nervous System
CI	Confidence Interval
cAMP	Cyclic Adenosine Monophosphate
DHIC	Detrusor Hyperactivity - Impaired Contractility
DO	Detrusor Overactivity
DM	Diabetes Mellitus
DSD	Detrusor Sphincter Dyssynergia
EMG	Electromyography
EAS	External Anal Sphincter
GSUI	Genuine Stress Urinary Incontinence
IBD	Inflammatory Bowel Disease
IBS	Irritable Bowel Syndrome
IAS	Internal Anal Sphincter
ICI	International Consultation on Incontinence
IPSS	International Prostate Symptom Score
ISD	Intrinsic Sphincter Deficiency
LUTS	Lower Urinary Tract Symptoms
MRI	Magnetic Resonance Imaging
MS	Multimple Scerosis
NO	Nitric Oxide
NOS	Nitric Oxide Synthase
NGF	Nerve Growth Factor
OAB	Overacive Bladder
PMC	Pontine Micturition Center
PFD	Pelvic Floor Dysfunction
POP	Pelvic Organ Prolapse
POPQ	Pelvic Organ Prolapse Quantitation
PNTML	Pudendal Nerve Motor Terminal Motor Latency
RRP	Radical Retropubic Prostatectomy
RCOG	Royal College of Obstetricians and Gynaecologists
SSRI	Selective Serotonin Re-uptake Inhibitor
SUI	Stress Urinary Incontinence
TURP	Transurethral Prostatectomy
TUIP	Transurethral Incision of the Prostate
TTX	Tetrodotoxin
VLPP	Valsalva Leak Point Pressure

Pathophysiology of Urinary Incontinence, Fecal Incontinence and Pelvic Organ Prolpase

J. MOSTWIN

A. BOURCIER, F. HAAB, H. KOELBL, S. RAO, N. RESNICK, S. SALVATORE, A. SULTAN, O. YAMAGUCHI

For this third International Consultation on Incontinence, the Committee on Pathophysiology was reorganized to consider causes of pelvic prolapse and fecal, as well as urinary, incontinence. For many women, childbirth and pregnancy contribute to the development of urinary as well as fecal incontinence, therefore these two conditions have been naturally integrated into a single chapter. Special problems of the elderly have also been included for this ICI.

We have also been asked to consider pathophysiological mechanisms underlying pelvic organ prolapse. These three areas of our concentration, urinary incontinence, pelvic organ prolapse and fecal incontinence, are loosely interconnected by virtue of similar location within the body. In the case of women, childbirth and pregnancy may contribute to one or all of these conditions. Yet there are also neurological factors, and gender specific factors which must be considered in the evaluation of any given patient. Thus, we have tied to provide a balanced overview of the subject, keeping in mind both the common and the distinct qualities of the various conditions, while organizing them in a logical, narrative manner that makes any one section of the chapter easy to read.

Other than the re-organization of the Committee, there have been only incremental increases in our understanding of urinary incontinence over the past few years, whether men's or women's. We have thus retained much of the original body of knowledge that appeared in the previous two Consultations in this chapter, so that the reader seeking a comprehensive review of the subject can find it here without needing to examine previous, sometimes difficult to find, editions. Because of the growing length of the report, however, we have omitted a number of figures from the first two ICI reports, as well as many of the tables regarding men's incontinence.

In the area of women's stress incontinence, intrinsic urethral function continues to receive increased attention. As newer pharmacological agents to provide neural stimulation of the striated sphincter appear, and the limits of vaginal suspensory operations for correction of urethral dysfunction are reported, considerations of pathophysiology have shifted from the 50 year old paradigm reagrding urethral mobility associated with vaginal prolapse in the genesis of incontinence. However, these newer directions should be considered against the background of half a century of observation and practical clinical experience. We therefore continue to recommend a balanced approach.

In the area of men's incontinence, the greatest concern remains the problem of sphincteric injury following radical pelvic surgery and brachytherapy. While many thousands of procedures are performed annually, our knowledge about sphincteric anatomy and function has progressed little since the last ICI. Instead, empiric methods of treatment and hopeful prevention have been advanced to treat affected individuals, and insofar as prosthetic implants remain an effective method of treatment, enthusiasm and urgency for further basic research into male sphincteric function remains limited. In contrast to this kind of sphincteric injury, the causes of incontinence associated with bladder outlet obstruction and prostatic enlargement have been well characterized, and little new knowledge has appeared in recent years.)

Finally, with respect to fecal incontinence and pelvic prolapse, two new areas for this Committee's concern, the sections addressing them may appear to provide some overlap and possible redundancy. Because this is not a textbook on the subject, we have preferred to allow the narrative quality of each section to remain intact so as to facilitate reading and avoid a fragmented tone to the final chapter.

A. THE OVERACTIVE BLADDER

I. INTRODUCTION

The most common problem with urine storage arises when the bladder fails to remain relaxed until an appropriate time for urination. The symptom syndrome is called "overactive bladder"(OAB), which refers to the symptoms of urgency, with or without urge incontinence, usually with frequency and nocturia. According to the ICS terminology as of 2002, OAB symptoms are suggestive of urodynamically demonstrable detrusor overactivity(involuntary detrusor contraction) during the filling phase which may be spontaneous or provoked. This may be further characterized as neurogenic when there is a relevant neurological condition. Common neurogenic causes include stroke, Parkinson's disease, multiple sclerosis and spinal injury. Non-neurogenic etiologies may be related to outflow obstruction, aging, female anatomical incontinence, but most cases are idiopathic. This section focuses on pathophysiology of the overactive bladder and reviews studies that have provided insights into the mechanisms underlying bladder overactiviy.

II. NEUROGENIC DETRUSOR OVERACTIVITY

1. Suprapontine lesions (Figure 1)

It is generally accepted that suprapontine lesions such as cerebrovascular disease and Parkinson's disease produce detrusor overactivity. The patient with a suprapontine lesion loses voluntary inhibition of micturition, which corresponds to uninhibited overactive bladder according to a classification by Fall et al [1, 2].

Brain transection studies in animals with an intact neuroaxis showed that suprapontine areas generally exert a tonic inhibitory influence on the pontine micturition center (PMC) [3, 4]. In humans, the cerebral cortex (medial frontal lobes) and the basal ganglia are thought to suppress the micturition reflex. Thus, damage to the brain induces bladder overactivity by reducing suprapontine inhibition.

Recently, the mechanism of overactive bladder induced by cerebral infarction or Parkinson's disease has been further studied using animal models[5-7]. In the central nervous system, a glutamatergic pathway is known to play a role in both excitatory and inhibitory regulation of micturition [5, 8, 9]. Central dopaminergic pathways also have dual excitatory and inhibitory influences on reflex bladder activity [10, 11]. It has been demonstrated that in the rat cerebral infarction model, bladder overractivity is mediated by NMDA glutamatergic and D2 dopaminergic excitatory mechanisms [7], suggesting that cerebral infarction may alter a balance between the facilitatory and inhibitory mechanism that results in upregulation of an excitatory pathway and downregulation of a tonic inhibitory pathway. Similarly, neuropharmacological studies in a monkey model for Parkinson's disease have shown that detrusor overactivity may result from a loss of dopaminergic inhibition mediated by D1 receptors [12, 13].

2. Spinal cord lesions (Figure 2)

A spinal cord lesion above the lumbosacral level eliminates voluntary and supraspinal control of micturition, leading to bladder overactivity mediated by spinal reflex pathways [14, 15]. Disruption below the level of the pons leads to unsustained and uncoordinated detrusor contractions often associated with uncoordinated sphincter overactivity (detrusor-sphincter dyssynergia, DSD). Impairement or loss of bladder sensation is a typical feature.

Electrophysiologic studies of the effect of capsaicin on voiding reflexes have shown that the afferent limb of the micturition reflex in chronic spinal cats,consists of unmyelinated C-fiber afferents, whereas in normal cats it consisits of myelinated A- d afferents [14, 16, 17]. Since C-fiber bladder afferents in the cat usually do not respond to bladder distension [18], a considerable reorganization of reflex connections takes place in the spinal cord following the interruption of descending pathways from the brain. In humans with spinal cord lesions, neurogenic detrusor overactivity is likely to be mediated by capsaicin-sensitive C-fiber afferents. Clinical experience with capsaicin supports the role of these C-fiber afferents in the pathophysiology of neurogenic bladder overactivity. Capsaicin has been used for the treatment of neurogenic bladder overactivity in patients with spinal cord injury or multiple sclerosis. When administered intravesically, capsaicin increases bladder capacity, reduces micturition contraction pressure, decreases autonomic dysre-

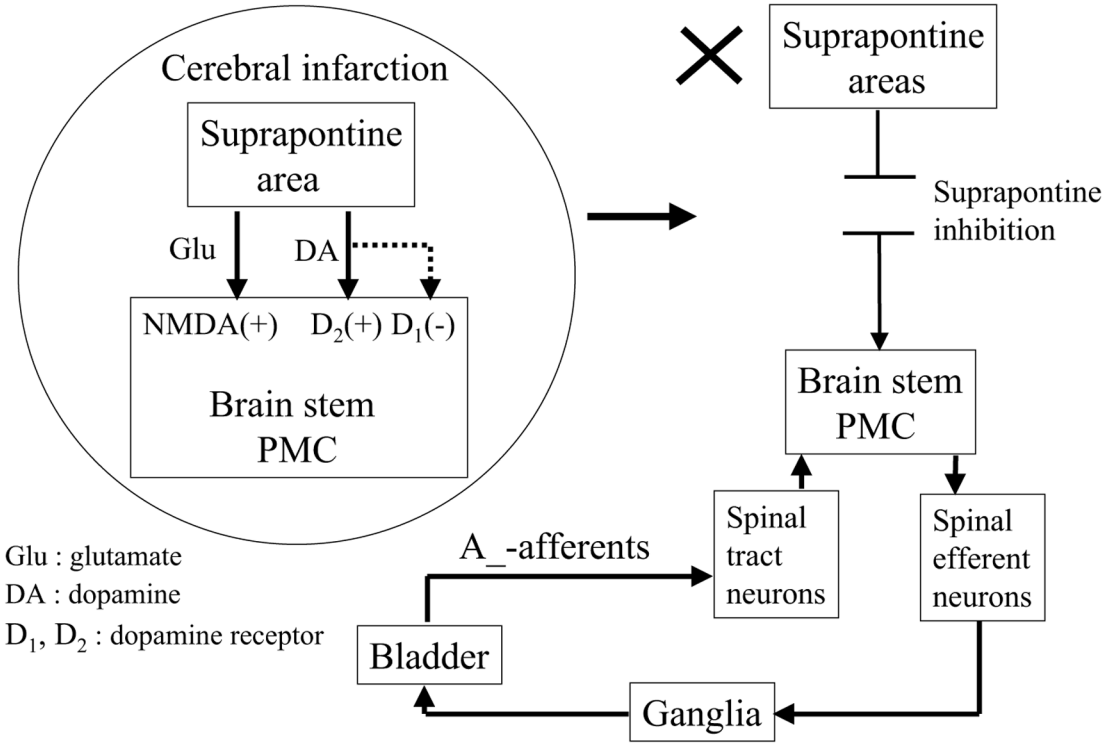


Figure 1. Suprapontine lesions causing detrusor overactivity

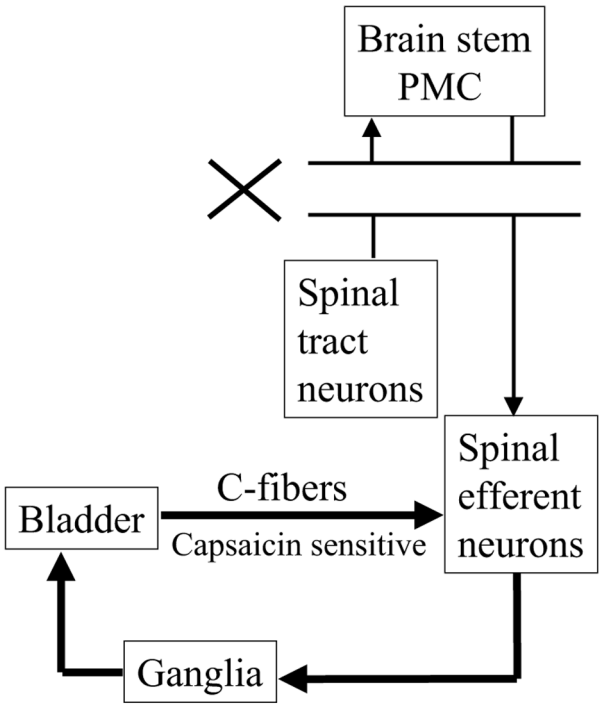


Figure 2. Spinal cord lesions causing detrusor overactivity

flexia and reduces the frequency of incontinence [19-21]. More recently, resineferatoxin, an ultra-potent analogue of capsaicin, has also used [22, 23].

In addition to changes in reflex pathways(i.e, C-fiber afferent-mediated micturition reflex), it has been demonstrated that a functional outlet obstruction resulting from DSD may alter the properties of bladder afferent neurons. For example, in chronic spinal animals, afferent neurons innervating the bladder increase in size, a change prevented by urinary diversion[24]. These observation suggest that some factors released in the obstructed bladder may be responsible for the neural change. Subsequently, the factors have been identified as nerve growth factor (NGF) [25].

Another type of plasticity in C-fiber bladder afferent neurons is evident as a change in excitability. Whole cell-patch clamp recordings have shown that hypertrophied bladder afferent neurons exhibit increased excitability due to a shift in expression of sodium channels from high-threshold tetrodotoxin(TTX)-resistant to low-threshold TTX-sensitive channels [26, 27]. In normal animals, TTX-resistant sodium channels are mainly expressed in C-fiber afferent neurons[28, 29].

III. NON-NEUROGENIC DETRUSOR OVERACTIVITY

1. Outflow obstruction (Figure 3)

Detrusor overactivity associated with outflow obstruction has long been recognized[30]. Sixty percent of patients with benign prostatic obstruction(BPO), exhibit this on filling cystometry. Following transurethral prostatectomy(TURP), the involuntary contractions disappear in two-thirds.

The hypothesis that denervation underlies obstructed non-neurogenic detrusor overactivity comes from the morphological studies of Gosling et al [31]. They demonstrated a reduction in acetylcholine esterase (AChe)staining nerves in obstructed human bladder muscle. Pharmacological studies performed on detrusor biopsies from patients with bladder outlet obstruction[32] have shown that muscle strips from patients with detrusor overactivity exhibit denervation supersensitivity to acetylcholine (the main excitatory neurotransmitter to the human bladder) and a reduction in nerve-mediated responses, as compared with strips from normal, stable bladder. Similar pharmacological and morphological evidences of denervation have been shown in studies using animal models of detrusor overactivity caused by urethral obstruction [33-35], demonstrating that there were significant increases in sensitivity to acetylcholine and other agonists such as high potassium, and the response to intramural nerve stimulation was significantly reduced (despite increased responsiveness of the muscle to exogenous acetylcholine), with both cholinergic and non-cholinergic(purinergic) neurotransmission being affected. These changes suggests a post-junctional supersensitivity secondary to partial denervation of the obstructed detrusor muscle, and may be the basis of unstable bladder behavior.

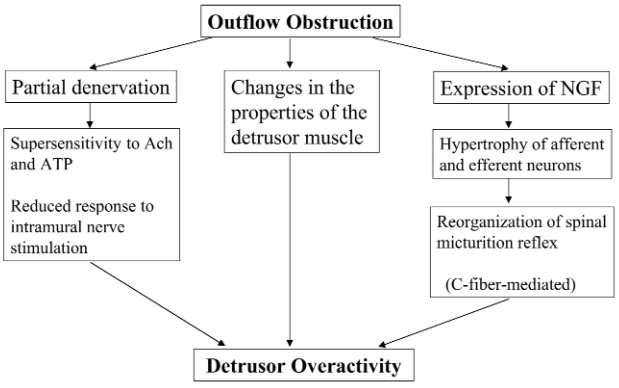


Figure 3. Outflow obstruction causing detrusor overactivity

However, it is not clear how denervation develops in outflow obstruction. One possibility is that there is a reduction of blood flow due to the effect of raised intravesical pressure during voiding or the increased tissue pressure of hypertorophied bladder wall during filling. Such hemodynamic change has been demonstrated in a canine model of outlet obstruction [36]. Thus, the role of ischemia in changes in bladder function and structure following outlet obstruction has been well characterized. A more recent study using iNOS knockout mice [37] suggests that generation of NO soon after obstruction is necessary to prevent detrusor dysfunction, since NO produces vasodilation and decreases platelet aggregation.

Obstruction can alter the properties of the detrusor muscle. In the obstructed guinea pig bladder, the detrusor muscle shows a decrease in force development, suggesting a deterioration in detrusor contractility [38]. The cable properties of detrusor cells are also changed [39]. The length constant is reduced, suggesting a decrease in cell to cell propagation of electrical activity. The time constant of the cell membrane is prolonged, leading to greater instability of membrane potential. This may facilitate depolarization of the the cell and activate L-type calcium channels. Such a mechanism could be further amplified by depolarizing currents supplied by a purinergic system, which has been shown to emerge in human obstructed bladder [40]. These findings suggest that, in general, individual cells are more irritable while synchronous activation is damaged, findings that are consistent with the abnormal bladder behavior of obstructed bladder, i.e., the decreased contractility coexisting with bladder overactivity.

A different interpretation for the mechanism underlying the development of detrusor overactivity is a possible reorganization of spinal micturition reflexes following outlet obstruction. Partial urethral ligation in a rat model results in hypertrophy of bladder afferent as well ass efferent neurons [41, 42]. This hypertrophy of bladder neurons is accompanied by increased expression of NGF in the bladder as well as in sacral autonomic centers[25], leading to facilitation of the spinal micturition reflex [41, 42]. Similarly, in patients with outflow obstruction, a spinal reflex may be responsible for the development of detrusor overactivity. This reflex is thought to be mediated by C-fibers and clinically detected as a positive response to the ice water test. C-fiber neurons are also known to contain tachykinin and other peptides as

neurotransmitters. It has been suggested that in rats with bladder outlet obstruction, tachykinins can influence via NK receptors both the spinal and supraspinal control of the bladder [43, 44].

2. Aging

Although the International Prostate Symptom Score (IPSS) questionnaire was developed to asses voiding dysfunction associated with prostatic enlargement, the questions deal mostly with voiding symptoms, and are not specific for outlet obstruction. When the IPSS questionnaire has been administerd to women as well as men,the scores of older men are similar to that of older women.[45]. This suggests that lower urinary tract symptoms (LUTS) may be a similar sign of aging in both men and women. The prevalence of urgency syndromes, in particular, increases with age, independent of the presence of outflow obstruction or neurogenic disorder. A study of incontinent institutionalized elderly revealed that approximately 61% of the women and 59% of the men (without obstruction) had detrusor overactivity [46]. However, in the elderly, the boundaries between neurogenic and non-neurogenic are uncertain, since age-associated neurogenic diseases such as subclinical cerebrovascular disorders, autonomic neuropathy and chronic brain failure commonly occur. Computerized tomography, magnetic resonance imaging or SPECT sometimes can detect the presence of cerebral lesions in elderly patients with detrusor overactivity [47, 48]. This may distinguish neurogenic from idiopathic deturusor overactivity in a considerable number of older patient

With regard to aging-related detrusor overactivity, Elbadawi et al. have proposed a possible explanation based on detailed ultrastructural study[49-51]. Electron microscopy of detrusor biopsies have revealed a characteristic structural pattern in specimens from the elderly with this detrusor overactivity. The main ultrastructural features of this dysfunctional pattern were abundant distinctive protrusion junctions and abutments which were proposed to mediate electrical coupling between the muscle cells and to be involved in generation of myogenic contraction in the overactive bladder. In addition, if the patients had impaired detrusor contractility, there was superimposed widespread degeneration of muscle cells and nerve axons, which matched the special group of elderly patients with DHIC (detrusor hyperactivity with impaired contractility) [52].

Age-dependent alterations in detrusor function also have been evaluated. Cystometry of conscious rats shows that bladder compliance decreases with aging [53]. In the rat detrusor muscle, the relaxant response to noradrenalin or isoproterenol has been shown to decrease with age, a change which may be related to decreased density of a -adrenoceptors and decreased cyclic adenosine monophosphate (cAMP) production [54]. In addition, age-related changes in cholinergic and purinergic neurotransmission have been studied recently in human detrusor muscle, showing that during electrical nerve stimulation, acetylcholine (Ach) release is decreased while ATP release is increased with aging [55, 56]. These changes in neurotransmission may contribute to the changes in bladder function in the elderly.

3. Pelvic floor disorders

Detrusor overactivity is known to be associated with female stress urinary incontinence as a result of pelvic floor relaxation. After surgical correction, this disappears in approximately two-thirds of these patients [57]. This may suggest that afferent nerve activity from pelvic floor and urethra is involved in detrusor inhibition during bladder filling. Thus, the decreased afferents due to pelvic floor deficiency can lead to involuntary detrusor contraction. External and direct pudendal nerve electrical stimulation shows good clinical results in the treatment of the overactive bladder [58, 59], thereby supporting this hypothesis.

The relationship of urethral distention or perfusion in the genesis of bladder overactivety was considered in a series of experiments performed between 1914 and 1941 by Barrington.

4. Idopathic detrusor overactivity

The diagnosis of idiopathic detrusor overactivity requires the exclusion of all known causes, but this should include all situations where etiology is unknown. Thus, the term is used to apply to a wide range of different conditions that may have a common final pathophysiologic pathway[60]. The following mechanisms are considered to be involved in the pathophysiology of idiopathic detrusor overactivity.

5. Sensory afferent activation (Figure 4)

Neuropeptide-containing sensory nerves have been found innervating the human bladder [61]. These sensory afferents are capsaicin-sensitive, unmyelinated C-fibers. They usually transmit sensation of bladder fullness, urgency and pain. Local release of tachykinins(substance P, CGRP) and other peptides

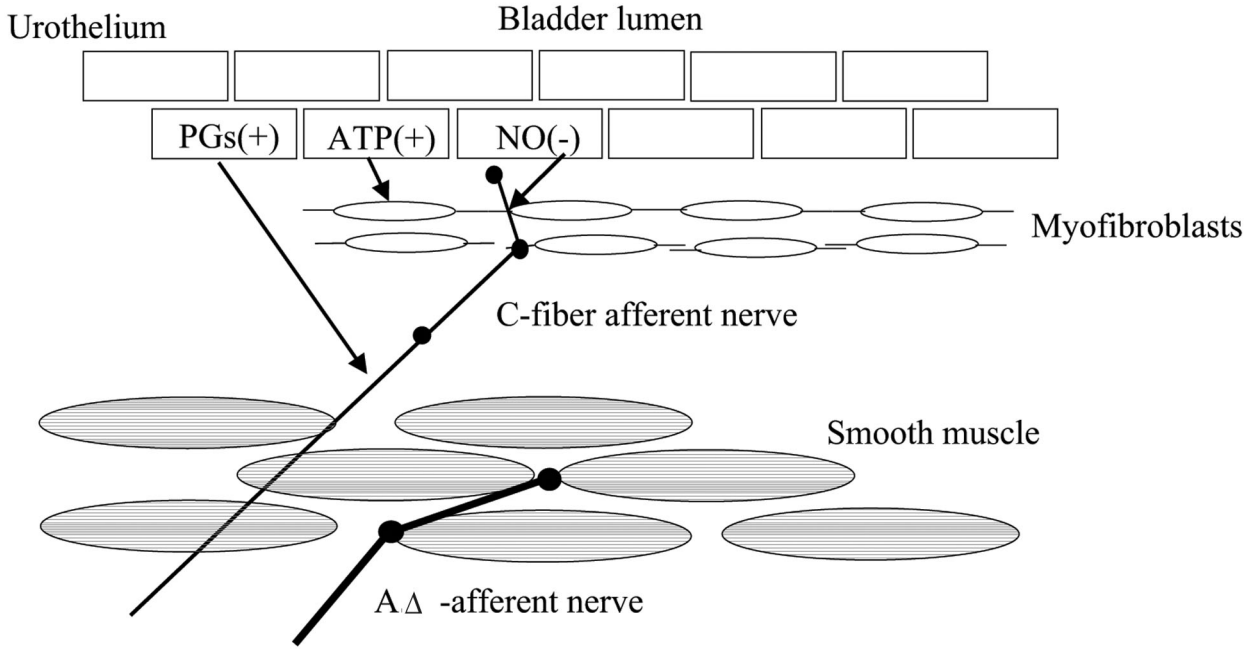


Figure 4. Afferent activation mechanism

from these sensory nerves in the bladder wall may produce diverse biological effects, such as detrusor muscle contraction, facilitation of neural transmission and increased vascular permeability [61].

Recently, a role of the urothelium in afferent activation has becomes the focus of intense interest. The C-fiber afferents generally have endings in the suburothelial layer of the bladder wall, but in some cases, they also penetrate the urothelium [61, 62]. Ferguson et al [63] demonstrated that ATP was released from the urothelium by bladder distension. In addition, ATP receptors(P2X3) are expressed on sensory afferent nerves [64, 65]. Thus, bladder filling causes a release of ATP from the urothelium, and ATP, in turn, can activate P2X3 receptors on afferent nerve terminals to evoke a neural discharge. Supporting this view, P2X3-deficient mice exhibite marked bladder hyporeflexia, associated with decreased voiding frequency and increased bladder capacity [66, 67].

In human the bladder, this sensory process seems to be more complex than originally thought. In studies of human bladder [68], P2X3 receptors could not be seen to co-localize exclusively with sensory nerve fibers containing calcitonin gene-related peptide (CGRP), whereas $P2X_3$ receptor immunoreactivity was found near myofibroblasts(so-called interstitial cells). Moreover, these myofibroblasts make close appositions with C-fiber nerve endings[69]. Thus, their contractile phenotype and intimate association with nerve suggest that myofibroblasts may respond to ATP and mechanically alter afferent nerve function[70].

In addition to ATP, prostanoids and nitric oxide(NO) are synthesized locally in both mucosa and muscle, and they are also released by bladder distension [71-74]. It is most likely that a cascade of stimulatory(eg.ATP, prostanoids, tachykinins) and inhibitory (eg.NO) mediators are involved in the transduction mechanisms underlying the activation of sensory afferent fibers during bladder filling [75].

This urothelial afferent transduction process suggests that up-regulation of the afferent activation mechanisms(eg. an increased generation/release of ATP, increased sensitivity of afferent nerves to mediators, increased number of afferent nerves) can induce detrusor overactivity, causing the symptoms of OAB. Smet et al [76] have shown that the density of nerve fibers immunoactive for substance P and CGRP was significantly higher in women with idiopathic detrusor overactivity than in normal age-matched women.

Furthermore, intravesical vanilloids (capsaicin and resineferatoxin) have been shown to improve OAB symptoms in patients with idiopathic detrusor overactivity as well as with hypersensitivity disorders [77-79]. These results may support the above hypothesis, but information on bladder sensory mechanisms is still limited.

6. Myogenic basis

Brading and Turner [80, 81] have emphasized that myogenic changes(regardless of etiology) may contribute to the pathophysiology of idiopathic detrusor overactivity. On the basis of observation that denervation is consistently found in detrusor biopsy specimen from patients with various forms of non-neurogenic detrusor overactivity [82], they have proposed that partial denervation of the detrusor may alter the properties of smooth muscle, leading to increased excitability and increased coupling between cells. Thus, local contraction(activity) that occurs somewhere in the detrusor will spread throughout the bladder wall, resulting in coordinated myogenic contraction of the whole bladder. However, recent electrophysiological studies [83] have shown that gap junction coupling is reduced rather than increased in detrusor muscle from patients with detrusor overactivity, suggesting the opposite effect on intercellular communication. Thus, it remains to be seen whether local activity spreads throughout the bladder wall. Regardless, as Brading has stated[80], the changes in smooth muscle properties seem to be a necessary prerequisite for the production of involuntary detrusor contraction.

7. Acethylcholine(Ach) release

It is clear from a clinical point of view that in patients with idiopathic detrusor overactivity, antimuscarinic drugs can improve symptoms, reduce urgency and increase bladder capacity. This suggests that in these patients, these is Ach release during bladder filling, leading to an increase in detrusor tone or involuntary bladder contraction.

Recently, using microdialysis technique, Yoshida et al. [84] found that there is a basal Ach release in human detrusor muscle. This release of Ach increased when bladder strips were stretched. They also showed that the released Ach is of non-neuronal origin, and, at least partly, is generated by the urothelium. In addition, Yossepowitch et al. [85] inhibited Ach breakdown with a cholinesterase inhibitor in a series of patients with LUTS. They found significant changes in bladder sensation, a decrease in bladder capacity, and an induction or amplification of involuntary detrusor contractions in 78% of the patients with the symptoms of OAB, but in none with no specific complaints suggesting the OAB. Such an effect requires Ach release during bladder filling.

Thus, it has been suggested that, during the storage phase, ACh may be released from a non-neuronal source(possibly the urothelium), or from postganglionic cholinergic neurons that may be activated by increased afferent activity via reflex pathways in the pathologic condition. Such a release of Ach can enhance the myogenic contractile activity of the detrusor, which seems to be a trigger stimulation for inducing an involuntary contraction, as postulated in the myogenic theory of detrusor overactivity.

It is assumed that all these mechanisms described above may contribute in concert to the pathophysiology of idiopathic detrusor overactivity (**Figure 5**).

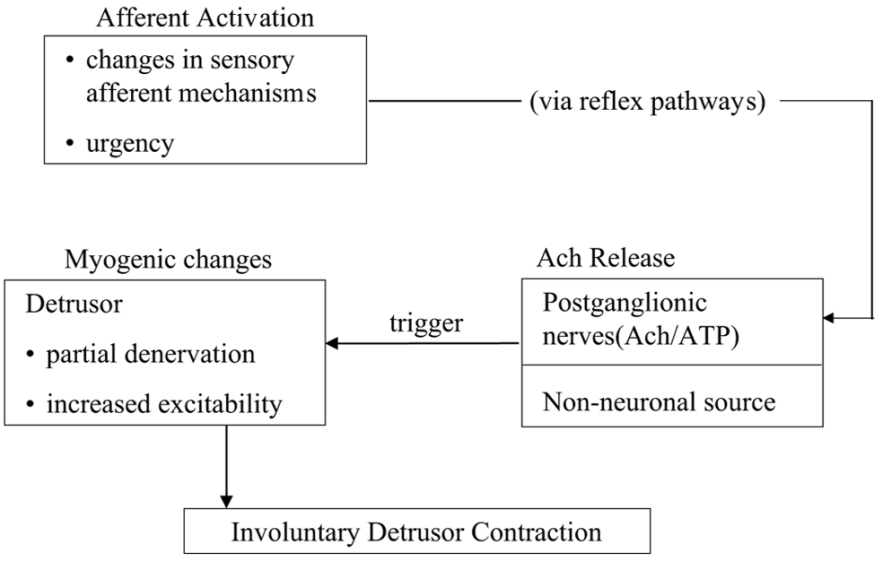


Figure 5. Idiopathic causes for detrusor activity

B. PREGNANCY, CHILDBIRTH AND THE PELVIC FLOOR

Reduction in both perinatal and maternal mortality rates in recent decades has focused increasing attention on maternal morbidity and the long-term sequelae of childbirth. Antenatal education encourages expectant mothers to anticipate normal vaginal delivery, leading to an early restoration of normal pelvic function after the performance of routine pelvic floor exercises. Not least because of improved investigative techniques available during the past decade, the incidence and mechanisms of obstetric injury to the pelvic floor have come under scrutiny. A survey of female British obstetricians [86] revealed that one third indicated a personal preference for elective caesarean delivery of their own hypothetical uncomplicated singleton pregnancy; a general fear of pelvic floor trauma was cited as the most common reason for this choice. Despite being based on incomplete prognostic data, this sentiment may be echoed increasingly among obstetric patients and may lead to an unselective, and even misguided, increase in caesarean delivery rates.

Epidemiological studies have reported prevalence of stress incontinence ranging from 23 to 67 percent during pregnancy and 6 to 29 percent after childbirth, but little is known about how the condition affects women at this time. However, the prevalence of urinary incontinence may be nearly the same 8 weeks postpartum as during pregnancy.

It is important that contributory obstetric factors are identified and their occurrence minimized. Vaginal birth has been recognized as being potentially traumatic to the pelvic floor. Women who have sustained significant anal sphincter injury are at greater risk of further damage of fecal incontinence with subsequent deliveries.

I. EFFECTS OF PREGNANCY ON PELVIC FLOOR FUNCTION

In spite of the great advances that have been made in many areas of obstetric care, ignorance still persists regarding the fundamental physiological facts about the impact of pregnancy and delivery on lower urinary tract function. There is a striking dearth of prospective studies regarding the relationship of pregnancy and delivery to the problem of urinary incontinence among women. Further research may reveal that stress incontinence in women is related, at least in part, to the pregnant state itself, rather than to trauma sustained at delivery. If true, this has significant implications for subsequent research efforts investigating the etiology of female urinary incontinence.

Cutner and Cardozo have summarized the few papers that do exist as follows [87]: “Lower urinary tract symptoms are so common in early pregnancy that they are considered normal. Their progression throughout the antepartum period and their resolution postpartum has been documented by several authors. However, the data are confusing and the underlying causes remain uncertain. The effects of normal pregnancy on the physiology of the lower urinary tract remain largely not investigated, in spite of the common pronouncements on this subject in the obstetrical literature. [88-91].”

It is commonly assumed that stress incontinence develops (at least in part) as the result of delivery trauma to the pelvic floor. However, several researchers have documented that many young nulliparous women suffer from occasional stress incontinence which is a significant clinical problem in as many as 5 % [92-94]. In a study of the relationship of pregnancy to stress inconti nence, Francis [88] found that 40 % of primigravid women had a history of occasional stress incontinence before becoming pregnant, and that if such a history was present their stress incontinence invariably became worse during pregnancy. If incontinence developed during pregnancy, it tended to disappear after the puerperium, but recurred with subsequent pregnancies and became progressively worse, eventually becoming a clinical problem when these women were no longer pregnant. Francis concluded that in women who deve lop stress incontinence in middle life, pregnancy itself, rather than parturition, revealed the defect and made it worse. Similar conclusions have been reached by other researchers [95-97]. The prevalence of persistent stress urinary incontinence is reported to be significant ly higher in grand multiparae compared with nulliparae[98].

II. PATHOPHYSIOLOGIC MECHANISMS OF BIRTH INJURY TO THE PELVIC FLOOR

Vaginal delivery, notably the first, is strongly associated with later surgery for stress incontinence, but the asso ciation is modified by maternal conditions

and inter ventions during delivery. Vaginal delivery may initiate damage to the continence mechanism by direct injury to the pelvic floor muscles, damage to their motor inner vation, or both. Additional denervation may occur with aging, resulting in a functional disability many years after the initial trauma. Physical and emotional health problems are common after childbirth, and are fre quently not reported to health professionals despite the fact that many women would like more advice and assistance in dealing with them.

There would seem to exist four major mechanisms by which childbirth (vaginal delivery) might contribute to the increased risk of urinary incontinence among women:

1. injury to connective tissue supports by the mechanical process of vaginal delivery, especial instrumental vaginal delivery (forceps > ventouse delivery) (**Figure 6**);
2. vascular damage to the pelvic structures as the result of compression by the presenting part of the fetus during labor;
3. damage to the pelvic nerves and/or muscles as the result of trauma during parturition;
4. direct injury to the urinary tract during labor and delivery. The physiolgic changes produced by pregnancy may make pregnant women more susceptible to injury from these pathophysiological processes (**Figure 7**).

Vaginal delivery causes partial denervation of the pel vic floor (with consequent re-innervation) in most women having their first baby. Pelvic floor muscle strength is impaired shortly after vaginal birth, but for most women returns within two months. In a few this is severe and is associated with urinary and fecal inconti nence. For some it is likely to be the first step along a path leading to prolapse and/or stress incontinence [99]. There is a growing body of evidence that multi parity, forceps delivery, increased duration of the second stage of labor, partially due to epudiral anaesthesia, third degree perineal tear and high birth weight (> 4000 g) are important factors leading to pudendal nerve damage [100-103].

Peschers et al showed that pelvic floor muscle strength is significantly reduced three to eight days postpartum in women following vaginal birth but not in women after caesarean delivery. Six to ten weeks later palpa tion and vesical neck elevation on perineal ultrasound do not show any significant differences to antepartum values, while intravaginal pressure on perineometry remains significantly lower in primiparae, but not in multiparae. Pelvic floor muscle strength is impaired shortly after vaginal birth, but for most women returns within two months [104].

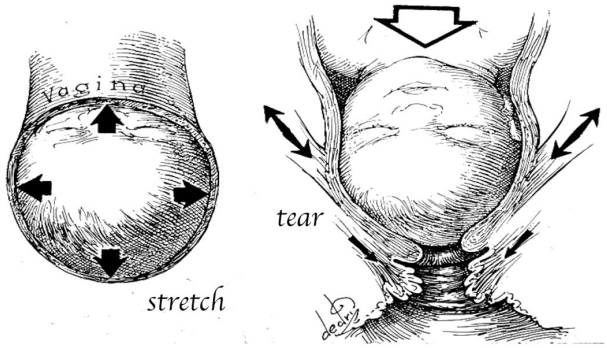


Figure 6. Labor stretches and tears vaginal wall. From: Randall and Nichols, Vaginal Surgery, 1989, Williams and Wilkins. [189]

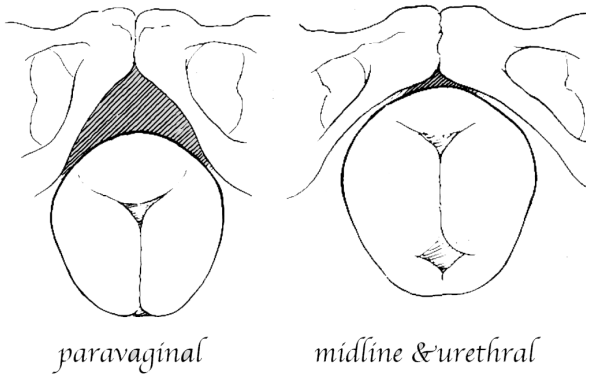


Figure 7. Urethra and vagina are compressed during labor. The pubic angle can affect the structures that are compressed. From: Randal and Nichols, Vaginal Surgery, 1989, Williams and Wilkins. [189]

There also is EMG evidence of re-innervation in the pelvic floor muscles after vaginal delivery in 80%. Main ly women who have a long active second stage of labor and heavier babies show the most EMG evidence of nerve damage. An elevation in perineal body position as well as a decrease in the area of the urogenital hiatus and of the levator hiatus at two weeks postpartum sug gests a return of normal levator ani geometry after vaginal delivery in most patients [105].

The pudendal nerve terminal motor latency (PNTML) measured 48-72 h after delivery is increased in women delivered vaginally compared to nulli-

parous control subjects. Multiparity, forceps delivery, increased dura tion of the second stage of labor, third degree perineal tear and high birth weight are important factors leading to pudendal nerve damage [100]. Compared with spon taneous vaginal births, women having forceps or ven touse extraction have increased odds for perineal pain, sexual problems, and urinary incontinence [101]. Vagi nal delivery, notably the first, is strongly associated with later surgery for stress incontinence, but the asso ciation is modified by maternal conditions and inter ventions during delivery [106]. Women with three or more birth deliveries were more likely to have inconti nence and excessive pelvic floor descent [106]. There is no evidence to suggest that at five years after delivery use of the ventouse or forceps has specific maternal benefits or side effects [107]. Meyer et al. found that, after spontaneous and instrumental deliveries, 21% and 34% of women complained of stress urinary inconti nence and 5.5% and 4% reported fecal incontinence, respectively. Substantial bladder neck hypermobility was present together with diminished functional ure thral length and intravaginal and intra-anal pressures. Only 22% of patients with stress urinary incontinence during pregnancy had such incontinence after delivery [108]. Women with postpartum urinary stress inconti nence have significantly greater antenatal bladder neck mobility than those women who were continent post partum [109].

III. EPIDURAL ANALGESIA DURING LABOUR

Regional anaesthesia for the relief of labor pain has become more popular during the past 20 years. Despite interest in its possible obstetric consequences, little attention has been paid to its potential effects on the pelvic floor and perineal injury. The available published data describe conflicting results. Some studies suggest that epidural analgesia, by enabling relaxation of the pelvic floor, leads to greater control of delivery of the fetal head and consequently fewer perineal lacerations [110], but prolongation of the second stage may also increase the incidence of pudendal nerve damage [103, 111]. Robinson et al. [112]recently examined the relation ship between epidural analgesia and perineal damage, and found that the rate of significant perineal injury was higher with epidural analgesia (16,1 % compared with increased use of operative intervention.) Episiotomy and instrumental delivery were responsible for this dif ference. Such an association may partly explain why institutions are reporting increased rates of significant perineal injury, paralleling local increases in epidural usage [106].

1. Role of episiotomy

Episiotomy is a widely performed intervention in child birth, despite equivocal scientific evidence regarding its benefit. It is one of the few surgical procedures perfor med without the patients consent and is the most com monly performed surgical procedure in the United States. There is a widespread assumption that it may do more harm than good [106, 112]. Restrictive episiotomy policies appear to have a number of benefits com pared to routine episiotomy policies.

Proponents of routine episiotomy claim that it avoids spontaneous uncontrolled tears and long _term relaxa tion of the pelvic floor, but these advantages are diffi cult to substantiate. There is no evidence that either first or second-degree perineal tears cause long-term consequences [89], so any argument that episiotomy prevents such spontaneous tears is inconsequential. A growing body of evidence suggests that episiotomy offers no protection against third and forth-degree tears, which are associated with adverse sequelae. A recent overview by Myers-Helfgott and Helfgott emphasized the absence of scientific evidence to sup port a role for liberal elective episiotomy in the reduc tion of third-degree lacerations during childbirth [90]. Indeed, several reports have implicated routine episio tomy in the genesis of major perineal and anal sphinc ter tears, even after controlling for confounding variables [91-93, 113]. In particular, midline episiotomy is associated with significantly higher rates of third and fourth-degree perineal tears than are mediolateral episiotomies [95-97]. Midline episioto my is not effective in protecting the perineum and sphincters during childbirth and may impair anal conti nence [114]. Coats et al., in a randomized controlled trial of 407 women, found that with midline episiotomy, 11,6 % of patients experienced lacerations of the anal canal versus 2 % who experienced these complications in association with mediolateral episio tomies. This association is compounded when instru mental delivery is employed, with anal sphincter injury rates of 50 % reported with the use of midline episioto my and forceps [115]. In spite of these data, midline episiotomy is still bewilderingly widespread, presuma bly because it is perceived to heal better and cause less postnatal discomfort.

Restrictive episiotomy policies appear to have a num ber of benefits compared to routine episiotomy policies. There is less posterior perineal trauma, less suturing and fewer complications, no difference for most pain measures and severe vaginal or perineal trauma, although there was an increased risk of anterior perineal trauma with restrictive episiotomy [116, 117].

Women who have episiotomies have a higher risk of fecal incontinence at three and six months postpartum compared with women with an intact perineum. Com pared with women with a spontaneous laceration, epi siotomy triples the risk of fecal incontinence at three months and six months postpartum, and doubles the risk of flatus incontinence at three months and six months postpartum. A non-extending episiotomy (that is, second degree surgical incision) triples the risk of fecal inconti nence and doubles the risk of flatus incontinence post partum compared with women who have a second degree spontaneous tear. The effect of episiotomy is independent of maternal age, infant birth weight, dura tion of second stage of labor, use of obstetric instrumen tation during delivery, and complications of labor. The refore, midline episiotomy is not effective in protecting the perineum and sphincters during childbirth and may impair anal continence and should be restricted to speci fied fetal-maternal indications [114, 118-121].

2. Pelvic floor muscle exercise

Practice of pelvic muscle exercise by primiparas results in fewer urinary incontinence symptoms during late pregnancy and postpartum [122]. The benefits from pelvic floor muscle training are still present one year after delivery [123].

In a prospective matched controlled trial Morkved and Bo evaluated the long term effect of a postpartum pel vic floor muscle training course in the prevention and treatment of urinary incontinence. All women partici pated in a matched controlled study evaluating the effect of an eight-week pelvic floor muscle training program in the prevention and treatment of urinary incontinence in the immediate postpartum period and one year after delivery. Registration of continence sta tus was assessed by structured interview and a standar dized pad test. At the one year follow up, significantly more women in the control group than in the training group reported stress urinary incontinence and/or sho wed urinary leakage at the pad test. These investigators concluded that a specially designed postpartum pelvic floor muscle training course was effective in the pre vention and treatment of stress urinary incontinence.

The benefits from pelvic floor muscle training are still present one year after delivery [123]. Sampselle et al demonstrated that practice of pelvic muscle exercise by primiparas results in fewer urinary incontinence symp toms during late pregnancy and postpartum [122][146]. Miller determined the characteristics of women in whom pelvic floor electrical stimulation will reduce stress uri nary incontinence. They used electrical stimulation for 15 minutes twice daily or every other day for 20 weeks. At the end of 20 weeks, those with a 50% reduction in leakage episodes on voiding diary (responders) were compared with those who did not show a 50% reduc tion (non-responders). Significant subjective and objective improvements were noted among responders by 10 and 14 weeks, respectively. Compliance was higher in responders during weeks 12-15 of the study. It was concluded that a minimum of 14 weeks of pelvic floor stimulation was necessary before significant objective improvements were seen [124].

3. Perineal trauma

Awareness of perineal damage after vaginal delivery has increased in recent years, due in part to better understanding of its consequences, improved methods for accurate neurophysiological evaluation and accu mulation of data on prognosis. Fecal incontinence represents a distressing social handicap, and vaginal delivery is now recognized as its principal cause [125]. Obstetricians should have an awareness of the causes, symptoms, appropriate investigation and treatment options available for this complication of childbirth. Limiting episiotomy can be strongly recommended. In the absence of strong data to the contrary, women should be encouraged to engage in perineal massage if they wish and to adopt the birth positions of their choi ce. Factors shown to increase perineal integrity include avoiding episiotomy, spontaneous or vacuum-assisted rather than forceps birth, and in nulliparas, perineal massage during the weeks before childbirth. Second stage position has little effect [126]. Further informa tion on techniques to protect the perineum during spon taneous delivery is badly needed. Wherever possible, women with postpartum fecal incontinence should be assessed in a specialized clinic, which has developed a close liaison with physiotherapy, dietetic and colorectal surgical advisers.

Episiotomy, forceps use, and birth weight are important predictors of third and fourth-degree tears.

However, determinants of sulcus tears appear to be present befo re pregnancy. Third and fourth-degree tears are related to physician management. Exercise mitigates the poten tial for severe trauma induced by episiotomy [127].

Eason et al. have systematically reviewed techniques proposed to prevent perineal trauma during childbirth and performed a meta-analysis of the evidence gathered from randomized controlled trials regarding their effi cacy. The conclusion was that avoiding episiotomy decreased perineal trauma (absolute risk difference 0.23, 95% confidence interval (CI] -0.35, -0.11). In nul liparas, perineal massage during the weeks before giving birth also protected against perineal trauma (risk difference -0.08, CI -0.12, -0.04). Vacuum extraction (risk difference -0.06, CI -0.10, -0.02) and spontaneous birth (-0.11, 95% CI -0.18, -0.04) caused less anal sphincter trauma than forceps delivery. The mothers position during the second stage had little influence on perineal trauma (supported upright versus recumbent: risk difference 0.02, 95% CI -0.05, 0.09). Factors shown to increase perineal integrity include avoiding episiotomy, spontaneous or vacuum-assisted rather than forceps birth, and in nulliparas, perineal massage during the weeks before childbirth. Second-stage posi tion has little effect. Further information on techniques to protect the perineum during spontaneous delivery is sorely needed [128].

C. PATHOPHYSIOLOGY OF SUI IN WOMEN: URETHRAL STRUCTURE, SUPPORT AND FUNCTION

The factors necessary for the urethra to remain closed at rest and during increased abdominal pressure have been well characterized, but their functional inter-relationships are still not fully understood. These factors include: 1) healthy, functioning striated sphincter controlled by pudendal innervation, 2) well vascularized urethral mucosa and sub- mucosa, 3) properly aligned and functioning intrinsic urethral smooth muscle, and 4) intact vaginal wall support.

I. THE FEMALE UROGENITAL DIAPHRAGM: URETHRAL SPHINCTER LOCATION

Detailed descriptions of the urogenital diaphragm have been made by Max Brodel working with Howard Kelly[129], Oelrich [130] and further expanded by DeLancey [131]. These reports have provided clear descriptions of the urethral rhabdosphincter. The proximal one-third of the urethra is shown surrounded by a sleeve of striated muscle continuous with a longer ascending cone which extends to the vaginal introitus. Manometric and electrophysiological recordings from this proximal one-third of the urethra have shown that it generates the highest level of resting pressure and electromyographic activity (**Figure 8**).

This portion of the urethra is an intra-pelvic structure located immediately posterior to the pubic bone. In the past, much has been made of the loss of this intra-pelvic position in stress incontinence. It had been suggested that when the urethra descended away from its intra-abdominal position, intra-abdominal forces no longer constricted it during straining. This concept has survived and been modified into the "hammock hypothesis" [132]which suggests that the posterior position of the vagina provides a backboard against which increasing intra-abdominal forces compress the urethra. Data supporting this hypothesis are drawn from urethral pressure transmission studies showing that continent patients experience an increase in intra-urethral pressures during coughing. This pressure increase is lost in stress incontinence and may be restored following successful operations designed to stabilize or elevate the sub-urethral vaginal wall [133-142].

The urethra is supported posteriorly and inferiorly by the anterior vaginal wall. The superior vaginal sulcus, most clearly found in nullipara, exists at this junction of the lower and middle third of the vaginal wall. This point represents the two lateral insertion points of the vaginal " hammock." Portions of the pubococcygeus muscle attach to these to sulci within the pelvis and can produce elevation during voluntary contraction.

Immediately anterior to the proximal urethra are found the reflections of the endopelvic fascia. The most prominent of these, the pubo-urethral ligaments, are sufficiently condensed to form distinct and recognizable ligaments on either side of the pubis. Although these structures form one continuous complex, they are distinguished by their names, as posterior and anterior pubo-urethral ligaments. The posterior pubo-urethral ligaments, which can be seen at the time of retropubic surgery, are the more familiar of these. These are strong fascial condensations which most likely maintain their characteristics throughout life. Previous investigators,

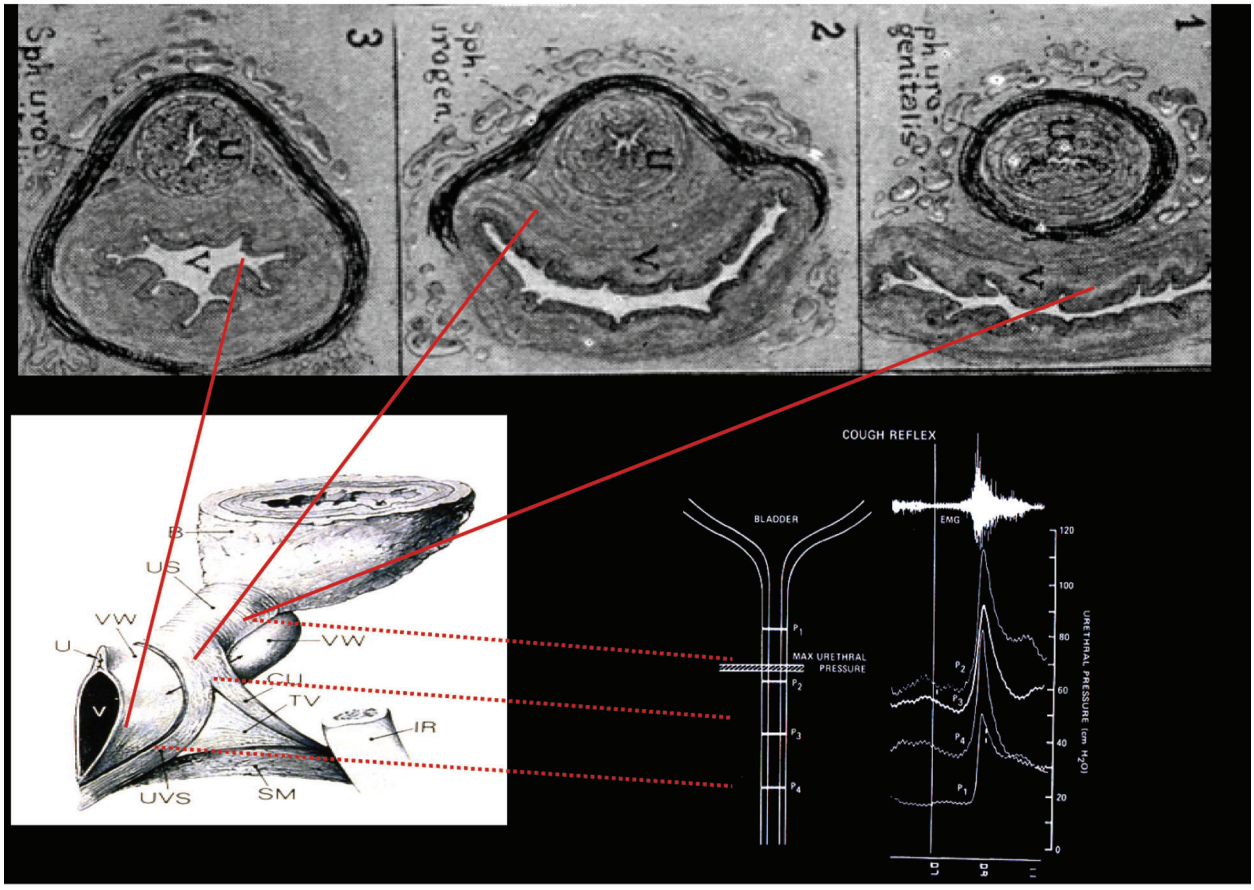


Figure 8. The high pressure zone of the urethra is also the area of greatest electromyographic activity, and is also the region that is surrounded by striated muscle from the urogenital diaphragm. Composite diagram from Oelrich [130]; Kelly & Burnam [554]

however, have suggested that elongation of these structures may be responsible for the loss of urethral support seen in stress incontinence.

While the lower one-third of the vagina is oriented more vertically in the nullipara, the upper two-thirds of the vagina deviate horizontally. This orientation is due 1) to the posterior attachments of the cervix by the cardinal and utero-sacral ligaments and 2) to the anterior position of the levator hiatus. Barium vaginograms have demonstrated this horizontal angulation of the upper two-thirds of the vagina, and show that during coughing and stressful maneuvers, the levator hiatus is shortened in an anterior direction by the contraction of the pubococcygeus muscles. Thus, the pelvic organs receive support from the shape and active contraction of the levator muscles.

A schematic diagram of the factors necessary for urogenital diaphragm support and function is provided in **Figure 9.**

II. EFFECT OF CHILDBIRTH, VAGINAL PROLAPSE AND URETHRAL POSITION ON URINARY CONTINENCE

Labor and delivery alter vaginal and pelvic anatomy and innervation in several ways as has been discussed in other sections of this chapter. Each of these may contribute to the eventual development of urinary incontinence:

1. Direct crushing or traction on the pudendal nerve has been discussed above and has previously been suggested as a primary cause of sphincteric incompetence in stress incontinence.
2. Cardinal and utero-sacral ligaments may be stretched or torn, resulting in anterior displacement of the uterus during straining or under the influence of gravity.

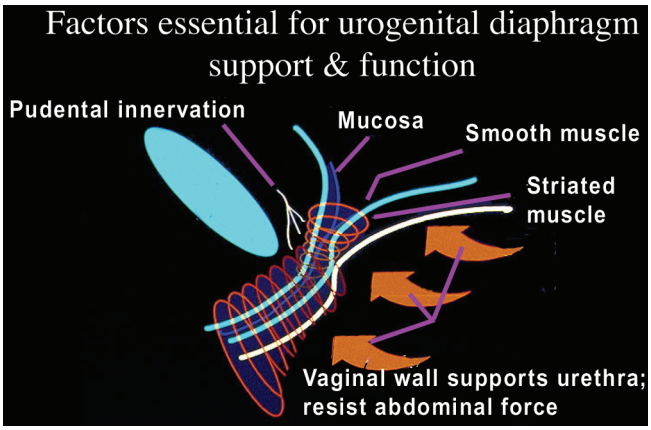


Figure 9. Factors essential for urogenital diaphragm support and function

3. The vagina itself may be torn away from its intrapelvic attachments with subsequent loss of the superior vaginal sulcus. There may be direct attenuation of the vaginal wall itself, manifested by loss of vaginal rugae and a thin appearance. Cullen Richardson has suggested four distinct kinds of vaginal injuries: paravaginal, central, distal, and cervical, the first two being the most commonly seen in women with stress incontinence. These defects have been identified by sonographic examination [143].
4. Finally, stretching, tearing and avulsion of the levator muscles result in a longer and wider levator hiatus. Consequently, the perineum is displaced anteriorly and posteriorly under stress and temporarily fails to support the pelvic organs. These changes in the levator hiatus with or without associated relaxation of cervical support result in chronic anterior displacement of pelvic organs with a loss of both active and passive organ support during rest and especially during straining.

In the patient with stress urinary incontinence these changes typically give rise to a rotational descent of the proximal urethra away from its retropubic position. Radiographic images of stress urinary incontinence in women have noted this and generated our earliest concepts of this condition. Jeffcoate and Roberts [144], using lateral cystourethrograms, concluded:

"…the most common characteristic anatomical change, present in four out of five cases of incontinence, is loss of the posterior urethro-vesical angle so that the urethra and trigone tend to come into line."

In 2002, fifty years later, perineal sonogrpahic studies of urethrovesical angle differences in incontinent and normal patients have found excellent correlation between angle and degree of incontinence, suporting these original observations [145].

Hodkinson, using a suspension of barium paste placed in the bladder and a small bead chain in the urethra, produced images of the urethra at rest and during maximum straining in women with stress urinary incontinence [146, 147]. He concluded:

"…it is clear that the distinguishing topographic pathological feature is depression of the urethrovesical junction to the lowest level of the bladder during the peak of the straining effort. It is also clear that the spatial relationships of the bladder and urethra to the symphysis make no difference in either the incidence or severity of stress incontinence."

These kinds of radiographic studies, however, cannot distinguish between lateral or central defects in vaginal wall support (**Figure 10**). Therefore, while urethral movement can be identified as an important finding in stress incontinence, one cannot determine

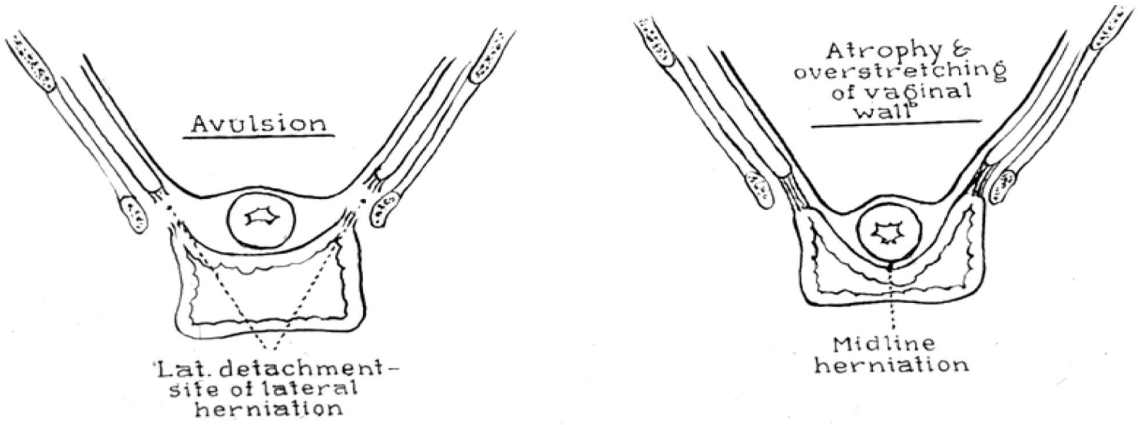


Figure 10. Loss of support from lateral or midline defect may appear the same on ultrasonic, radiographic or MRI images. The clinician must examine the patient to determine the location of vaginal weakness contributing to rotational descent.

the exact location of the vaginal defect. Because the proximal urethra rotates out of the focal plane of ultrasonograhic probes or MRI, coronal images of vaginal relaxation have not yet shown anatomical detail at the moment of incontinence. They cannot distinguish central from paravaginal defects. For this, an examination of the patient is required.

Although we have considerable knowledge about anatomical defects in the majority of patients with GSUI, less is understood about the exact effect of these defects, and indeed, vaginal position itself, on urethral closure. Early experience with operations for stress incontinence showed that not all women with stress urinary incontinence had vaginal prolapse, that correction of vaginal relaxation did not always correct stress incontinence, and that women who redeveloped stress incontinence symptoms after apparently successful surgery did not necessarily show a recurrence of their prolapse[148].

III. EMERGING CONCEPTS OF URETHRAL WEAKNESS AND ISD

The idea that primary urethral weakness could cause urinary incontinence independent of vaginal weakness appeared in a proposed classification by Blaivas et al [149]. In their classification, they named this Type III incontinence to distinguish it from Types I and II, each of which showed movement, while Type III did not. This term still remains in the contemporary literature, though it has now been largely replaced by the term intrinsic sphincter deficiency (ISD), focusing attention on urethral elements which appear to be independent of vaginal position and mobility. These elements include pudendal innervation, striated sphincter mass and function, and urethral smooth muscle, mucosa and submucosal cushions.

When ISD was first introduced as a concept to explain surgical failures and the presence of stress incontinence in the absence of vaginal mobility, the diagnostic tendency was to consider the cause of stress incontinence as a dichotomy, due either to hypermobility (displacement, or prolapse of the vaginal wall) or ISD. The typical patient with ISD was described as having low urethral closure pressures, a "stovepipe" appearance on cystoscopy, and opening or funneling of the urethra under resting or minimal increases in intra-abdominal pressures on radiographic images. The common causes were thought to be surgical injury, ischemia following previous pelvic or vaginal surgery or radiation damage. It appears now, that these examples of ISD may have represented the most advanced or extreme forms.

IV. HYPERMOBILITY VS. ISD: FROM DICHOTOMY TO CONTINUUM

Currently, there appears to be a shift away from this simple categorization of stress incontinence as being due either to hypermobility or ISD. This has arisen in part because of the development of the concept of Valsalva Leak Point Pressure (VLPP) [150, 151] and more recent analyses of long term results of stress incontinence surgery [152].

VLPP emerged as an alternative method to study urethral closure during stress for studies of urethral bulking with collagen. Investigators recognized that improvements in continence following urethral bulking did not correlate with urethral closure pressures, but did correlate with the amount of pressure required to produce leakage in the absence of intrinsic detrusor contraction. Although VLPP still lacks specific anatomic or theoretical grounding and many uncertainties related to standardization of recording methods and associated prolapse remain, low VLPP (without specified or established values) has been widely embraced as an indicator of ISD.

Just as the concept of VLPP blurred the previous distinction between simple ISD and simple hypermobility, long term outcome studies of correction of hypermobility have suggested that there may be more urethral weakness among patients with hypermobility than had been previously considered. Long term outcome studies of stress incontinence surgery have shown that there is a much greater failure rate of many of the commonly performed stress incontinence operations than had been generally appreciated, and that slings providing direct sub-urethral support seemed to provide the greatest long term protection against recurrence of incontinence [152]. Since slings had traditionally been the procedure of choice for recurrent incontinence or "Type III" (now ISD) incontinence, the possibility that ISD was more common than previously thought was more widely considered. Recently, Horbach and Ostergaard have found that age is a significant, indepenedent predictor of ISD in the setting of genuine stress incontinence [153], suggesting that age-related reduction in muscle mass, slowed reflexes or repeated episodes of prolapse may all contribute to the condition.

These two developments have led to a growing clinical impression that some degree of ISD may exist in many patients who, until recently,, were thought to have only hypermobility as a cause of their incontinence. A typical expression of this approach can be found in the conclusion of Kayigil et al. [154] following examination of 50 patients; “The high rate of intrinsic sphincteric deficiency in patients with urethral hypermobility indicates that the incidence with stress incontinence may be greater than previously believed, and may influence the apparently higher failure rates after bladder neck suspension.” In contemporary clinical practice, this impression has given rise to a growing tendency to recommend suburethral sling surgery as a form of primary surgical treatment for all women with stress incontinence, where formerly this approach was reserved almost exclusively for patients with recurrent stress incontinence or significant ISD [155, 156].

1. Direct studies of urethral function

As recognition of the importance of urethral function has increased, so too have the number of investigations of urethral position, urethral closure and transmission pressure profiles, Valsalva leak point pressure measurements and electromyographic examinations of the pudendal nerve and the striated sphincter.

a) Studies of urethral position

Stress incontinence is frequently associated with loss of urethral position. This has been the primary pathophysiological paradigm since the observations of Hodginson and Jeffcoate and Roberts. Similar observations are still reported today [157, 158]. Even when some displacement is seen in continent nulliparous females, incontinent women show a greater degree of mobility [159].

Successful suspensory operations, whether by sling or paraurethral suspension stabilize urethral position [148]and, when studied, increase pressure transmission during stress. It is not clear if the active contraction of urethral support seen in the female is restored after surgery, nor is it known if it is necessary for continence. It has been suggested that passive support alone is what restores continence after suspension.

b) Studies of urethral pressure and resistance

Stress incontinence is generally thought to be characterized by a decrease in urethral transmission profiles and resting closure pressure. Although not perfectly correlated, low resting pressures and low leak point pressures are found more commonly in patients with severe incontinence which may be more refractory to suspensory operations. Sonographic studies have recently shown a relationship between low urethral resistance and decreased urethral smooth and skeletal muscle layers [160].

Improvement in transmission pressures is associated with successful outcomes after suspensory operations for SUI. [133, 140, 141, 161-163]. The exact mechanism for this increase in transmission is not clear. Increased exposure to intra-abdominal forces has been suggested [142, 164, 165]. Compression against the pubis by the pelvic viscera has been suggested [166]. The final position of the urethra, however, may not be the key variable [133].

c) Electrophysiological studies of urethral function

Snooks and Swatch [100, 167, 168] first brought attention to the importance of urethral denervation after childbirth and its possible contributions to urinary and fecal incontinence. Stress incontinence is frequently associated with a decline in the electrophysiological function of the pudendal nerve [169], the striated urethral sphincter [170], and the pelvic floor muscles [171, 172]. Most recent studies continue to support the finding of prolonged pudendal nerve terminal motor latency in SUI [173].

Electromyographic studies of normal sphincteric function show that in continent women, pressures begin to rise in the urethra before rising in the bladder, suggesting an active muscular component [174]. Experimental studies of urethral function and the role of Onuf’s nucleus in the sacral spinal cord have led to recent practical innovations in the development of serotonin uptake inhibitor agents in the treatment of SUI [175]. Most electrophysiological studies have concentrated on motor rather than sensory innervation, however, and the role of urethral sensation in GSUI is unknown.

There is a need for a hypothesis which would integrate these various observations regarding hypermobility, ISD and pudendal nerve function, place them within the context of an abnormal pelvic floor and provide a model to guide research and studies of the natural history of the condition.

2. Role of advanced imaging in understanding pathophysiology

Radiographic imaging has provided considerable insight into pathophysiology of stress incontinence, ever since the advent of bead chain cystograms and

simple static and straining lateral cystograms. Magnetic resonance imaging (MRI) and real time ultrasonography, in addition to showing the events of stress incontinence on both a global pelvic and local urethral scale, have suggested a relationship of the proximal urethra to vaginal wall movement.

3. Magnetic Resonance Imaging

Dynamic fastcan MRI can visualize all compartments of the female pelvis during increased intra-abdominal straining[176]. MRI is comparable to standard cystography in demonstrating cystocele defects [177]. Using the pubococcygeal line as a reference marker, the normal displacement of bladder base, cervix or cervical cuff, and the rectum can be identified and compared to women with prolapse. The urethra is shown in the context of global pelvic relaxation [178]. Although most MRI studies have been descriptive rather than quantitative, they still show far more soft tissue detail than earlier radiographic studies and continue to offer promising research opportunities. Recent studies have utilized an endovagoinal coil to obtain higher resolution images of the urethra [179].

Dynamic MRI with cine-loop reconstruction produces vivid, intuitively appealing images which can show movement of all compartments of the relaxed pelvis during straining [178]. Static MRI shows details of urethral and peri-urethral anatomy and the striated sphincter can be clearly seen [180]. Pending further improvements in resolution, MRI remains a most promising tool for studying details of urethral movement [181]. Ultrasonogrpahy, however, is simpler and less expensive, and, for now, provides better visualization of moving structures.

4. Real time ultrasonography

Several sonographic approaches have been used for the study of stress incontinence: suprapubic, translabial and transperineal. As resolution of sonographic probes has improved, the detail previously best seen with the transrectal approach may now be seen by a transperineal approach. Earlier studies with a transrectal approach have shown that funneling of the proximal urethra was the sonographic sign most-frequently associated with loss of urine [182]. In about half the patients with SUI in this study, funneling was seen only with straining. In the other half, some degree of funneling was already present at rest, increasing with straining and present with actual leakage. Enhanced views of the urethra are possible with sonographic contrast material [183, 184]. Most recently, 3-D reconstruction from translabial views of the urethra has been used to compare findings in normal volunteers and those with ISD [185].

The most recent sonographic study of women with SUI found funnelling at rest in 109 of 330 patients, and found that the degree of vaginal relaxation as well as the parameters of intrinsic urethral function, including VLPP and urethral closure pressures, were worse in patients with funneling than without. The authors of this study concluded that: “In primary genuine stress incontinence, bladder neck funneling on ultrasound cystourethrography implies the potential coexistence of poor anatomic support and an intrinsic sphincter defect. [186].” Ghoniem et al [187] also found that urethral funneling was more likely to be associated with low closure pressures, low VLPPs, and a higher incidence of ISD in patients with SUI. Ultrasound has been used to identify paravaginal defects prior to Burch colposuspension to guide surgical midification, and then repeated after surgery to show correction of the defects [188].

Urethral movement and funneling seen by ultrasound resemble the rotational descent previously described by Nichols and Randall [189]. It is also consistent with the previously cited descriptions of Jeffcoate and Roberts, and that of Hodginson. Improved soft tissue detail seen with ultrasound has permitted an extension of these original observations. The anterior and posterior walls of the proximal urethra appear to move differently during increases in intra-abdominal pressure. At first, they appear to move together: the urethra begins its descent as a single unit. At some point, however, the anterior urethra becomes arrested in its rotational movement and appears to move more slowly. The posterior portion of the urethra continues to descend along with the vaginal wall [182, 190]. This difference in movement suggests a shearing apart of the two walls, leading to the appearance of funneling, which can be seen as urine leaks out of the urethra.

Anatomic correlation suggests that the pubourethral ligaments may restrict the movement of the anterior urethral wall, facilitating downward traction by the prolapsing vagina during stress, contributing to the shear. At the level of the pubis, the posterior portion of the pubourethral ligament travels beneath the pubis to form an anterior portion, which supports the clitoris in women, and the corpora cavernosa in men. Both Nichols and Milley [191] and Zacharin [192-194] have previously suggested that the posterior pubourethral ligaments might support the urethra,

and their laxity might contribute to the descent of the urethra in stress incontinence. These studies, however, suggest a different interpretation. Longitudinal and cross-sectional views of the proximal urethra show that the ligaments travel along only the anterior portion of the urethra as they pass beneath the pubis to emerge as the anterior pubourethral ligaments. The vagina and its bilateral attachments forming the lateral sulcus support the posterior part of the urethra. It is more likely that the vaginal wall and its attachments become weaker than the strong condensations of endopelvic fascia forming these ligaments. Therefore, the pubourethral complex, even if attenuated, probably remains stronger than the underlying vaginal wall. Sonographic examination of the prolapsing urethra thus suggests arrest of anterior urethral wall movement by the pubourethral complex, while the vaginal wall continues to rotate, pulling the posterior wall of the urethra along with it (**Figure 11**).

These anatomical considerations, combined with current knowledge about pudendal nerve activity in normals, prolapse or stress incontinence, suggest an inter-relationship regarding urethral closure and vaginal movement. As intra-abdominal pressure increases, the proximal urethra experiences two kinds of forces, which may lead to opening. The first of these is a shearing force produced by the unequal separation of the anterior and posterior urethral walls from the pubis during straining. This is the effect of vaginal mobility on urethral closure. The second is an expulsive force, produced by the transmission of intra-abdominal forces to the bladder, which must be resisted by the urethra if opening is to be prevented. The urethra resists this primarily by intrinsic closure of the pudendally innervated striated sphincter, aided by vaginal support (**Figure 12**).

It is likely that these shearing and expulsive forces are generated simultaneously as intra-abdominal pressure rises. One can easily imagine that the urethra can be brought to a continence threshold beyond which urethral closure cannot be maintained.

One can further imagine that repeated episodes of prolapse may eventually stretch, tear or attenuate sphincter mass and contribute to a chronically weakened urethra manifested by low VLPP or low urethral closure pressures, characteristic of ISD.

After severe or prolonged untreated prolapse and stress incontinence, vaginal support alone may not be sufficient to correct the deficiencies of an exhausted sphincter. Although theoretical rather than evidence-based, such considertions may direct future research efforts towards a more integrated hypothesis regarding stress incontinence in women.

The relative contributions of abnormal vaginal mobility and intrinsic urethral function should be considered as part of a continuum rather than a dichotomy. Current research and interest has concentrated mostly on ISD as the primary cause of SUI in women, but the relationship of the many factors affecting urethral support and function should remain a perspective in interpreting emerging findings.

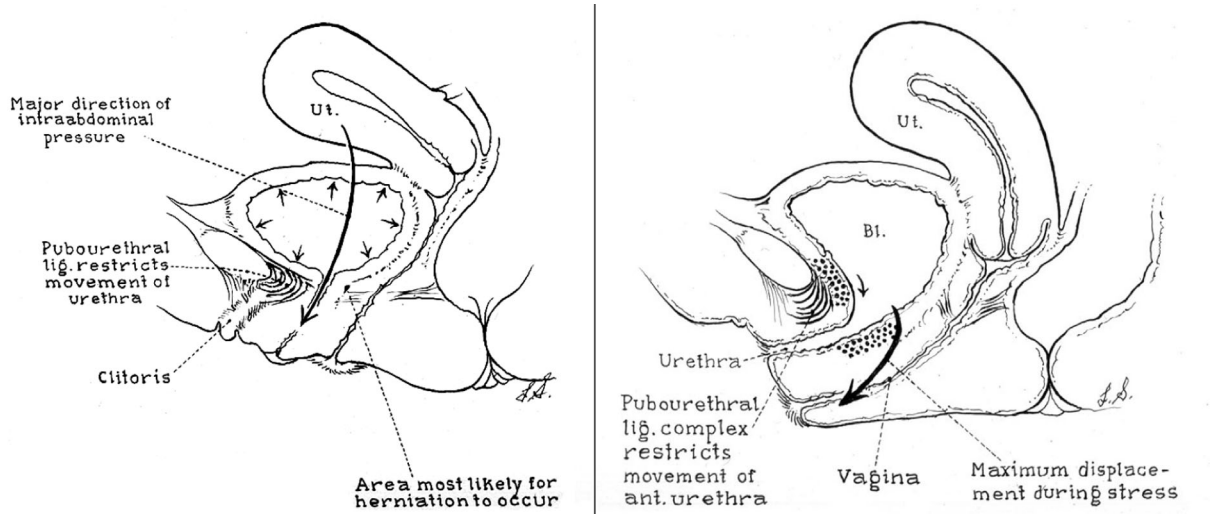


Figure 11. Effect of vaginal movement on urethral closure. Anterior portion of proximal urethra is slowed in its movement by anterior suspensory tissues, while posterior portion of urethra is displaced by rotating vaginal wall.

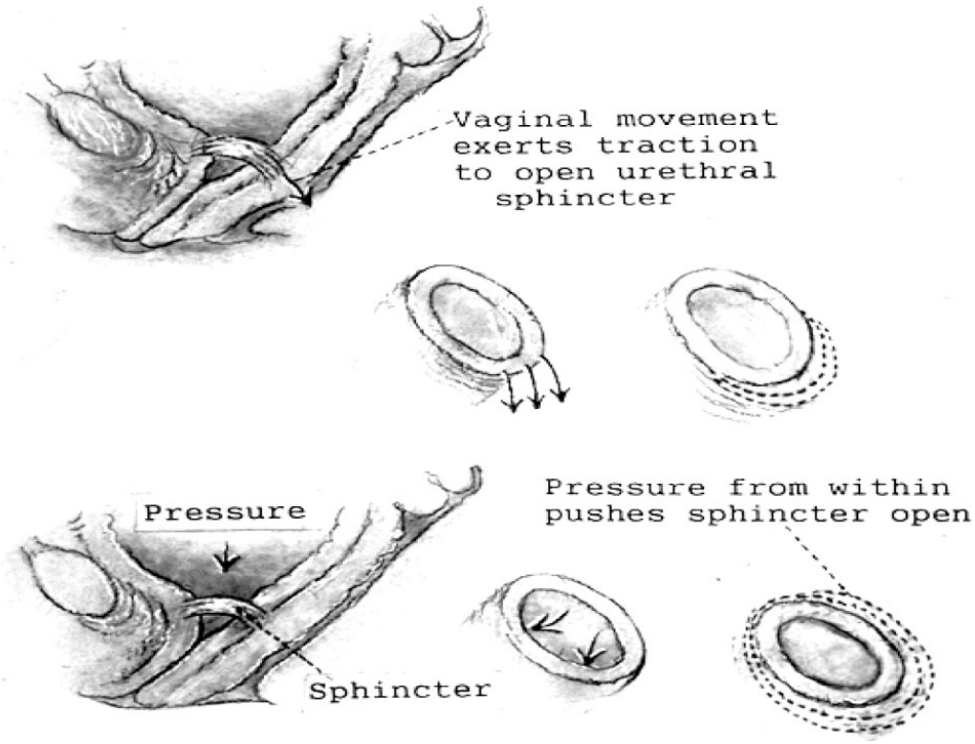


Figure 12. External traction of the urethra by vaginal movement and internal pressure from urine in the bladder distending the urethral walls may work simultaneously against urethral resistance to result in leakage.

V. CONCLUSIONS

We are approaching a new classification of stress incontinence which will integrate hypermobility and urethral dysfunction as inter-related elements on a spectrum of change. Certain concepts have stood the test of time, and they are included below, along with conclusions:

1. Many patients with GSUI show urethral mobility (Level 2), though it is not yet known what it is about that mobility which permits urethral opening during stress.
2. Some patients who present with minimal mobility or who have recurred after successful surgery have primary or residual sphincteric insufficiency.
3. Sphincteric insufficiency is related to a decline in striated sphincter muscle mass and function as measured by electrophysiological studies of pudendal nerve and sphincter function, and MRI and sonographic estimates of muscle mass (Level 1). If repeated episodes of vaginal traction can be shown to enhance sphincteric damage, then the effect of early treatment of stress incontinence and prolapse on future development of ISD should be investigated, since advanced ISD remains a difficult aspect of SUI to treat.
4. Successful operations can restore urethral position but probably do not restore urethral function. A good surgical outcome probably requires a certain reserve of urethral function. It is in the area of functional understanding of urethral anatomy that the greatest progress is likely to be made.

D. PELVIC ORGAN PROLAPSE

Pelvic organ prolapse (POP) has a strong inter-relationship with the urinary tract. Urinary incontinence commonly co-exists with POP and the converse relationship is also true. Thus, it is important for incontinence specialists to have a well-grounded understanding of POP in order to provide optimal patient care for the many women worldwide whose quality of life is impacted by pelvic floor disorders.

This section will provide an overview of evidence relating to POP, especially its interaction with the urinary tract. In addition, the significant gaps in knowledge will be highlighted focusing on high-priority opportunities for additional research.

I. ETIOLOGY OF PELVIC ORGAN PROLAPSE

Most of the literature regarding risk factors for POP is based on epidemiological studies, case control studies, and observational studies. A major qualification of the interpretation of epidemiological data is that association does not mean causation. Many epidemiological associations have been embraced without thoughtful confirmatory experiments.

1. Pregnancy

Until recently the few studies that examine the association of POP with pregnancy implicate vaginal delivery as an important risk factor for POP. However research is now focusing also on modifications of the pelvic structures occurring during pregnancy itself. O'Boyle et al. [195] prospectively examined 129 nulliparous pregnant women (mean age 21 years) using the POPQ staging system[196] in the first, second and third trimester. Statistical comparison was performed only in a total of 36 women. These authors found significant physiologic alterations produced by pregnancy involving all the vaginal segments. However Point Aa seemed to be the measurement which mostly determined the increase in POPQ stage as gestation progressed and the assignment to the final stage in most cases. Points Aa, Ba, Ap and Bp were significantly different from the first to the second and to the third trimesters. Interestingly there was also a significant increase in Pb from the third to the third trimester. Although this study only has small number it is the first and only one which objectively describes the effect of pregnancy on the pelvic floor in women presumed to have no support defects. Further research in this field would be recommended.

Sze et al. [197] examined 94 nulliparous women using the POPQ staging system at 36-week antepartum and 6-week postpartum. They did not show any significant difference in prolapse occurrence between women who delivered vaginally or by cesarea section when this was performed in the active phase of labor. These authors did not demonstrate also a difference in terms of racial predisposition for prolapse between Caucasian and Black women.

2. Mode of delivery

The mode of delivery, parity and the presence of lacerations at delivery were retrospectively considered by Uustal Fornell et al. [198]. These authors mailed a questionnaire on urinary and fecal incontinence and prolapse symptoms to 1000 40 year old and 1000 60 year old women with a 67% response rate. **Table 1** shows the univariate associations between prolapse symptoms and obstetric history.

3. Parity

In the Oxford Family Planning Association prolapse epidemiology study parity was the strongest risk factor for the development of POP with an adjusted relative risk of 10.85 (4.65-33.81)[199].

While the risk increased with increasing parity, the rate of increase slowed after two deliveries. Samuelsson et al also found statistically significant associations of increasing parity and maximum birth weight with the development of POP[200]. These same relationships relating POP to increasing parity and birth weight were observed in the case control study of women who developed prolapse under the age of 45 and in a clinical observational study of women over age 18 [201, 202]. Finally, a study of 21,449 Italian women attending menopausal clinics demonstrated a significant association between uterine prolapse and vaginal birth (or for 3 births compa-

Table 1. Univariate reationship of prolapse symptoms to obstetric history.

	Pelvic heaviness	**Genital bulge**	**Digitation by defecation**
Vaginal delivery compared to cesarean section only	1.8 (0.7-5.1)	Not applicable	2.9 (0.7-2.8)
Vaginal delivery compared to nulliparous	1.8 (1.0-3.1)	7.4 (1.0-53.9)	1.2 (0.0-7.4)
Sphincter rupture compared to no sphincter rupture	2.9 (1.3-6.8)	1.2 (0.2-7.0)	3.0 (1.3-7.3)
Three or more births compared to one or two births	1.5 (1.1-2.1)	2.0 (1.1-3.7)	1.4 (0.9-2.0)
Large tear at delivery compared to no tear at delivery	2.1 (1.3-3.4)	1.1 (0.5-2.6)	2.1 (1.2-3.7)

red to none being 3.0 (2.1-4.3) but not with delivery of a baby weighing >4500 grams [203]. To date, specific events of the birth process have not been studied sufficiently to identify them as risk factors for POP. Rinne & Kirkinen found no significant relationship of POP with forceps or vacuum delivery or the duration of the second stage of labor [201]. Klein et al found an association between episiotomy and diminished pelvic floor strength three months post partum but not with subjective symptoms of bulging[204]. In contrast, Taskin et al showed that routine episiotomy when combined with antepartum[205]. Kegel exercises were as effective as Cesarean delivery in avoiding advanced POP two months after delivery in a group of 100 women who had their management determined by the day of their enrollment for prenatal care. Sartore et al [206] compared 254 primiparous women who received mediolateral episiotomy to 265 women with intact perineum or first and second degree spontaneous laceration at 3 months after delivery. They concluded that mediolateral episiotomy does not against genital prolapse.

4. Aging

Virtually all studies examining prolapse or surgery for prolapse demonstrate an increased prevalence with aging. Comparing 368 controls with 87 women with severe prolapse Swift [207] found that advancing age together with increasing weight of infants delivered vaginally, a history of hysterectomy and a history of previous surgery were the strongest etiologic predictors of severe prolapse using a stepwise multiple logistic regression analysis, the odds ratios being 1.1184, 1.2362, 2.3688 and 5.0878 respectively. Few studies look at the effect of menopause on POP risk and results are conflicting; Swift showed a significant increased risk with menopause while Olsen and the Progetto Menopausa Study Group did not [202, 203, 208]. Versi [209] did not find correlation between prolapse and menopausal age. On the other hand, examining the periurethral region, Goepel [210] fiund an altered metabolism of connective tissue with a significant decrease of collagen and vitronectin expression in women with prolapse regardless their continence status.

5. Constipation

Evidence linking constipation to POP relate to data linking POP to pelvic floor denervation and neuropathy. While vaginal childbirth has been implicated as a major inciting event for pelvic neuropathy and prolapse, chronic constipation with repeated prolonged defecatory straining efforts has been shown to contribute to progressive neuropathy and dysfunction [211, 212]. In one case control study, constipation and straining at stool as a young adult before the onset of recognized POP was significantly more common in women who subsequently developed POP (61%) than in women who did not develop PFD (pelvic floor dysfunction) (4%)[213]. In 185 women subdivided into those with (n=69) and without (n=116) posterior vaginal wall prolapse, Fialkow[214] found that subjects with posterior vaginal wall prolapse were more likely to have difficult defecation (included the need to have defecation by digitation) compared to women without prolapse.

The Swedish prolapse study provided evidence for progressive decreases in pelvic floor muscle strength with increasing age and parity. This decrease in pelvic floor muscle strength was a significant independent determinant of the risk of POP, again supporting an association between pelvic neuromuscular dysfunction and prolapse[200]. DeLancey [215] have recently shown that women with genital prolapse are 2.5 times more likely to have major levator ani muscle loss and generate 43% less force during maximal pelvic muscle contraction compared to age matched controls. Looking at 309 women with prolapse and stress incontinence, Busacchi [216] found a reduction in peptide-containing nerve supply to the perineal muscles, concluding that this provides a morphologic basis suggesting that neural abnormalities contribute to the pathogenesis of genital prolapse and urinary incontinence.

6. Occupational stress and physical labor

Occupational physical stress has been examined as a contributing factor for POP. One report has implicated the extreme stress associated with airborne training (including parachute jumps) with pelvic floor dysfunction and prolapse in women previously subjected to laparoscopic uterosacral ligament transection [217]. A study using the Danish National Registry of Hospitalized Patients included over 28,000 assistant nurses (who are traditionally exposed to repetitive heavy lifting) aged 20-69 and compared their risk of surgery for POP and herniated lumbar disc (a condition associated with heavy lifting at work) to the risk in over 1.6 million same-aged controls [218]. The odds ratio for the nurses compared to controls was 1.6 (1.3-1.9) for POP surgery and 1.6 (1.2-2.2) for disc surgery, suggesting that heavy lifting may contribute to POP. An Italian study demonstrated an increased risk of prolapse with

lower levels of education, a possible indicator of harder physical labor, although this was not specifically investigated [203].

7. Obesity

Obesity is another condition that is associated with chronically increased abdominal pressure [219]. Looking at the prevalence of reproduction-related illnesses in a rural community of 557 women in Lebanon, Deeb et al. [220] they found a high prevalence of prolapse and obesity. Some studies have demonstrated significant relationships between increasing weight and body mass index and the risk of POP or surgery for POP [199, 203]. Others have not demonstrated this correlation or have demonstrated a loss of correlation once analysis was corrected for confounders such as age, parity, or pelvic muscle strength [200, 201]. Another medical condition associated with chronic episodic increases in abdominal pressure is chronic pulmonary disease. Fornell [198] reported an ratio of 1.4 (0.4-5.0 95% CI) of defecation by digitation when associated to chronic bronchitis using univariate analysis. One case control study examined this and reported significantly more pulmonary disease (such as asthma) in women < 45 years of age who developed prolapse (14%) compared to controls (2.4%) [201]. Strinic et al. [221] have recently compared 40 women with genital prolapse with 40 controls for their ventilatory function. Women with prolapse showed a significant decrement in the peak expiratory flows (-26%). Also the forced vital capacity and the forced expired volume were decreased by –9% and –16% respectively. All these findings were considered typical for reduced strength of the expiratory muscle suggesting a possible link between the lack of collagen and the impairment of pulmonary function in women with prolapse.

8. Hysterectomy

In the Oxford Family Planning Study the incidence of surgical POP repair was higher for women who had undergone a prior hysterectomy for reasons other than prolapse (29 per 10,000) and highest for women who had undergone hysterectomy for prolapse (158 per 10,000) [199]. Marchionni et al demonstrated some degree of vaginal vault prolapse 9-13 years after hysterectomy in 11.6% of women who had the hysterectomy for prolapse and in 1.8% of women who had the hysterectomy for other benign disease [222]. Compared to total abdominal hysterectomy, subtotal hysterectomy does not seem to increase the risk for vaginal vault prolapse as described by Gimbel et al [223]; Thakar[224] reported a 2% rate of cervical prolapse after subtotal hysterectomy. Swift also demonstrated a significant association of POP with a prior history of hysterectomy or prolapse surgery [202]. This was confirmed by Fornell 4 which reported an odds ratio of 7.1 (3.9-12.9 95% CI) for defecation by digitations and of 2.0 (0.8-4.9 95% CI) for women who had a history of hysterectomy using a univariate analysis.

9. Previous surgery for prolapse

While any prolapse procedure can fail for a variety of reasons, it has been suggested that certain procedures have higher risks of specific pelvic support defects. These include anterior and/or posterior vaginal wall descent formation after Burch colposuspension and anterior superior segment prolapse after sacrospinous ligament fixation [225-227]. In a study on 127 women undergoing Burch colposuspension with a mean follow-up of 12.4 years Langer [228] reported an overall complaint of anatomical defects in 19% of women. Another study by Demirci [229] on 220 women with a mean follow-up of 18 months showed cystocele in 18 (8%), rectocele in 32 (15%) and enterocele in 35 (16%) after Burch. More recently Kwon [230] reported 17.6% of stage II anterior prolapse, 32.4% of stage II posterior prolapse and 8.8% stage II uterine prolapse after Burch colposuspension, although this study was limited in numbers. The occurrence of posterior vaginal wall prolapse after Burch colposuspension can be significantly prevented by obliterating the cul-de- sac, the approximation of the uterosacral ligaments being more effective than the Moschcowitz procedure, as recently reported by Langer [231]. Out of 122 women undergoing vaginal sacrospinous fixation for vaginal vault or uterine prolapse, Nieminen [232] 26 (21%) had recurrence, being in 14 cases an anterior wall descent.

a) Vaginal route for surgical prolapse correction

In addition, there is evidence that the vaginal route of prolapse correction is associated with damage to the pudendal nerve and results in anatomic outcomes and higher re-operation rates than abdominal route prolapse surgery [233, 234]. This last data is however controversial. In fact in a RCT comparing abdominal and vaginal prolapse surgery, [235] the abdominal approach showed significant higher scores on the discomfort/pain domain (mean difference 7.1, 95% CI 1.1-13.2), overactive bladder domain (mean difference 8.7, 95% CI 0.5-16.9) and obstructive micturition domain (mean difference 10.3, 95% CI

0.6-20.1); pelvic examination was similar in the two groups although prolapse symptoms were more frequent in the abdominal group. Re-operation was more likely in women undergoing abdominal procedures compared to vaginal ones (odds ratio 11.2, 95% CI 1.4-90.0).

b) Laparoscopc laser procedures

Finally, there have been five case reports implicating laser laparoscopic uterosacral ligament ablation for chronic pelvic pain as a cause of uterine prolapse in young women [217, 236].

10. Collagen synthesis abnormalities

There are data that link clinical, laboratory, and genetic syndromes of abnormalities of collagen to pelvic organ prolapse [237, 238]. Recently Visco [239] reported a differential gene expression in the pubococcygeus muscle related to actin, myosin and extracellular matrix proteins comparing women with prolapse to controls. Boreham [240, 241] showed an altered smooth muscle bundle architecture both in the anterior and posterior vaginal wall of women with pelvic organ prolapse compared to normals. It is controversial whether women with prolapse have a different collagen content or fiber quality in the parametrium compared to controls [242, 243].

In addition, Rinne and Kirknen linked POP in young women with a history of abdominal hernias, suggesting a possible connection with abnormal collagen[201]. Uustal et al. [198], using an univariate analysis, reported an odds ratio of 1.9 when prolapse symptoms such as pelvic heaviness and defecation by digitations were associated with a medical history of surgery for groin hernia.

11. Pelvic and axial skeleton

Finally, there is evidence from several case control studies that variations in axial and pelvic skeletal structure can be associated with increased risks of POP. These include increasing degrees of thoracic kyphosis, a decrease in lumbar lordosis and in vertical orientation of the pelvic inlet, and an increase in the transverse diameter of the pelvic inlet [244-246]. In a case control study Handa [247] compared 59 women with pelvic floor disorders with controls using standardized pelvimetry techniques during MRI. After controlling for age, race and parity, using a multiple logistic regression analysis, pelvic floor disorders were significantly associated with a wider transverse inlet (odds ratio 3.425) and a shorter obstetrical conjugate (odds ratio 0.2333). The association between early age, advanced stage POP and the severe disruption of pubic bone and pelvic muscle structure in women with bladder exstrophy is well recognized [248].

II. ASSOCIATED PELVIC CONDITIONS

1. Urinary tract dysfunction and prolapse

Detrusor overactivity is known to be associated with female stress urinary incontinence as a result of pelvic floor relaxation. After surgical correction, this disappears in approximately two-thirds of these patients [249]. This may suggest that afferent nerve activity from pelvic floor and urethra is involved in detrusor inhibition during bladder filling. Thus, the decreased afferents due to pelvic floor deficiency can lead to involuntary detrusor contraction. External and direct pudendal nerve electrical stimulation shows a good clinical result in the treatment of the overactive bladder [214, 250], thereby supporting this hypothesis.

Animal experiments performed by Barrington in the first half of the twentieth century have also suggested a mechanism by which urethral relaxationmay evoke reflex detrusor contraction: when urine enters a relaxed proximal urethra, the desire to void may be evoked, an extention of his experimental observations in anesthetized rabbits, that water running through the urethra, or mechanical distention of the urethra produced a bladder contraction [251-253].

a) Bladder overactivity

Women with anterior vaginal wall support defects often have bladder neck hypermobility with urodynamic stress incontinence, as well as concurrent defects of uterine and posterior wall support. Schick et al [254] looked at 255 women with urodynamic stress incontinence and found a statistically significant correlation between urethral hypermobility and the degree of urethral incompetence assessed with the abdominal leak point pressure ($P = 0.0049$). However, with greater degrees of anterior vaginal wall prolapse (Stage III and IV) fewer women have symptoms of stress incontinence [255]. Severe prolapse can descend and obstruct the urethra, making assessment and management of the continence mechanism in such patients problematic [200, 255-257]. Multiple studies have described an occult incontinence rate after various methods of reducing

the prolapse during preoperative testing of 23-62% [258-261]. However, Bump et al described an only 4% de novo incontinence rate in women with Stage III or IV prolapse who had been randomized to a bladder neck plication procedure as their only prophylaxis, also concluding that preoperative barrier testing was not useful in identifying women who required a urethropexy [227]. Klutke et al determined that preoperative barrier testing was most useful in identifying those women who do not leak with reduction of the prolapse, since such patients did not undergo urethropexy and had better outcomes with regard to both USI and DO rates [262]. Because of this uncertainty, the least invasive method of bladder neck stabilization seems preferred for such patients [263].

b) Voiding dysfunction

Pelvic organ prolapse can also negatively affect voiding function [264], although one study noted that the majority of women with severe prolapse still void effectively [265]. Looking at 228 women with urinary tract disorders and/or prolapse, Dietz et al [266] found that enterocele had the worst effect on voiding function ($P<0.001$), whereas the relationship between anterior vaginal wall prolapse and voiding was complex: using ultrasound the finding of an intact retrovesical angle was related to difficulties in voiding ($P<0.001$); funnelling and opening of the retrovesical angle was associated with improved voiding ($P<0.001$).

Fitzgerald found that preoperative voiding studies with the prolapse reduced by a pessary was the best predictor of normalization of residuals post operatively [267].

The impact of pelvic organ prolapse on the upper urinary tract is not well described in the surveyed literature, consisting primarily of case reports of acute and acute or chronic renal failure attributed to ureteral obstruction by Stage IV uterine or vaginal vault prolapse. Hydroureter and hydronephrosis was demonstrated in such cases, resolving post repair [250, 268-271].

2. Gastrointestinal dysfunction and POP

Since 1965 colorectal surgeons focused their attention to the rectal side of the rectocele [272]. Amongst gynaecologists Khan and Stanton [249] firstly reported on bowel function after posterior colporrhaphy. Since then gynaecologists have been paying increasing attention to the correlation between bowel disorders and genital propapse.

Unfortunately repeated reports document disparities between physical exam and defecography in patients with prolapse, particularly those with large vaginal eversions. Two series of defecographies in consecutive patients with prolapse and/or evacuation disorders describe defecographic findings that changed the patients diagnosis (though not always the management) in 46 of 62 of cases and noted enteroceles that were not found on physical exam in approximately 50% of cases [273-275].Use of defecography as a gold standard for exam in these series raises concerns, since normal asymptomatic women may have focal defecographic abnormalities, but it is clear that it is challenging to assess the posterior compartment in severe prolapse. For instance, sigmoidoceles are present in 4-11% of reported series, and are nearly always missed on physical exam [275-277]. Relatively few of the published studies of outcomes of posterior compartment repairs provide an analysis of gastrointestinal co-morbidities as risk factors for failure. However, the prevalence of abnormal colonic transit time is approximately 20% in patients presenting with evacuation disorders [278]. An abnormal preoperative colonic transit study is the most consistently cited risk factor for failure of rectocele repair to relieve evacuatory symptoms, regardless of the surgical technique [279-281]. Recently Goh et al [282] reviewed the management of rectocele and clearly describe the complexity of clinical conditions resulting from the possible combination of various gynaecological and colorectal symptoms with anatomical abnormalities and the different surgical approaches. They claim for a "need for standardization in definitions of a rectocele and outcome measures". Recognition of the multifactorial etiology of constipation and evacuatory symptoms is advisable to help avoid disappointing surgical results and in fact as stated by Goh et al. "the best method of surgical approach is currently unclear." [282]

a) Fecal incontinence

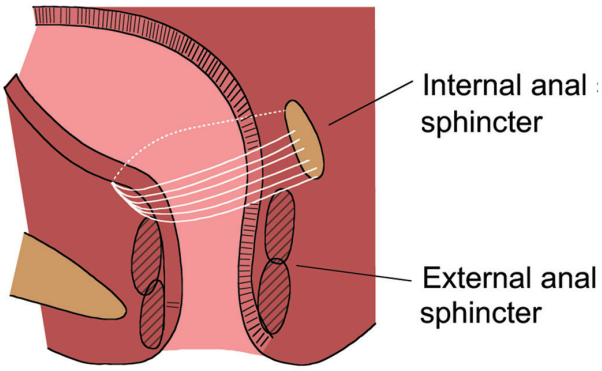
Fecal incontinence is a more frequent complaint among women with incontinence and prolapse than in the general population, being reported between 15% and 29% of patients presenting for an urogynaecological evaluation [283-287]. There is some evidence that rectocele repair can diminish both maximal anal resting and squeeze pressures, possibly contributing to the development of incontinence in patients already at risk with abnormal preoperative manometry [288]. No data are available concerning anal continence after transvaginal posterior repair, while some concern has been raised both after transanal and combined trans-vaginal/trans-anal procedures for the treatment of rectocele [289, 290].

E. FECAL INCONTINENCE: GASTROENTEROLOGICAL PERSPECTIVE

Fecal continence is maintained by the structural and functional integrity of the anorectal unit. Consequently, disruption of the normal anatomy or physiology of the anorectal unit leads to fecal incontinence. Fecal incontinence is often due to multiple pathogenic mechanisms and rarely due to a single factor [291].

I. STRUCTURE AND FUNCTION OF THE ANORECTUM

The rectum is a hollow muscular tube, 12 cm to 15 cm long, composed of a continuous layer of longitudinal muscle that interlaces with the underlying circular muscle[292]. The anus is a muscular tube 2 cm to 4 cm long. At rest, it forms an angle with the axis of the rectum of approximately 900; during voluntary squeeze the angle becomes more acute, approximately 70o; during defecation, the angle becomes more obtuse, about 110o to 130o. A schematic drawing is provided in **Figure 13**.



1. The anal sphincter

The anal sphincter consists of two muscular components: the internal anal sphincter (IAS), a 0.3 cm to 0.5 cm thick expansion of the circular smooth muscle layer of the rectum, and the external anal sphincter (EAS), a 0.6 cm to 1.0 cm thick expansion of the striated levator ani muscles. Morphologically, both sphincters are separate and heterogenous[293]. The EAS is a predominantly slow-twitch, fatigue-resistant muscle[294, 295]. The IAS generates mechanical activity, with a frequency of 15 to 35 cycles per minute, and ultra-slow waves at 1.5 to 3 cycles per minute[296, 297]. The ultra-slow waves generate pressures fluctuating between 20 mm Hg and 50 mm Hg in 10% of control subjects [298-300]. The IAS contributes approximately 70% to 85% of the resting sphincter pressure, but only 40% after sudden distention of the rectum and 65% during constant rectal distention [301]. Thus, the IAS is chiefly responsible for maintaining anal continence at rest [301].

The anus is normally closed by the tonic activity of the IAS. This barrier is reinforced during voluntary squeeze by the EAS. The anal mucosal folds, together with the expansive anal vascular cushions, provide a tight seal [302, 303]. These barriers are further augmented by the puborectalis muscle, which forms a flap-like valve that creates a forward pull and reinforces the anorectal angle[304].

2. Nerve structure and sensation

The anorectum is richly innervated by the sensory, motor, and autonomic nerves and by the enteric nervous system. The principal nerve is the pudendal nerve, which arises from the second, third, and fourth sacral nerves (S2, S3, S4) and innervates the EAS. The pudendal nerve is a mixed nerve that subserves both sensory and motor function. [305] Pudendal nerve block creates a loss of sensation in the perianal and genital skin and weakness of the anal sphincter muscle, but it does not affect rectal sensation[301]. It also abolishes the rectoanal contractile reflexes, suggesting that pudendal neuropathy may affect the rectoanal contractile reflex response.

It is not completely understood how humans perceive stool contents in the anorectum. Earlier studies failed to demonstrate rectal sensory awareness[306, 307]. But more recent studies have confirmed that balloon distention is perceived in the rectum and that such perception plays a role in maintaining continence[308, 309]. Furthermore, sensory conditioning can improve both hyposensitivity [310, 311] and hypersensitivity[312] of the rectum. Mechanical stimulation of the rectum can produce cerebral evoked responses, [313] confirming that the rectum is a sensory organ.

Although there are no organized nerve endings, both myelinated and unmyelinated nerve fibers are present in the rectal mucosa, and the myenteric plexus [307, 314]. These nerves most likely mediate the distention or stretch-induced sensory responses as well as the viscero-visceral, [315] the recto-anal inhibito-

ry, and the recto-anal contractile reflexes[314]. The sensation of rectal distention is most likely transmitted along the S2, S3, and S4 parasympathetic nerves[314]. Rectal sensation and the ability to defecate can be abolished completely by resection of the nervi erigentes[316]. If parasympathetic innervation is absent, rectal filling is only perceived as a vague sensation of discomfort. Even paraplegics or persons with sacral neuronal lesions may retain some degree of sensory function, but virtually no sensation is felt if lesions reach the higher spine[309, 317]. Thus, the sacral nerves are intimately involved with the maintenance of continence.

It has been suggested that bowel contents are periodically sensed by anorectal "sampling,"[318, 319] the process by which transient relaxation of the IAS allows the stool contents from the rectum to come into contact with specialized sensory organs, such as the Krause end-bulbs, Golgi-Mazzoni bodies and genital corpuscles, and the sparse Meissner's corpuscles and Pacinian corpuscles in the upper anal canal [306, 307, 314]. Specialized afferent nerves may exist that subserve sensations of touch, temperature, tension, and friction, but are incompletely understood[314]. Incontinent patients appear to sample rectal contents infrequently[319].

The role of anorectal temperature sensation is also subject to debate[320-322]. The likely role of anal sensation is to facilitate discrimination between flatus and feces and the fine-tuning of the continence barrier, but its precise role needs to be characterized.

3. Rectal distension

Rectal distention is associated with a fall in anal resting pressure known as the rectoanal inhibitory reflex. The amplitude and duration of this relaxation increases with the volume of rectal distention[323]. The arrival of flatus mimics sudden rectal distention and this is associated with a fall in anal pressure[324].

Although this process may facilitate discharge of flatus, rectal distention is also associated with an anal contractile response, a subconscious reflex effort to prevent release of rectal contents, such as flatus[325-327]. The amplitude and duration of the rectoanal contractile reflex also increases with rectal distention up to a maximum volume of 30 ml [323]. Abrupt increases in intraabdominal pressure, such as those caused by coughing or laughing, are associated with increases in anal sphincter pressure[328]. This may be achieved through multiple mechanisms, including reflex contraction of the puborectalis[329].

4. Anal endovascular cushions

The blood-filled vascular tissue of the anal mucosa also plays an important role in producing a more perfect closure of the anus. An in vitro study showed that even during maximal involuntary contraction, the internal sphincter ring was unable to close the anal orifice completely and a gap of approximately 7 mm was left open. This gap was filled by the anal cushions[330]. Anal cushions may exert pressures of up to 9 mmHg and thereby may contribute 10% to 20% of resting anal pressure[331].

II. PATHOGENIC MECHANISMS AND ETIOLOGY

Fecal incontinence occurs when one or more mechanisms that maintain continence is disrupted to an extent that other mechanisms are unable to compensate. Hence, fecal incontinence is often multifactorial1, [291, 332] In a prospective study, 80% of patients with fecal incontinence had more than one pathogenic abnormality[291]. Although the pathophysiological mechanisms often overlap, they may be categorized under the four subheadings shown in Table 2. For each category, the probable cause(s) and the mechanism through which it leads to fecal incontinence is also summarized in **Table 2**.

1. Structural abnormalities

a) Anal sphincter muscles

Disruption or weakness of the EAS muscle causes urge-related or diarrhea-associated fecal incontinence. In contrast, damage to the IAS muscle or the anal endovascular cushions may lead to a poor seal and an impaired sampling reflex. These changes may cause passive incontinence or fecal seepage, often under resting conditions. In most patients, both sphincters may be defective. The extent of muscle loss can influence the severity of incontinence.

The most common cause of anal sphincter disruption is obstetric trauma [333, 334] However, it is unclear why most women who have sustained an obstetric injury in their 20's or 30's typically present with fecal incontinence in their 50's. The injury may involve the EAS, the IAS, the pudendal nerves, or a combination of these structures. In a prospective study, 35% of primiparous (normal anti-partum) women showed evidence of anal sphincter disruption following vaginal delivery[333, 334] Other important risk factors include forceps-assisted delivery, prolonged second stage of labor, large birth weight,

Table 2. Pathophysiologic mechanisms underlying fecal incontinence

CATEGORY	CAUSE	MECHANISTIC EFFECT
Structural		
Anal sphincer muscle	Hemorrhoidectomy, anal dilatation	Loss of sampling reflex due to neuropathy
Rectum	Inflammation, IBD/ radiation; Prolapse; aging; IBS	Lost accomodation &sensation; hypersensitivity
Puborectalis	Excessive perineal descent; aging; trauma	Obtuse anorectal angle sphincter weakness
Pudendal Nerve	Obstetrical/surgical injury excessive straining perineal descent	Sphincter weakness sensoryloss/impairment
CNS, Spinal cord, ANS	Head or spinal cord injury, Back surgery, MS, DM, stroke, avulsion	Lost sensation/reflexes secondary myopathy, loss of accomodation
Functional		
Anorectal sensation	Obstet, CNS, ANS injury	Loss of stool awareness Rectoanal agnosia
Fecal impaction	Dyssynergic defecation	Fecal retention & overflow; Impaired sensation
Stool characteristics		
Volume and consistency	Infection, IBD, IBS, drugs, metabolic abnormalities	Diarrhea & urgency Rapid stool transport Impaired accomodation
Irritants	Bile salt malabsorption/ laxatives	Diarrhea
Hard stool/Retention	Dyssynergia/drugs	Fecal retention & overflow
Miscellaneous		
Mobility/cognition	Aging, dementia. disability	Mulitfactorial changes
Psychosis	Willful soiling	Mulitfactorial changes
Drugs	Anticholinergics; Laxatives Antidepressants Caffeine/muscle relaxants	Constipation Diarrhea Alteredsensation/constipation Relaxed sphincter tone
Food intolerance	Lactose, fructose, sorbitol	Diarrhea/flatus malabsorption

and occipito posterior presentations[334-336]. Furthermore, perineal tears, even when carefully repaired, can be associated with incontinence and patients may either present several years following delivery[336].

Episiotomy is believed to be a risk factor for anal sphincter disruption. In one study, medial episiotomy was associated with a nine-fold higher risk for anal sphincter dysfunction[337]. However, in a large 30-year retrospective cohort study, the prevalence of frequent fecal incontinence was 6.9% for women whose index delivery was complicated by anal sphincter disruption, 18% for the control group, and 0% for women who had ceserean section; bothersome incontinence was experienced by 27.6%, 25.8%, and 15.2% of the respective groups. This study suggests that regardless of the type of delivery, fecal or flatus incontinence occurs in a surprisingly large number of middle-aged women. This raises the issue of whether age-related changes that affect the pelvic floor are a predisposing comorbid problem in the pathogenesis of fecal incontinence [338].

Whether anal sphincter pressures change with aging is debatable [339, 340]. In both men and women 70 years of age there was a 30% to 40% decrease in sphincter pressures compared to patients 30 years [341]. In another study, elderly subjects were found to have lower sphincter pressures, [342] but many were taking medications that may have affected muscle function. In contrast, other studies that have examined anal pressures have reported only insignificant decreases with age[343]. However, in all age groups squeeze pressure has been shown to be significantly lower in women than in men.[339, 343, 344]. Furthermore, in women, there appears to be a rapid fall in squeeze pressure after menopause[344, 345]. Recently, estrogen receptors have been identified in the human striated anal sphincter[346]. In an

experimental study of adult rats, ovariectomy led to atrophy of the striated anal sphincter muscle, [346-348] which suggests that the strength and vigor of the pelvic floor muscles is influenced by hormones. Also, in older women, pudendal nerve terminal motor latency [PNTML] is prolonged [341, 349] and there is excessive pelvic floor descent on straining [341, 342]. These mechanisms may lead to progressive damage to the striated anal sphincter muscle due to repeated stretch injury during straining [212, 349, 350]. An anal endosonography study also showed that aging was associated with an increase in the thickness and echogenecity of the internal sphincter muscle [351].

Other causes of anatomic disruption include iatrogenic factors such as anorectal surgery for hemorrhoids, fistula, or fissures. Anal dilation or lateral sphincterotomy may result in permanent incontinence due to fragmentation of the anal sphincter apparatus [352, 353]. Contrary to the belief of many surgeons, hemorrhoidectomy can cause incontinence by inadvertently damaging the IAS [354] or through the loss of endovascular cushions. Accidental perineal trauma or a pelvic fracture may also cause direct sphincter trauma leading to fecal incontinence. Interestingly, a study of homosexual men showed that although the anal resting pressure of the subjects was lower and the anal sphincters were thinner than those of controls, there was no evidence of sphincter injury from ano-receptive intercourse [355]. These results suggest that anal intercourse may not cause sphincter trauma, at least in men. Finally, in the absence of traumatic structural defects, internal sphincter dysfunction may also occur because of myopathy, [356] internal sphincter degeneration, [357] or as a complication of radiotherapy [358, 359].

b) Puborectalis muscle

Sir Allan Parks believed that the pressure exerted by the anterior rectal wall together with the puborectalis muscle was fundamental to maintaining continence as it formed a flap valve mechanism[360]. This concept was disputed in another study that imaged the rectum radiologically while simultaneously measuring rectal and anal canal pressures, as well as anal electromyogram (EMG) activity, during defecation maneuvers [361]. The authors concluded that continence was maintained primarily by increased activity of the EAS muscle and the puborectalis muscle and that rectal pressures were consistently lower than those generated within the anal canal [361]. Similar observations were made by another group [362]. Also, after successful sphincter repair, continence was associated with higher sphincter pressures and not with an altered anorectal angle [363]. These findings suggest that an obtuse anorectal angle may represent an epiphenomenon in patients with incontinence.

The nerve supply for the upper portion of the puborectalis muscle arises from direct branches of the anterior S3 and S4. Thus, the puborectalis muscle and the external anal sphincter have separate neurological innervation. Consequently, pudendal blockage does not abolish voluntary contraction of the pelvic floor [364] but completely abolishes EAS function.11, [301, 364] It has been suggested that continence can be preserved following division of the EAS and IAS provided the puborectalis muscle is intact [365]. Moreover, division of the puborectalis muscle posteriorly does not produce incontinence as long as anal sphincter pressures are normal [366]. Thus, although the puborectalis plays an integral role in maintaining continence, its precise role is poorly understood.

c) Neuropathy

An intact innervation of the pelvic floor is essential for maintaining continence. Sphincter degeneration secondary to pudendal neuropathy and obstetric trauma may cause fecal incontinence in women[350]. The neuropathic injury is often sustained during childbirth, probably due to stretching of the nerves during elongation of the birth canal or through direct trauma during the passage of the fetal head. The nerve damage is more likely to occur when the fetal head is large, when the second stage of labor is prolonged, and when forceps are applied, especially high forceps delivery or if there is prolonged labor [334, 336, 350, 362, 367, 368]. Damage to the innervation of the pelvic floor musculature is usually asymmetrical [369]. Subsequent vaginal deliveries may further damage the pudendal nerves [333]. In another study of women who sustained obstetric sphincter injury, the only risk factor associated with the development of fecal incontinence was prolonged PNTML [370].

1. Autonomic neuropathy

The role of extrinsic autonomic innervation is somewhat controversial. Animal studies have shown that the pelvic nerves convey relaxatory fibers to the rectum [371]. Consequently, these nerves may play a role in accommodating and storing feces and gas

[372]. Damage to the pelvic nerves may lead to impaired accommodation and rapid transit through the rectosigmoid region, overwhelming the continence barrier mechanisms. Sympathetic efferent activity, as studied by stimulating the pre-sacral sympathetic nerves, tends to relax the IAS, [372, 373] whereas parasympathetic stimulation may cause contraction of the anal sphincter.

The upper motor neurons for voluntary sphincter muscle lie close to those innervating the lower limb muscles in the para sagital motor cortex adjacent to the sensory representation of the genitalia and perineum in the sensory cortex[368]. Consequently, damage to the motor cortex from central nervous system (CNS) lesions may lead to loss of bowel control and to incontinence. In some patients with neurogenic incontinence there is damage to both the sensory and motor nerve fibers, resulting in sensory impairment [308, 374, 375]. This can impair conscious awareness of anal filling[376] as well as the associated reflex responses in the striated pelvic floor sphincter muscles.

Approximately 10% of patients with fecal incontinence may have lesions more proximal than the intra pelvic or perianal nerves. The primary abnormality in these patients is cauda equina nerve injury[368] which may be occult and not evident through clinical evaluation. These patients have a prolongation of nerve conduction along the cauda equina nerve roots without an abnormality in PNTML muscles[368, 377, 378]. In a minority of patients, however, there is a combination of peripheral and central lesions [377]. Other disorders such as multiple sclerosis, diabetes, and demyelination injury (or toxic neuropathy from alcohol or traumatic neuropathy) may also lead to incontinence [379-385].

d) Rectal accommodation and reservoir function

The rectum is a compliant reservoir that stores stool until social conditions are conducive for its evacuation [385, 386]. If rectal wall compliance is impaired, a small volume of stool material can generate high intrarectal pressure that can overwhelm anal resistance and cause incontinence [387]. Etiologies include radiation practitis, ulcerative colitis, [387, 388] or Crohn's disease, an infiltration of the rectum by tumor or following radical hysterectomy [359]. Likewise, rectal surgery, in particular pouch surgery, [389] and spinal cord injury, [390, 391] may also be associated with loss of rectal compliance.

III. FUNCTIONAL MECHANISMS

1. ANORECTAL SENSATION

An intact sensation not only provides a warning of imminent defecation, but also helps to discriminate between formed stool, liquid feces, or flatus. Elderly persons, [392] physically and mentally challenged individuals, and children with fecal incontinence [393] often show blunted rectal sensation. This impaired sensation may lead to excessive accumulation of stool, causing fecal impaction, mega-rectum (extreme dilation of the rectum), and overflow [392, 393]. Impaired rectal sensation may also occur as a result of neurological damage such as multiple sclerosis, diabetes mellitus, or spinal cord injury[382, 390].

Less well known is the fact that analgesics (particularly opiates) and antidepressants may also impair rectal sensation and produce fecal incontinence. That the rectum is important in preserving continence has been shown elegantly through surgical studies in which preservation of the distal 6 cm to 8 cm of the rectum, along with its parasympathetic nerve supply, helped subjects avoid incontinence[394]. In contrast, both rectal sensation and the ability to defecate can be abolished completely by resection of the nervi erigentes [316].

An intact "sampling reflex" allows the individual to choose whether to discharge or retain rectal contents. Conversely, an impaired "sampling reflex" may predispose a subject to incontinence [319]. However, the role of the sampling reflex in maintaining continence remains unclear. In children who have had colonic pull through surgery, some degree of sensory discrimination is preserved [395]. Because the anal mucosal sensory zone is absent, it has been suggested that sensory receptors (possibly located in the puborectalis muscle) may play a role in facilitating sensory discrimination [395]. Also, traction of this muscle is a more potent stimulus for triggering both defecation and rectal distention [395].

Because abolition of anal sensation by the topical application of 5% lidocaine did not reduce resting sphincter pressure —— although it partially affected voluntary squeeze pressure and did not affect the ability to retain saline infused into the rectum —— the role of anal sensation in maintaining fecal continence has been questioned [308].

2. Dyssynergic defecation and incomplete stool evacuation

In some patients, particularly the elderly, prolonged retention of stool in the rectum or incomplete evacuation may lead to seepage of stool or staining of undergarments [392]. A majority of these patients show obstructive or dyssynergic defecation, [396] and many of them also exhibit impaired rectal sensation, [396, 397] whereby anal sphincter and pudendal nerve function is intact, but the ability to evacuate a simulated stool is impaired [396]. Similarly, in the elderly and in children with functional incontinence, the prolonged retention of stool in the rectum can lead to fecal impaction [393]. Fecal impaction may also cause prolonged relaxation of IAS tone, which allows liquid stool to flow around impacted stool and to escape through the anal canal [393].

3. C. Descending perineum syndrome

In women with long-standing constipation and a history of excessive straining for many years (perhaps even without a childbirth), excessive straining may lead to progressive deenervation of the pelvic floor muscles [212]. Most of these patients demonstrate excessive perineal descent and sphincter weakness, [212] which may lead to rectal prolapse; however, fecal incontinence is not an inevitable consequence. Whether or not incontinence develops will depend on the state of the pelvic floor and the strength of the sphincter muscles [398].

IV. STOOL CHARACTERISTICS

The consistency, volume, and frequency of stool and the presence or absence of irritants in stool may also play a role in the pathogenesis of incontinence [292, 385] In the presence of large-volume liquid stools, which often transit the hind-gut rapidly, continence can only be maintained through intact sensation and a strong sphincteric barrier. Similarly, in patients with bile salt malabsorption, or lactose or fructose intolerance or rapid dumping of osmotic material into the colon, the colonic transit is too rapid for both gaseous and stool contents and can overwhelm the continence mechanisms [385, 387].

V. MISCELLANEOUS

A variety of medical conditions and disabilities may predispose to fecal incontinence, particularly in the elderly. Immobility and lack of access to toileting facilities are primary causes of fecal incontinence in this population [399]. Several medications may inhibit sphincter tone — — for example, anticholinergics and antispasmodics. In contrast, stimulants such as caffeinated products, fiber supplements, or laxatives may cause diarrhea.

VI. TOPICS FOR FURTHER INVESTIGATION AND RESEARCH

The study of anorectal function tests in healthy subjects stratified for age, gender, and parity can help define normal values and physiologica chnages.

What is the utility of the diagnostic tests of anorectal function, both for understanding the key pathophysiological mechanisms and for predicting treatment outcomes?

Why do women who suffer obstetric injury in their 20's typically present with incontinence in their 50's? A prospective study of anorectal sphincter function in both nulliparous and multiparous women at periodic intervals over a 20- to 30-year would be indicated.

Further considerations:

1) examine the role of the puborectalis muscle in maintaining continenece;

2) the role of anal mucosal sensation in maintaining continence, particularly in patients with fecal seepage, and to develop tests for evaluating this function.

3) mechanisms responsible for fecal seepage.

4) pathophysiological basis for the rectoanal sampling reflex.

5) role of rectal accommodation and compliance in maintaining continence.

F. CHILDBIRTH AND FECAL INCONTINENCE: OBSTETRICAL PERSPECTIVE

Pregnancy and childbirth have a significant impact on the emotional and physical wellbeing of a woman. It is reported that as many as 91% of women report at least one new symptom eight weeks post-partum. [400] A fall in maternal mortality accompanied by an increase in female life expectancy (80 years in the United Kingdom) has now shifted the focus of attention towards identification of factors that may minimise morbidity. Although pre-existing bowel symptoms may be aggravated during pregnancy and childbirth, the development of symptoms de novo is a more frequent occurrence. Obstetric trauma is the commonest cause of fecal incontinence. However, the onset of symptoms may occur many years after delivery with a peak incidence in the perimenopausal years. This may reflect the effect of contributory factors such as the process of aging, the effect of the menopause or progression of neuropathy. This section focuses on the association between obstetric trauma and fecal incontinence. However to avoid confusion, the term anal incontinence is used to include incontinence to flatus, liquid and solids.

The mechanism that maintains continence is complex and affected by various factors such as mental function, lack of a compliant rectal reservoir, enhanced colonic transit and changes in stool consistency and volume. However the most important factors appear to be an anatomical intact anal sphincter complex and neurological function. In about 80% of women with presumed "idiopathic" anorectal incontinence there is histological evidence of denervation of the striated pelvic floor muscles, particularly the puborectalis and external sphincter. [401] This feature has also been demonstrated electro-physiologically by means of an increased fibre density in patients with idiopathic fecal incontinence, indicating re-innervation following denervation. [402] Another finding in these patients is a conduction delay in pudendal nerves as measured by pudendal nerve terminal motor latency (PNTML). [403].

Although Hertz in 1909 suggested that pelvic floor damage may result from a normal vaginal delivery, objective scientific evidence for this was only produced in 1984[350] and a follow-up of 14 patients 5 years later[404]. These authors studied 122 women,71 after delivery with manometry, perineometry, PNTML and EMG, and 51 before and after delivery with EMG. This study demonstrated an increase in anal sphincter striated muscle fibre density in the vaginal delivery group at 2 months post-partum indicating evidence of re-innervation following denervation. The fibre density was not altered following elective caesarean section. Thirty three percent of primiparae and 50% of multiparae had prolonged PNTML within 48 hours of delivery. However by 2 months, the PNTML had returned to normal in 60% of these women, indicating that damage to pudendal nerve conduction is reversible. Multiparity, forceps delivery, increased duration of the second stage of labour, third degree perineal tears and high birth weight were important factors leading to pudendal nerve damage. In the 5 year follow-up study of 14 women, only multiparae who did not have a forceps delivery were selected; the denervating process was found to be progressive in the majority of women, and 5 women suffered from stress incontinence of urine, 3 of whom were also incontinent to flatus.

In another prospective neurophysiological study, Allen et al [405] studied 96 nulliparous women with EMG, PNTML and vaginal pressure measurements during pelvic floor contraction. They found evidence of re-innervation in the pelvic floor muscles of 80% of primiparae 2 months after vaginal delivery. The only obstetric factors associated with re-innervation were a high birth weight and a longer active stage of labour. Forty five of the original 96 women were studied again six years later, and they concluded that changes in pelvic floor neurophysiology occur in time and do not appear to be related to further childbearing. [406]

A third prospective study[407] measured anal pressures, anal sensation and the perineal plane in 72 antenatal women and repeated 72 hours post-partum and in 41 women 2 months postpartum. Anal sensation was unchanged. Cornes et al. [408] measured anal sensation in 96 primiparae within 10 days after delivery, and measurements were repeated in 74 women 6 months after delivery. They found that at 6 months anal sensation had returned to normal. Anal sensation remained unchanged after caesarean section. In women who had a torn external sphincter, only impairment of sensation in the upper anal canal persisted at 6 months. More than half the women who admitted to persistent anal incontinence had normal anal sensation. Chaliha et al [409] measured anal electro-sensitivity before and after childbirth

and found it unchanged. Anal sensation in isolation therefore probably plays a minor role in the development of obstetric related fecal incontinence.

I. MECHANICAL TRAUMA

Until the recent advent of anal ultrasound, mechanical trauma to the anal sphincters was suspected only when there was a history of a difficult vaginal delivery, particularly a third or fourth degree tear. Consequently, when anal endosonography was performed in patients believed to be suffering from "neurogenic" fecal incontinence unsuspected internal and external sphincter defects were identified. [410] The sonographic appearance of external anal sphincter defects has been verified histologically to represent fibrosis[411]13 while the appearance of internal sphincter defects have been validated prospectively in patients undergoing lateral internal anal sphincterotomy[412]. Trauma identified by ultrasound may be occult or recognised (third/fourth degree tear).

1. Occult anal sphincter trauma

To date Sultan et al [413] have performed the only prospective study (before and after childbirth) to demonstrate both occult anal sphincter trauma and pudendal nerve damage during childbirth in both primiparous and multiparous women (n=150). Thirty five percent of primiparous women and 44% of multiparous women developed anal sphincter defects during vaginal delivery. Thirteen percent and 23% respectively developed defaecatory symptoms (fecal urgency and/or anal incontinence) after delivery. Only 2 of the 150 women (both primiparous) had tears of the anal sphincter recognized at the time of delivery. A strong association was demonstrated between the presence of any defect and the development of symptoms. Only 4% of multiparous women sustained new sphincter damage following a subsequent delivery. The single independent factor associated with anal sphincter damage was forceps delivery. The 23 women delivered by caesarean section remained asymptomatic and none developed sphincter defects. No relationship was demonstrated between latency measurements and defaecatory or urinary symptoms.

Donnelly et al [414] interviewed 219 nulliparae regarding bowel habits in the third trimester and performed anal vector manometry. At 6 weeks postpartum 184 women returned and the same bowel symptom questionnaire was completed and anal vector manometry plus PNTML measurements were performed. Anal endosonography was performed in 81 women with altered fecal continence or abnormal physiology. Instrumental vaginal delivery and a passive second stage of labour prolonged by epidural analgesia were significantly associated with the greatest risk of anal sphincter trauma and impaired fecal continence. As instrumental delivery is a known risk factor (8 fold increased risk of sphincter trauma), early use of oxytocin was recommended to shorten the second stage. A continuation of the same study[415] reported that pudendal nerve latencies were prolonged and the squeeze pressure increment was reduced in those women who had a caesarean section in the late first stage (>8cm cervical dilatation) or second stage.

Chaliha et al [409] measured anal sensation and manometry in 286 nulliparae during the third trimester and repeated in 161 women postpartum when anal endosonography was also performed. Anal endosonography revealed sphincter defects in 38% of women and this was associated with the presence a lowering of anal squeeze and resting pressures. Threshold anal electrosensitivity remained unchanged and bore no relationship to symptoms. Postpartum sphincter defects were associated with perineal laceration and vaginal delivery.

Abramowitz et al [416] performed a prospective study of 233 women who had anal endosonography performed before and 6 to 8 weeks after childbirth Of the 233 women (118 primiparae) 202 had a vaginal delivery. Postpartum anal incontinence in the 233 women was reported by 13% of primiparae and 8.5% of multiparae, and anal sphincter defects in 21% and 12% respectively. However the prevalence of anal sphincter defects amongst those that had a vaginal delivery (n=202) was 26% and 13% respectively. Previous studies[417, 418] including others mentioned in Table 3 & 4 have shown that the first delivery is at greatest risk for anal sphincter trauma but this study is at variance as it claimed that secundiparous females have the same risk as primiparous women. However, this finding remains unsubstantiated and is further disputed by a more recent prospective study[419].

Fynes et al 21 undertook a prospective study of 59 previously nulliparous women through 2 successive pregnancies and found that 34% had anal sphincter injury after their first delivery but only 2 new injuries occurred after the second delivery, confirming the findings in Sultan's study15. An important finding in

this study was that 42% of women (5 of 12) who had occult sphincter injury during their first delivery (squeeze pressure increment < 20mmHg or anal sphincter defect > one quadrant) developed anal incontinence after the second delivery.

Willis et al [420] performed anal vector manometry, endosonography, PNTML and rectal sensibility at the 32 weeks and 6 weeks postpartum. Using the Kelly-Holschneider score they reported anal incontinence in 5% and identified occult injuries in 19%. PNTML and rectal sensibility was unaffected by vaginal delivery.

Nazir[421] et al performed vector manometry and endoanal ultrasound in 73 nulliparous woman at 25 weeks and 5 months postpartum (**Table 3**). There was no correlation between vector manometry and anal endosonography or clinical variables.

Belmonte-Montes[422] performed anal endosonography in 98 nulliparous women 6 weeks before and 6 weeks after delivery and after excluding 20 third degree tears found occult sphincter injuries in 13%. Seventy five percent of women with defects were symptomatic and there was a good correlation between defects and symptoms. However it is not clear as to how many with occult defects were symptomatic (Table 3).

In 3 further studies[423-425]25-27 anal ultrasound was performed only after delivery and defects were identified in 11.5 to 34% (**Table 4**). Varma et al [423] studied 159 postnatal women (105 primiparous and 54 secudiparous) and found occult anal sphincter defects in 11.5% of primiparous and 19% of secundiparous vaginal deliveries but 80% of forceps deliveries. None of their patients suffered fecal incontinence but only 72% of questionnaires were returned. However their cohort had a low forceps rate and a high caesarean section rate (25%) and a low forceps rate (4%).

Results discussed in this section are listed in Table 3 & 4.

2. Third/fourth degree obstetric tears

It is unclear as to whether the sonographic anal sphincter defects described above represent tears that have been missed at delivery or true "occult" defects that may not be visible to a trained doctor or midwife. Groom and Patterson-Brown [426] conducted a study in which they demonstrated that the rate of third degree tears rose to 15% when all "2nd degree tears" were examined by a second person, confirming that at least some tears are being missed. This reflects inadequate training and was highlighted by Sultan et al [427] who reported that 91% of doctors who had done at least 6 months of training in obstetrics and 60% of midwives indicated inadequate training in perineal anatomy, and 84% and 61% respectively reported inadequate training in identifying 3rd degree tears. Another possible reason for under-diagnosis is that tears of the anal sphincter have been wrongly classified and therefore anal sphincter tears have been under-reported. Any involvement of the anal sphincter should be classified as third degree. However 41% of doctors and 16% of midwives classified a torn anal sphincter as a 2nd degree tear[427]. Sultan and Thakar reviewed every relevant text book (n=65) in the library of the Royal College of Obstetricians and Gynaecologists (RCOG) and found that there was a lack of consistency in classification and in about 40% the classification was omitted or wrong[428]. Furthermore previous classifications are incomplete because they do not incorporate depth of external sphincter rupture or involvement of the internal sphincter. This therefore has epidemiological, clinical and medicolegal implications. If a third degree tear is incorrectly classified as second degree, then inappropriate repair could result in sub-optimal outcome (see below). Sultan[429] has therefore proposed the following classification to be incorporated in the 29th RCOG green top guidelines[430]:

First degree: laceration of the vaginal epithelium or perineal skin only.

Second degree: involvement of the perineal muscles but not the anal sphincter.

Third degree: disruption of the anal sphincter muscles and this should be further subdivided into:

3a: <50% thickness of external sphincter torn.

3b: >50% thickness of external sphincter torn.

3c: internal sphincter torn also.

Fourth degree: a third degree tear with disruption of the anal epithelium.

An isolated rectal tear without involvement of the anal sphincter is rare and should not be included in the above classification.

Primary sphincter repair of a third or fourth degree obstetric tear is usually performed by obstetricians using the end-to-end repair technique[336]35. However as shown in **Table 5**, anal incontinence occurs in 15 to 59% and in addition, urgency can affect a further 6[336, 431] to 28%. Frank fecal

Table 3. Prospective studies of "occult" anal sphincter injury and anal incontinence, excluding fecal urgency before/after vaginal delivery

Study	Parity	Vaginal delivery Numbers	FU in weeks postpartum	Sphincter Defects	Anal incontinence
Sultan et al 93[413]	Primi Multi	79 48	6 6	33% 44%	5% 19%
Donnelly et al 98[414]	Primi	168	6	35%	25%
Rieger et al98 [424]	Primi	37	6	41%	8%
Zetterstrom et al 99 [425]	Primi	38	9	20%	18%
Fynes et al 99[419]	Multi	59	6-12	37%	17%
Abramowitz et al 00[416]	Primi Multi	202 including multi	8	26% 13%	15% 10%
Chaliha et al 01[409]	Primi	130	12	19%	13%
Belmonte-Montes et al 01[422]	Primi	78	6	13%	?
Nazir et al 02[421]	Primi	73	20	19%	25%
Willis et al 02[420]	Primi; Multi	42	12	10%	5%
MEAN (excluding Willis&al)	Primi; Multi			28% 31%	16% 15%

Table 4. Studies of "occult" anal sphincter injury during vaginal delivery and anal incontinence excluding fecal urgency (postnatal).

Study	Vaginal delivery	Parity	FU postpartum	Defects	Anal incontinence
Varma et al 99[423]	78	Primi	4 weeks	11.5%	0%
	31	Multi	4weeks	19%	0%
Damon [532] *	197	Primi	3 months	34%	6%
Faltin [533] **	150	Primi	3 months	28%	15%

*Ultrasound performed < 1 week after delivery

** anal ultrasound performed immediately after delivery before perineal repair

Table 5. Prevalance of anal incontinence after primary anal sphincter rupture

Authors	Year	Country	N	Follow-up Months	Anal incontinence
Sangalli et al [431]	2000 S	witzerland	177	13 years	15%
Wood J et al [534]	1998	Australia	84	31	17%*
Walsh et al [535]	1996	UK	81	3	20%
Sander et al [536]	1999	Denmark	48	1 2	1%
Crawford et al [537]	1993	USA	35	12	23%
Sorensen et al [538]	1993	Denmark	38	3	24%
Nielsen et al [539]	1992	Denmark	24	12	29%
Go & Dunselman[540]	1988	Netherlands	20	6	30%
Fenner et al [541]	2003	USA	165	6	30%
DeLeeuw [440]	2001	Netherlands	125	14 years	31%
Wagenius[542]	2003	Sweden	186	4 years	33%
Uustal Fornell et al [543]	1996	Sweden	51	6	40%
Poen et al [433]	1998	Netherlands	117	56	40%
Sultan et al [336]	1994	UK	34	2	41%
Zetterstrom et al [544]	1999	Sweden	46	9	41%
Sorensen et al [545]	1988	Denmark	25	78	42%
Tetzschner et al [370]	1996	Denmark	72	24-48	42%
Williams et al [546]	2003	UK	124	?	42%
Kammerer-Doak et al [547]	1999	New Mexico	15	4	43%
Haadem et al [548]	1988	Sweden	62	3	44%
Bek & Laurberg[549]	1992	Denmark	121	?	50%
Davis et al [550]	2003	UK	52	3.6	50%
Fitzpatrick et al [432]	2000	Ireland	154	3	53%
Nazir et al [551]	2003	Norway	100	18	54%
Gjessing H et al [552]	1998	Norway	38	12-60	57%
Goffeng et al [553]	1998	Sweden	27	12	59%
MEAN					37%

* Includes 2 with secondary sphincter repair

incontinence affected 9% (range 2 to 23%). In five studies[336, 432] anal endosonography was performed to demonstrate persistent anal sphincter defects following repair in 40 to 91% of women. Forceps delivery, first vaginal delivery, large baby, shoulder dystocia and a persistent occipito-posterior position have been identified as the main risk factors for the development of a third/fourth degree tear[336, 416, 417, 433].

The most popular method of repair of the external sphincter is the end-to-end technique but colorectal surgeons prefer the overlap technique for secondary repair because of better outcome[434]. It is now known that like other incontinence procedures outcome can deteriorate with time and one study has reported 50% continence at 5-year follow-up[435].However some women in this study had more than one attempt at sphincter repair[435]. Sultan et al. were the first to describe the overlap technique for acute anal sphincter rupture and in addition advocated the separate identification and repair of the internal sphincter. Compared to matched historical controls who had an end-to-end repair, anal incontinence could be reduced from 41% to 8% using the overlap technique and separate repair of the internal sphincter[434].

However as the two operators performing the repair had a specialised knowledge of the anal sphincter anatomy it could have biased their results and they therefore recommended a randomised trial. The only published randomised trial published to date is by Fitzpatrick et al in Dublin[432] who found no significant difference between the 2 methods of repair although there appeared to be trend towards more symptoms in the end-to-end group.

There were methodological differences in that the torn internal sphincter was not identified and repaired separately and they used a constipating agent for 3 days after the repair. Nevertheless as the authors concur, a better outcome would be expected with both techniques as a consequence of focused education and training in anal sphincter repair. Fernando et al [436] performed a multicentrerandomised trial of end –to-end vs overlap using the the technique described by Sultan et al. [434] At one year follow-up they found significantly more urge fecal incontinence in the end-to-end group (24% vs 0; P=0.006)[436].

A summary of studies reporting the prevalence of anal incontinence following primary repair of obstetric anal sphincteer rupture is listed in Table 5.

a) Management of subsequent pregnancy

All women who sustained a third/fourth degree tear should be assessed in hospital by a senior obstetrician 6 to 8 weeks after delivery. Some centres have established dedicated multidiscliplinary perineal clinics. It is important that a careful history is taken regarding bowel, bladder and sexual function. As these symptoms are embarrassing, a structured questionnaire may be useful. A careful vaginal and rectal examination should be performed to check for complete healing, scar tenderness and sphincter tone[437, 438]. We recommend that all women should have ano-rectal investigations (endosonography and manometry) but if such facilities are unavailable locally then at least symptomatic women should be referred for investigations (Fig 2)[428]. Mild incontinence (fecal urgency or flatus incontinence) may be controlled with dietary advice, constipating agents (loperamide or codeine phosphate), physiotherapy or biofeedback. However women who have severe incontinence should, in addition, be offered secondary sphincter repair by a colorectal surgeon. Asymptomatic women must be advised to return if symptoms develop.

There are no randomised studies to determine the most appropriate mode of delivery. Women who have had a successful secondary sphincter repair for fecal incontinence should be delivered by caesarean section[439]. Some women with fecal incontinence may chose to complete their family prior to embarking on anal sphincter surgery. It remains to be established whether these women should be allowed a vaginal delivery as it could be argued that damage has already occurred and risk of further damage is minimal and possibly insignificant in terms of outcome of surgery.

Very few text books discuss management in a subsequent pregnancy but some indicate that caesarean section should be considered particularly after a difficult repair[428]. It has been suggested that a caesarean section should be performed even after transient anal incontinence[370] but this has been questioned[439].

In order to counsel women with previous 3rd/4th degree tears appropriately, we find it useful to have a symptom questionnaire, anal ultrasound and manometry results. If vaginal delivery is contemplated then these tests should be performed during the current pregnancy unless performed previously and found to be abnormal. Current evidence suggests that if a large sonographic defect (> one quadrant) is pre-

sent or if the squeeze pressure increment is less than 20 mmHg then the risk of impaired continence is increased to 42% after a subsequent delivery[415]. Our policy is to counsel these women and offer a caesarean section especially especially to those who are symptomatic. Asymptomatic women who do not have compromised anal sphincter function can be allowed a normal delivery by an experienced accoucher. Although 11% of textbooks recommend a prophylactic episiotomy[428] there is limited evidence that an elective episiotomy prevents subsequent anal sphincter disruption[440] while o other studies have indicated that episiotomy may increase the prevalence of anal sphincter disruption. Preliminary results of our multicentre study (unpublished data) does not support the practice of prophylactic episiotomy and therefore we only be perform it if clinically indicated.

II. EFFECTS OF INSTRUMENTAL VAGINAL DELIVERY

Although only 4% of women delivered by forceps sustain a 3rd/4th degree tear, up to 50% of those that do tear have an instrumental delivery[336]. Vacuum extraction is associated with fewer 3rd /4th tears than forceps and this view is supported by 2 large randomised studies[441, 442]. A UK study[441] where mediolateral episiotomy is practised reported severe vaginal lacerations in 17% of forceps compared to 11% of vacuum deliveries and a Canadian study[442]69 where midline episiotomy is practised reported 3rd /4th tears in 29% of forceps compared to 12% of vacuum deliveries. In a Cochrane review (ten trials)[443] use of the vacuum extractor instead of forceps was associated with significantly less maternal trauma (odds ratio 0.41, 95% confidence interval 0.33 to 0.50) and with less need for general and regional anaesthesia. There were more deliveries with vacuum extraction (odds ratio 1.69, 95% confidence interval 1.31 to 2.19) and fewer caesarean sections were carried out in the vacuum extractor group. However the vacuum extractor was associated with an increase in neonatal cephalhaematomata and retinal haemorrhages. Serious neonatal injury was uncommon with either instrument.

Occult trauma to the anal sphincter has also been identified more frequently in forceps delivery occurring in up to 80 percent. [413, 423, 444]. A small randomised study (n=44) confirmed this by identifying occult anal sphincter defects in 79% of forceps compared to 40% of vacuum deliveries[413]. Trauma occurs more frequently when a second instrument is used to attempt vaginal delivery[413] and therefore if delivery fails with the appropriate technique and vacuum cup, one should resort to a caesarean section. Metal cups appear to be more suitable for 'occipito-posterior', transverse and difficult 'occipito-anterior' position deliveries[445]. The soft cups seem to be appropriate for straightforward deliveries as they are significantly more likely to fail to achieve vaginal delivery (odds ratio 1.65, 95% confidence interval 1.19 to 2.29). Although, they were associated with less scalp injury (odds ratio 0.45, 95% confidence interval 0.15 to 0.60), there was no difference between the two groups in terms of maternal injury. Farrell et al [446] performed a prospective study of 690 primigravid women and found that forceps delivery was associated with a higher incidence of flatal incontinence (RR 2.6) compared to vaginal delivery and both flatal (RR 2.6) and fecal (RR 3.6) incontinence compared to caesarean delivery. Vacuum delivery did not increase the risk of flatal incontinence. In qnother recently study by MacArthur et al [447] performed the largest questionnaire based multicentre study to establish the prevalence of fecal incontinence at 3 months post-partum. They reported a prevalence of 9.2%, with 4.2% reporting it more often than rarely. Forceps delivery was associated with almost twice the risk of developing fecal incontinence whereas vacuum extraction was not associated with this risk. These studies support the recommendation by the Royal College of Obstetricians and Gynaecologists (RCOG) that the vacuum extractor should be the instrument of choice[448].76

III. EPISIOTOMY

There is now considerable observational data to indicate that a reduction in episiotomy rate is not associated with an increase in anal sphincter rupture[449]. The Cochrane database[450] shows that restricting the use of episiotomy is associated with less posterior trauma. Although anterior perineal trauma was increased it had no effect on the development of urinary incontinence. Henrikssen et al [451, 452] performed an observational study in which they noted that when midwives who previously had a high episiotomy rate reduced their rate, the prevalence of ASR (anal sphincter rupture) also reduced. However this beneficial effect was abolished when midwives with a low rate of episiotomy attempted to reduce it even further. Based on this evidence, it was suggested that the ideal episiotomy rate should lie between 20 to 30% and no more. Midline episiotomies are more popular in North America as it is believed that

they are more comfortable and recovery is less complicated. However Coats et al [453]81 performed a randomised study of 407 primiparae and found 12% of midline episiotomies extended into the anal sphincter compared to 2% of mediolateral episiotomies. Although the perineum was significantly less bruised in the midline group and sexual intercourse commenced earlier, pain and wound breakdown was similar in both groups.

IV. DELIVERY TECHNIQUES

Pirhonen et al [454] compared the frequency of anal sphincter rupture in low risk deliveries between two Scandinavian countries (26 541 vaginal deliveries) and found the risk to be 13 times higher in Sweden (Malmo) vs Finland (Turku). They speculated that the only explanation for this was a difference in manual support given to the baby's head during crowning and pushing the perineum under the chin.

V. TRAINING

There is evidence from one study[427] that perineal anatomy is poorly understood by midwives and trainee doctors, who perform the bulk of deliveries in the UK. In this study 41% of trainees and 16% of midwives incorrectly classified a partial or complete tear of the EAS as 'second degree'. Inconsistency in classification of tears would allow many injuries to pass, unrecognised. It has been shown that hands-on workshops on perineal repair (www.perineum.net) can change practice[455] and therefore intensive and focused training in perineal anatomy and repair should therefore become an essential module in the programme for trainees.

VI. IRRITABLE BOWEL SYNDROME (IBS)

IBS affects 3-17% in selected populations and the cause remains unknown. Donnelly et al [456] recruited 312 primiparous women and reported that 11% of young primiparous women (n= 34 of 208) suffered from pre-existing IBS prior to their first pregnancy. Twenty four percent reported symptoms of impaired fecal continence in the puerperium but symptoms were found significantly more frequently in those with IBS compared to those with normal bowel habit (71% vs 18%). However women suffering from IBS are no more likely to incur mechanical or neurologic injury to the anal sphincter. Women with IBS delivered by caesarean section did not have altered continence postpartum. However 6 months postpartum there were no symptomatic differences between those with IBS and those without but only 90 of the 107 women who had either impaired fecal continence or abnormal anal manometry were studied. Treatment is directed towards the predominant symptom and although antispasmodics such as hyoscine, mebeverine and dicyclomine are used widely to relax intestinal smooth muscle, they should be avoided during pregnancy.

VII. CONCLUSIONS AND RECOMMENDATIONS

a) Compared to forceps the vacuum extractor is associated with less perineal and anal sphincter trauma; it should therefore be the instrument of choice (Level 1).

b) Compared to midline episiotomy, mediolateral episiotomy is associated with a lower risk of anal sphincter rupture (12% vs 2%). (Level 1)

c) Liberal use of episiotomy is not beneficial (Level 1). Restricting the rate of episiotomy to about 30% may reduce the risk anal sphincter injury.(Grade C)

d) A prolonged active second stage of labour is associated with denervation of the pelvic floor and one study has suggested that this also occurs with a prolonged passive second stage of labour with epidural analgesia. In these circumstances, early use of oxytocics in the second stage of labour may be useful. (Grade C)

e) Selective use of caesarean section should be considered, particularly in those who have evidence of compromised anal sphincter function and those who have had previous successful continence or prolapse surgery.(Grade C)

f) The value of antenatal pelvic floor exercises in the prevention of incontinence and prolapse could be of benefit but is currently being evaluated in randomised studies.

g) Modification in techniques of delivery of the baby may reduce anal sphincter injury and further research is needed.

g) A more focused training program for doctors and midwives needs to implemented. There is a poor understanding of perineal and anal sphincter anatomy and hence identification of anal sphincter trauma, incorrect classification and poor outcome of repair. (Grade D)

G. URINARY INCONTINENCE IN MEN: THE ROLE OF OBSTRUCTION AND PROSTATIC SURGERY

Concepts regarding male continence have arisen primarily through experience with spinal injury and neurological disease. Only recently has incontinence in aging men and women, and men with post-prostatectomy incontinence been studied more carefully. Progress has been limited by lack of knowledge about normal human anatomy and physiology and uncertainty regarding the existence and role of "internal" and "external" sphincters [457]. Urodynamic studies characterizing detrusor function and sphincter coordination in neurological injury and illness are abundant, but these have still not successfully solved the more recent problems of sphincteric injury following radical prostatectomy and brachytherapy for prostate cancer. Studies of normal and damaged sphincteric function in men remain limited. Urodynamic methods, electromyography and advanced imaging techniques such as magnetic resonance imaging (MRI) are powerful tools which could provide information about structure and function.

Incontinence in men may result from failure of the bladder to store, as in neurological injury or disease, or from direct sphincter injury following radical prostatectomy, or less frequently, simple prostatectomy (transurethral or open). Injury may be caused by pelvic trauma resulting in pelvic fracture with membranous urethral disruption, or by physical agents such as therapeutic radiation. Although pathophysiology may initially be classified into sphincteric and bladder causes, clinical experience sugggests considerable overlap between them. We have already discussed bladder dysfunction in the elderly and in neurological illness and injury. This following section focuses on post-prostatectomy incontinence.

I. THE SPHINCTER OF THE MALE

The anatomy of the male urogenital diaphragm has been well characterized by Oelrich[458] and Myers[459, 460]. Myers has developed many of hisinsights based on expperience withradicalprostatectomy. His work has included three dimensional magnetic resonance imaging reconstruction of the male urogenital diaphragm [460]. Anatomical studies clearly show that the urogenital diaphragm is a vertically oriented tapering sleeve of striated muscle surrounding the smooth muscle of the urethra, which is itself a continuation of detrusor fibers. The structures in men and women are remarkably similar, as underscored in the works on men and women by Oelrich as previously cited: the sleeve is quite narrow at the apex and wider at the base, partially open posteriorly in women to permit passage of the vagina, but completely closed in men where it is contiguous with the bulbospongiosus muscle. There are slips of pubococcygeus muscle of the levator ani investing the edges of the rhabdosphincter. However, the levator ani muscles do not encircle the urethra in men or women. Recent anatomical studies have confirmed these observations, particulalry those regarding the lack of posterior urethral support in men (as well as women) [461].

These two muscle groups, levator ani and urethral rhabdosphincter, differ as to type. Levators are predominantly fast-twitch, Type II, while periurethral striated muscles are predominantly Type I, slow twitch, providing sustained tone. Thus after radical prostatectomy it is possible to interrupt the stream voluntarily by forceful contraction of the levators, yet still have continuous sphincteric incompetence because of periurethral rhabdosphincter insufficiency.

The pubourethral complex stabilizes the urethra and permits the bladder to expand away from a fixed retropubic attachment and contract toward it during micturition. It seems likely that stabilization and accurate positioning of the male urethra and the ejaculatory ducts during vaginal penetration and seminal emission would be the primary function of these structures. Their presence in the female may be incidental, much as the mammary gland is in the male. It is not at all clear that pubourethral suspension by this fascial complex is essential for continence, although certain groups have recommended preservation of these structures following radical prostatectomy as a means of improving continence preservation after this operation.

II. POST-PROSTATECTOMY INCONTINENCE

In 1994, the Agency for Health Care Policy and Research published clinical guidelines for the diagnosis and treatment of benign prostatic hyperplasia[462]. The guidelines panel reviewed 27 articles

regarding transurethral prostatectomy and 30 articles regarding open prostatectomy to analyze treatment outcomes. The panel reported that the risk of total incontinence, defined as complete loss of voluntary control over micturition was of great concern to patients facing a treatment decision for BPH. In an overall ranking of 15 different outcomes, the panel's proxy judges ranked total incontinence of urine as the fourth most important outcome influencing a treatment decision. "The panel's review showed stress incontinence to occur in 1.9 percent and urge incontinence in 0.5 percent of patients following open prostatectomy. Average total urinary incontinence was 0.5 percent.

After TURP, 2.1 % of patients experienced stress incontinence, 1.9 % had urge incontinence, and 1.0% were reported to have total incontinence. The panel attempted to abstract data on urge incontinence, but found very few studies reporting this particular outcome, therefore a statistical analysis was not performed.

Turner-Warwick et al. [463] first directed attention to the relationship of bladder outlet obstruction, the symptoms of frequency, urgency and urge incontinence (now commonly known as LUTS: Lower Urinary Tract Symptoms) and the correlation of these symptoms with detrusor overactivity seen on cystometry. They noted that in 75% of men, symptoms were relieved by prostatectomy. Several contemporary explanations for the cause of persistent overactivity after obstruction endure.

These include denervation supersensitivity of the bladder muscle [464-466], alterations in collagen composition of the obstructed bladder [467], emergence of altered and increased sensory reflexes mediating the micturition reflex [468, 469], and physical changes in detrusor myocytes affecting electrical transmission [470].

Causes of sphincteric damage after transurethral or open prostatectomy for BPH include direct damage to endoluminal tissue distal to the verumontanum because of surgical error or loss of landmarks, unexpected infiltration of the sphincter by carcinoma with loss of urethral compliance, and electrocautery injury to the sphincter. Incontinence after simple prostatectomy is more likely due to bladder dysfunction than pure sphincteric injury[471]. Incontinence after radical prostatectomy, an operation now being performed commonly today, is more likely due to sphincteric injury.

III. RADICAL PROSTATECTOMY

Although experienced surgical centers report low rates of incontinence after radical prostatectomy, the overall prevalence in the general practicing community is unknown and may be higher. Initial urodynamic studies of incontinence after radical prostatectomy disagreed regarding etiology, although most suggest that sphincteric injury rather than bladder dysfunction was the primary cause of leakage. Further evidence has accumulated from studies since the last ICI report reinforcing the conclusion that sphincteric damage is the primary cause of incontinence after total prostatectomy.

Direct exposure and manipulation of the sphincter during radical retropubic prostatectomy (RRP) would suggest that sphincteric damage is the most likely cause of incontinence. Successful treatment with the artificial urinary sphincter prosthesis would also indirectly suggest that primary sphincteric injury is the major cause of incontinence, since outcome is usually not complicated by bladder dysfunction.

IV. ESTIMATES OF POST-PROSTATECTOMY INCONTINENCE

Initial estimates of incontinence, reviewed at the time of the first ICI report, were significant. In 1993, The American College of Surgeons Commission on Cancer reviewed the reported results of 2,122 patients treated by radical prostatectomy performed at 484 institutions in 1990 [472]. Only 58% reported complete continence, 23% reported occasional incontinence not requiring pads, 11.2% wore 2 or fewer pads per day, 4% wore more than 2 pads per day, and 3.6% were completely incontinent. In 1992, Fowler et al published the results of an outcomes study with worse results [473]. In this series of Medicare patients (age >65) surveyed by mail, telephone, and personal interview, over 30 percent reported currently wearing pads or clamps to deal with wetness; over 40 percent said they dripped urine during cough or when the bladder was full; 23 percent reported daily wetting of more than a few drops. Six percent had surgery after the radical prostatectomy to treat incontinence.

In an editorial critical of both reports, Walsh [474] noted that the ACS results showed 81.1% complete continence without pads. He noted also that 40% of

the men in the ACS series had Stage C or D (T3 or greater) disease which could decrease the rate of post-operative continence. In reviewing several reports from centers with broad experience (now referred to as "centers of excellence"), he noted that the incidence of significant urinary incontinence was low (2-5%) and the need for artificial sphincter was rare (0-0.5%) [474]. Further data have indicated that centers of excellence now reporting continence rates of approximately 88-95%.

There may be significant discrepancy between self-reported and objectively evaluated estimates of incontinence. Morten et al [475] reported on the results of 24 hour pad test at various intervals after prostatectomy: 8% of the patients were incontinent prior to surgery, 79% one month after surgery, 64% three months after surgery and 43% six months after surgery. The proportion of patients reporting problems with continence were 25% prior to surgery, 92% one month after, 81% three months after, and 50% 6 months after surgery. When directly questioned, 50% reported leaking only a few drops, a significant discrepancy between subjective perception and pad weights.

Prompted by the discrepancies between the Medicare report [473] and the reports from centers of excellence, Litweiler et al [476] reviewed continence results from 467 radical prostatectomies performed by 22 different private attending urologists in a community hospital in Texas. Of those questioned by telephone survey by an independent interviewer, 23% had been continent since surgery, 18.2% achieved delayed continence, and 58.8% were still incontinent at the time of interview. The majority of incontinent patients had stress incontinence (77.5%) while 59.8% had urge incontinence, 27.7% leaked only drops, and less than once a day. The authors concluded that these outcomes, better than the Fowler estimates, but not as good as the reports of centers of excellence were more representative of what private practitioners in America could expect with their patients.

Reports from more recent general experience as well as centers of excellence support the initial impression that incontinence varies from 2 to 10%, being worse in men as they approach the age of 70. Catalona [477] has reported that "Recovery of urinary continence occurred in 92% (1,223 of 1,325 men) and was associated with younger age ($p<0.0001$) but not with tumor stage ($p = 0.2$) or nerve sparing surgery ($p = 0.3$)." In a recent update, Walsh [478] reported that "Urinary continence, which was defined as wearing no pads, gradually improved during the first 12 months after surgery, and at 1 2 and 18 months, 93% of the patients were dry."

Estimates of post-prostatectomy continence may thus vary widely depending on how soon after surgery the results are reported, the experience of the operating surgeons and center reporting the results, the definitions of continence, the method of interview and record retrieval, and the consideration of subjective vs. objective results. It is also important to realize that growing familiarity with the operation, its surgical anatomy, and the preservation of continence, may yet improve these results in the future.

V. POSSIBLE CAUSES OF SURGICAL INJURY

Anatomical studies [458, 479] have emphasized that the urethral sphincter is a tubular structure that invests the urethra circumferentially from the pubis to the bladder neck, very much unlike the frequently described planar diaphragm on which the prostate is pictured sitting like a spinning top. Recognizing the importance of these findings, Myers [459] has drawn attention to the variability of prostatic apical anatomy and ways of avoiding injury during the operation. Myers has also suggested that some men may have congenitally short urethral sphincters which may function well enough while supplemented by additional functional length of the prostatic urethra but when shortened after prostatectomy, these urethrae may fall below a critical level of functional length [480]. A recent report of 211 patients studied by endorectal MRI coil has shown that continence is more likely to occur if the membranous urethral length is greater than 12 mm[481]. Concern about apical surgical margins,however, may limit widespread application of these insights.

The innervation of the periurethral striated sphincters is by the pudendal nerve traveling beneath the levator ani to branch within the pelvis [482] and beneath the pubis [483] The subpubic branches separate from the subpubic portion of the dorsal nerve of the penis after its division from the pudendal nerve. The branches migrate in a retrograde manner toward the sphincteric urethra. Whether these fibers are motor or sensory and what their role in post-prostatectomy incontinence might be has not yet been determined. These fibers could easily be injured by excessive cautery, suture placement into the dorsal vein complex or traction on the subpubic urethra at

the time of apical dissection. Hollabaugh et all have attempted to identify and preserve these branches by modifying their surgical technique. They reported improved continence after doing so [484]. A similar approach to identify and preserve apical branches which might innervate the sphincter was reported by Kaye et al [485].

Additional studies have suggested that denervation of the urethra or the bladder may occur during radical prostatectomy. John et al studied trigonal innervation by biochemical markers and found that "urinary incontinence was associated with decreased trigonal innervation, a high sensory threshold and low maximal urethral closure pressure" [486].

The gradual return of continence noted by many surgeons reporting from centers of excellence also suggest the possibility that denervation and re-innervation may be involved in post-prostatetcomy incontinence.

Uncertainty regarding the mechanism of post-prostatectomy incontinence has led to a number of different modifications in surgical technique. Preservation of the bladder neck is reported by some to have a better outcome, but there is concern about surgical cancer margins, despite reports indicating little difference when compared to conventional techniques [487-489]. Avoiding seminal vesicle removal during surgery has been suggested as a means to avoiding injury to sensory innervation [490], but again, there may be concerns about cancer margins and the significance of leaving these structures behind. Pubourethral ligament sparing has been advocated [491, 492]. Even intra-operative suburethral sling placement has been advocated [493]. One study has compared continence after perineal and retropubic approaches, finding little difference [494].

1.7.6 Urodynamic studies: urethral injury is more significant than bladder dysfunction

Urodynamic studies have been used to investigate whether bladder or sphincter dysfunction is responsible for post-prostatectomy incontinence. In reviewing published studies, it is important to know whether patients who underwent radical prostatectomy for cancer were considered separately from those who underwent treatment for benign prostatic hyperplasia: the latter group is well known to suffer from more bladder dysfunction.

In the review of 700 patients by Walsh et al [495], no one was sufficiently incontinent to require an artificial sphincter. Eight men with the most severe incontinence requiring more than one pad per day were evaluated. The average bladder capacity was 450 cc. None of the most incontinent had uninhibited bladder contractions. There was no correlation between potency and continence and no correlation between continence and preservation or removal of one or both neurovascular bundles. The authors concluded that anatomic factors rather than preservation of autonomic innervation were responsible for post-prostatectomy incontinence.

Chao et al [496] reviewed the video-urodynamic records of 74 men referred for incontinence after radical prostatectomy. 57% had sphincter weakness alone, 39% had combined sphincter weakness and evidence of detrusor overactivity and/or decreased compliance. Only 4% had detrusor overactivity alone. 42% of the patients voided by abdominal straining without evidence of intrinsic bladder contraction. The authors concluded that detrusor abnormalities are rarely the sole cause of incontinence, with sphincter weakness being present in 96%.

In an electromyographic study of motor units of the periurethral striated sphincter in 10 men after radical prostatectomy, 7 of whom were continent, all showed loss of motor units and diminished electromyographic activity [497]. More recent reports have substantiated these early findings [498].

Hammerer et al [499] performed thorough urodynamic evaluation 6-8 weeks in 53 of 88 men who underwent radical prostatectomy. Compared to preoperative values, they found a significant decrease in maximum urethral closure pressure (89.5 + 26.5 vs. 64.9+16.9) and also functional urethral profile length (62+11.3 vs. 26.2+8.5). Although there were slight changes in bladder capacity and threshold for voiding, there was no statistically significant change in compliance. The authors noted additionally that incontinent men showed a significantly smaller functional profile length (21.5 vs. 29.9 mm) and a lower maximal urethral closure pressure (51.3 vs. 67.7 cm H2O).

Several recent studies have further extended earlier findings that sphincteric damage is the primary cause of post-prostatectomy incontinence, and even when associated when detrusor overactivity, sphincteric injury remains the primary cause [500-502]. Groutz et al examined 83 incontinent men after radical prostatectomy, concluding "sphincteric incontinence is the most common urodynamic finding in patients with post-radical prostatectomy incontinence, although other findings may coexist" [503].

One recent disturbing study reported a high incontinence rate in men undergoing relief of obstruction following brachytherapy for prostate cancer. Hu et al [504] studied 109 men who underwent brachytherapy. Ten needed surgical relief of outflow obstruction. Seven of the ten were severely incontinent afterwards. They concluded "Permanent urinary incontinence is common in patients who require a TURP or TUIP after prostate brachytherapy"

VII. ROLE OF BLADDER DYSFUNCTION IN INCONTINENCE AFTER RADICAL PROSTATECTOMY

Only two earlier studies had suggested that bladder dysfunction might be significant. Goluboff et al [505] evaluated 56 men with post-prostatectomy incontinence, 31 after transurethral, 25 after radical. Detrusor overactivity alone was present in 34 patients (61%), including 24 (77%) after transurethral resection of the prostate and 10 (40%) after radical retropubic prostatectomy. Stress incontinence alone was present in only 3 patients (5%), including 1 (3%) after transurethral resection of the prostate and 2 (8%) after radical retropubic prostatectomy. Detrusor overactivity with stress incontinence was present in 19 patients (34%), including 6 (19%) after transurethral resection of the prostate and 13 (52%) after radical retropubic prostatectomy. Of these 19 patients 4 (21%) had poorly compliant bladders. These authors concluded that detrusor overactivity was much more likely to be the cause of incontinence than sphincteric weakness.

In an editorial, Leach had drawn attention to the high prevalence of detrusor overactivity and decreased compliance he had found in post-prostatectomy patients, many of whom had undergone radical prostatectomy. [506, 507]. Referring to a more recent prospective study of 26 men before and 3, 6 and 12 months after radical prostatectomy, he noted a high incidence of de novo bladder overactivity in the incontinent patients [508]. These results, however, differed from findings in patients studied an average of 3.8 years after surgery in whom a much lower incidence of bladder dysfunction was found [496].

Identification of sphincteric and bladder dysfunction preoperatively may indicate a higher risk of urinary incontinence after radical prostatectomy [509], but it remains to be determined if such patients should be excluded form potentially curative treatment on the basis of pre-operative urodynamic testing.

VIII. EXPERIENCE WITH THE ARTIFICIAL SPHINCTER

Experience with artificial sphincter suggests that treatment of sphincteric incompetence alone can produce satisfactory results in the majority of patients with incontinence after radical prostatectomy. The experience suggests that what bladder dysfunction may co-exist has been either under-reported, or has not significantly affected the outcome with artificial sphincters [510-516] [517].

IX. CONCLUSIONS REGARDING POST-PROSTATECTOMY INCONTINENCE

While definitions and rates of post-prostatectomy incontinence may vary, most urodynamic analyses of post-radical prostatectomy incontinence would suggest that sphincter damage is a significant contributing factor. Emerging studies of incontinence after radical prostatectomy reinforce this conclusion. Sensory denervation of the urethra may also be a factor in incontinence, but the site or mechanism of potential nerve injuury is still not clear. Two urodynamic reports have suggested that bladder dysfunction may be present, but it is important to distinguish between patients with incontinence following prostatectomy for cancer and benign disease as the latter group may have more accompanying pre-operative bladder dysfunction. Reported experience with the artificial urinary sphincter supports the conclusion that treatment of sphincteric competence results in good management of post-radical prostatectomy incontinence. One can imagine several possible ways in which the operating surgeon might injure the sphincter, but it is less clear how the bladder itself might be injured, although evidence of trigonal denervation in some studies suggest that this may happen.

Even though the reported incidence of bladder dysfunction after radical prostatectomy is limited to a few studies, its potential contribution to the overall problem should not be excluded. It is possible that post-prostatectomy sphincteric incompetence facilitates bladder dysfunction in four ways: 1. A weakened sphincter may be less likely to provide the necessary recruitment and reciprocal inhibition characteristic of the storage phase of the normal bladder; 2. urine distending an incompetent proximal urethra can provoke a feeling of impending urination and a bladder contraction, 3) diminished urethral or trigo-

nal sensitivity may diminish the normal guarding reflex, and 4) poor compliance may be evident in a chronically under-distended bladder.

Regardless of etiology, post-prostatectomy incontinence is a serious complication. If sufficiently prevalent it could lead to significant objection to surgical treatment of early prostatic cancer in younger men, the very group in whom cure is most desired and most likely to be achieved. For this reason, every effort should be made to determine the relative contributions of sphincteric and bladder damage to the etiology of this problem, and further refinements in anatomical understanding, surgical technique, accurate epidemiological reporting and further urodynamic testing of patients before and after surgery should be encouraged. Finally, improved outcome studies examining the consequences of incontinence and its true effect on quality of life must be undertaken if the problem is to be placed in a clinically useful and meaningful perspective.

H. CAUSES OF TRANSIENT INCONTINENCE IN OLDER ADULTS

I. BACKGROUND

Transient causes likely account for one-third of incontinent cases among community-dwelling older people (>65 years old), up to one-half of cases among acutely-hospitalized older people, and a significant proportion of cases among nursing home residentsc [518-520].

Most causes of transient incontinence in the older population lie outside the lower urinary tract but two points are worth emphasizing. First, the risk of transient incontinence is increased if, in addition to physiologic changes of the lower urinary tract, the older person also suffers from pathologic changes. Overflow incontinence is more likely to result from an anticholinergic agent in a person with a weak or obstructed bladder, just as urge incontinence is more likely to result from a loop diuretic in someone with detrusor overactivity and/or impaired mobility [521, 522].

This fact likely explains why some controversy persists regarding some causes of transient incontinence. It also emphasizes that continence depends on the integrity of multiple domains--mentation, mobility, manual dexterity, medical factors, and motivation, as well as lower urinary tract function. Although in younger individuals incontinence usually results from lower urinary tract dysfunction alone, incontinence in older patients often results from deficits in multiple domains that together result in incontinence [523].

Attention to any one or more of these risk factors can restore continence or at least improve it. Second, although termed "transient," these causes of incontinence may persist if left untreated, and so they cannot be dismissed merely because the incontinence is of long duration.

II. QUALITY OF DATA

In older people, continence status is often not absolute, especially in those who are frail. Infrequent leakage of small amounts may appear and disappear, and reporting accuracy varies as well [524].

Furthermore, ethical constraints and methodological issues preclude robust investigations of the conditions commonly impugned as causes of transient incontinence. Thus, it is not surprising that evidence supporting the association between these conditions and transient incontinence consists predominantly of case reports and case series.

III. RESULTS OF LITERATURE REVIEW

Transient causes of incontinence in older people are shown in **Table 6** and can be recalled using the mnemonic DIAPPERS [525].

Table 6. Causes of Transient Incontinence in Older People

D	Delirium
I	Infection (UTI, symptomatic)
A	Atrophic urethritis/vaginitis
P	Psychological (e.g. severe depression, neurosis)
P	Pharmacologic
E	Excess urine output
R	Restricted mobility
S	Stool impaction

1. Delirium

"D" is for delirium, a confusional state characterized by fluctuating inattentiveness and disorientation. Its onset occurs over hours to days, as contrasted with dementia, which develops over years. Delirium can result from almost any medication and from virtually any acute illness, including congestive heart failure, deep vein thrombosis, or infection.

Many of these conditions may present atypically in older patients, and if the patient becomes confused because of them, incontinence may be the first abnormality detected [526]. Delirium leads the list because, if unrecognized, it is associated with significant mortality. Thus, in this case, meticulous medical evaluation—not cystometry—is crucial.

2. Urinary infection

Symptomatic urinary infection is another cause of incontinence, although it is an uncommon one [518]. However, asymptomatic urinary infection, which is much more common in older people, is not a cause of incontinence [527, 528].

3. Atrophic vaginitis

Atrophic vaginitis in older women is frequently associated with lower urinary tract symptoms, which occasionally include incontinence. As many as 80% of such women attending an incontinence clinic are reported to have physical evidence of atrophic vaginitis, characterized by vaginal mucosal atrophy, friability, erosions, and punctate hemorrhages12. Atrophic vaginitis has been associated with urgency and occasionally a sense of "scalding" dysuria, but both symptoms may be relatively unimpressive.

More recent epidemiologic and clinical studies have called these beliefs into question since they have demonstrated an association with estrogen treatment and the onset of incontinence. Unfortunately, limitations in their design allow for the possibility of both bias and confounding. Further research is warranted.

4. Medications

Pharmaceuticals are one of the most common causes of incontinence in older people, with several categories of drugs commonly implicated [529]. (**Tables 7 & 8**) Of note, many of these agents also are used in the treatment of incontinence, underscoring the fact that most medications used by older people are "double-edged swords." The first category of relevant drugs is the long-acting sedative/hypnotics, such as diazepam and flurazepam, which can cloud an older patient's sensorium. "Loop" diuretics, such as furosemide or bumetanide, by inducing a brisk diuresis, can also provoke leakage. Drugs with anticholinergic side effects are a particular problem and include major tranquilizers, antidepressants, anti-parkinsonian agents (e.g., benztropine mesylate or trihexyphenidyl), first generation (sedating) antihistamines, anti-arrhythmics (disopyramide), antispasmodics, and opiates. By decreasing detrusor contractility, they can cause urinary retention and overflow incontinence. They also can cause confusion. Anticholinergic agents are particularly important to ask about for two reasons. First, older patients often take more than one of them at a time. Second, they are contained in many nonprescription preparations that older people frequently take without consulting a physician.

Adrenergically-active agents have also been associated with incontinence. Many alpha-adrenoreceptor antagonists (used mainly for treatment of hypertension) block receptors at the bladder neck and may induce stress incontinence in women [530]. Older women are particularly at risk because their urethral length and closure pressure normally decline with age. Thus, prior to considering other interventions for stress incontinence in a woman taking such a drug, substitution of an alternative agent should be tried and the incontinence re-evaluated. Calcium channel blockers can cause incontinence. As smooth muscle relaxants, they can increase residual volume, especially in older adults with impaired detrusor contractility. The increased residual urine may occasionally lead to stress incontinence in women with a weak urethral sphincter, or to overflow incontinence

Table 7 : Important anticholinergic drugs and drug side effects in the elderly

Drugs	Anticholinergic Effects
Antipsychotics	Dry mouth
Tricyclic Antidepressants (not SSRI's)	Constipation
Anti-parkinsonian agents	Confusion
First generation (sedating) antihistamines	Drowsiness, fatigue
Anti-arrhythmics (disopyramide)	Tachycardia
Antispasmodics	Inhibit detrusor contractility
Opiates	Urinary retention; Blurred vision;Increased ocular pressure

Table 7. Common Medications Affecting Continence

Type of Medication	Examples	Potential Effects on Continence
Sedatives/Hypnotics	Long-acting benzodiazepines(e.g., diazepam, flurazepam)	Sedation, delirium, immobility
Alcohol		Polyuria, frequency, urgency, sedation, delirium, immobility
Anticholinergics	Dicyclomine, disopyramide, antihistamines (sedating ones only, e.g., Benadryl®)	Urinary retention, overflow incontinence, delirium, impaction
Antipsychotics	Thioridazine, haloperidol	Anticholinergic actions, sedation, rigidity, immobility
Antidepressants (*tricyclics*)	Amitriptyline, desipramine; *not* SSRIs	Anticholinergic actions, sedation
Anti-Parkinsonians	Trihexyphenidyl, benztropine mesylate (*not* L-dopa or selegiline)	Anticholinergic actions, sedation
Narcotic analgesics	Opiates	Retention, impaction, sedation, delirium
α-Adrenergic antagonists	Prazosin, terazosin, doxazosin	Urethral relaxation may precipitate stress incontinence in women
α-Adrenergic agonists	Nasal decongestants	Urinary retention in men
Calcium channel blockers	All dihydropyridines*	Urinary retention; nocturnal diuresis due to fluid retention
Potent diuretics	Furosemide, bumetanide (***not*** thiazides)	Polyuria, frequency, urgency
NSAIDsThiazolidinediones	Indomethacin, COX-2 inhibitors Rosiglitazone, pioglitazone	Nocturnal diuresis from fluid retention
Angiotensin converting enzyme (ACE) inhibitors	Captopril, enalapril, lisinopril	Drug-induced cough precipitates stress incontinence inwomen and some men after prostatectomy
Vincristine		Urinary retention from neuropathy

Examples include amlodipine (Norvasc®), nifedipine, nicardipine, isradipine, felodipine, nimodipine (Adapted from: Resnick NM. Geriatric Medicine. In: Isselbacher KJ, Braunwald E, Wilson JD, Martin JB, Fauci AS, Kasper DJ (eds), *Harrison's Principles of Internal Medicine.* McGraw-Hill, 2002; p. 34.)

in men with concurrent urethral obstruction. Finally, angiotensin converting enzyme inhibitors, by inducing cough (the risk of which is age-related), may precipitate stress incontinence in older women whose urethra has shortened and sphincter weakened with age.

5. Diuresis

Excess urinary output can also cause incontinence, especially in individuals with impaired mobility, mentation, or motivation, particularly if they also have detrusor overactivity. Causes of excess output include excess intake, diuretics (including theophylline-containing fluids and alcohol), and metabolic abnormalities (e.g., hyperglycemia and hypercalcemia). Nocturnal incontinence can be caused or exacerbated by disorders associated with excess nocturnal excretion, such as congestive heart failure, peripheral venous insufficiency, hypoalbuminemia (especially in malnourished older people), and drug-induced peripheral edema associated with NSAIDs, thiazolidinediones, and some calcium channel blockers (e.g., dihydropyridines such as nifedipine, isradipine, and nicardipine). The role of caffeine and timing of drinking fluids (e.g. in the evening or before bedtime) is still not clear, but should nonetheless be considered a possible contributing cause for nocturia and nocturnal incontinence.

6. Restricted mobility

Restricted mobility is an easily understood but frequently overlooked cause of incontinence. In addi-

tion to obvious causes, restricted mobility may be associated with orthostatic or postprandial hypotension, poorly-fitting shoes, physical deconditioning, or fear of falling, all of which are common geriatric conditions.

7. Fecal impaction

Finally, fecal impaction has been implicated as the cause of incontinence in up to 10% of older patients seen in acute hospitals9 or geriatric incontinence clinics1. One possible mechanism involves stimulation of opioid receptors [531]. A clue to the presence of fecal impaction is the onset of both urinary and fecal incontinence, usually associated with oozing of loose stool around the impaction.

IV. SUMMARY

Aside from re-challenge data for alpha adrenergic agents (Level of Evidence = 2), the level of evidence for most of thse causes is Level 3-4. Nonetheless, because they are easily addressed and contribute to morbidity beyond the lower urinary tract, they are worth identifying even if the evidence is not strong.

V. RECOMMENDATIONS

Despite the current lack of compelling data, these seven "transient" causes of urinary incontinence should be searched for in older incontinent patients before embarking on more complex assessment and management. Their prevalence is high, their treatment is straightforward, and they contribute to morbidity beyond the urinary tract. Moreover, addressing them may improve the incontinence even if it does not eliminate it, and it may make the incontinence more amenable to subsequent therapy. (Grade of recommendation C)

VI. RESEARCH PRIORITIES

Further research should be performed on the mechanisms, prevalence, incidence, and remission rates of each of the known causes of transient incontinence, and possible additional causes should be identified as well.

Since older people are heterogeneous, studies should be conducted among several subgroups, including independent and homebound community-dwelling older people, bedfast and non-bedfast institutionalized older people, and acutely hospitalized older people.

REFERENCES

1. Fall, M., G. Geirsson, and S. Lindstrom, Toward a new classification of overactive bladders. Neurourol Urodyn, 1995. 14(6): p. 635-46.
2. Fall, M., B.L. Ohlsson, and C.A. Carlsson The neurogenic overactive bladder. Classification based on urodynamics. Br J Urol, 1989. 64: p. 368.
3. DeGroat, W.C., A.M. Booth, and N. Yoshimura, Neurophysiology of micturition and its modification in animal models of human disease, in The Autonomic Nervous System: Nervous Control of the Urogenital System, C.A. Maggi, Editor. 1993, Harwood Academic Publishers: London. p. 227-290.
4. Tang, P.C. and T.C. Ruch Localization of brain stem and diencephalic areas controlling the micturition reflex. J Comp Neurol, 1956. 106: p. 213.
5. Yokoyama, O., et al., The influence of anethesia on the development of bladder hyperactivity following middle cerebral occlusion in the rat. Soc. Neurosci. Abstracts, 1997. 23: p. 1522.
6. Yoshimura, N., et al., The dopamine D, receptor agonist SKF 38393 suppresses detrusor hyperreflexia in the monkey with parkinsonism. Neurpharmacology, 1993. 32: p. 315.
7. Yokoyama, O., et al., Glutamatergic and dopaminergic contributions to rat bladder hyperactivity after cerebral artery occlusion. Am J Physiol, 1999. 276(4 Pt 2): p. R935-42.
8. Chen, S.Y., et al., Glutamate activation of neurons in cardiovarcular reactive area of the cat brain stem affects urinary bladder motility. Am J Physiol, 1993. 265: p. F520.
9. Yoshiyama, M., J.R. Roppolo, and W.C. De Groat, Effects of MK801 on the micturition reflex in the rat-possible sites of action. J Pharmacol Exp Ther, 1993. 265: p. 844.
10. Kontani, H., T. Inoue, and T. Sasaki, Effects of apomorphine on urinary bladder motility in anesthetized rats. Jpn J Pharmaco, 1990. 52: p. 59.
11. Yoshimura, N., et al., Dopamine D-1 receptor-mediated inhibition of micturition reflex by central dopamine from the substantia nigura. Neurourol Urodyn, 1992. 11: p. 535.
12. Yoshimura, N., et al., The dopamine D1 receptor agonist SKF 38393 suppresses detrusor hyperreflexia in the monkey with parkinsonism induced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). Neuropharmacology, 1993. 32(4): p. 315-21.
13. Yoshimura, N., et al, Dopamine D-1 receptor-mediated inhibition of micturition reflex by central dopamine from the substantia nigura. Neurourol Urodyn, 1992. 11: p. 535.
14. DeGroat, W.C., A.M.Booth, and N.Yoshimura, Neurophysiology of micturition and its modefication in animal medels of human disease, in The Autonomic Nervous System, in Nervous Control of the Urogenital System, C.A. Maggi, Editor. 1993, Harwood Academic Publishers: London. p. 227-290.
15. Bors, E. and A.E. Comarr, Physiology of Micturition, Its Neurological Disorders and Sequelae. 1971, Baltimore: University Park Press.
16. de Groat, W.C., et al., Mechanisms underlying the recovery of urinary bladder function following spinal cord injury. J Auton Nerv Syst, 1990. 30 Suppl: p. S71-7.
17. de Groat, W.C., et al., Organization of the sacral parasympathe-

tic reflex pathways to the urinary bladder and large intestine. J Auton Nerv Syst, 1981. 3(2-4): p. 135-60.

18. Habler, H.J., W. Janig, and M. Koltzenburg, Activation of unmyelinated afferent fibres by mechanical stimuli and inflammation of the urinary bladder in the cat. J Physiol, 1990. 425: p. 545-62.
19. Fowler, C.J., et al., Intravesical capsaicin for neurogenic bladder dysfunction. Lancet, 1992. 339(8803): p. 1239.
20. Fowler, C.J., et al., Intravesical capsaicin for treatment of detrusor hyperreflexia. J Neurol Neurosurg Psychiatry, 1994. 57(2): p. 169-73.
21. Geirsson, G., M. Fall, and L. Sullivan, Effect of intravesical capsaisin treatment on postraumatic spinal detrusor hyperreflexia and the bladder cooling reflex. Neurourol Urodyn, 1994. 13: p. 346.
22. Chancellor, M.B. and W.C. de Groat, Intravesical capsaicin and resiniferatoxin therapy: spicing up the ways to treat the overactive bladder. J Urol, 1999. 162(1): p. 3-11.
23. Lazzeri, M., et al., Intravesical resiniferatoxin for the treatment of detrusor hyperreflexia refractory to capsaicin in patients with chronic spinal cord diseases. Scand J Urol Nephrol, 1998. 32(5): p. 331-4.
24. Kruse, M.N., L.A. Bray, and W.C. de Groat, Influence of spinal cord injury on the morphology of bladder afferent and efferent neurons. J Auton Nerv Syst, 1995. 54(3): p. 215-24.
25. Steers, W.D., et al., Nerve growth factor in the urinary bladder of the adoult regulates neuronal form and function. J Clin Invest, 1991. 88: p. 1709-15.
26. Yoshimura, N. and W.C.D. Groat, Changes in electrophysiological and pharmacological properties of rat bladder afferent neurons following spinal cord injury. J Urol, 1995. 149: p. 340A.
27. Yoshimura, N., O.Yoshida, and W.C.D. Groat, Regional differences in plasticity of membrane properties of rat bladder afferent neurons following spinal cord injury. J Urol, 1995. 153: p. 262A.
28. Arbuckle, J.B. and R.J. Docherty, Expression of tetrodotoxin-resistant sodium channels in capsaicin-sensitive dorsal root ganglion neurons of adult rats. Neurosci Lett, 1995. 185(1): p. 70-3.
29. Yoshimura, N., et al., Different types of Na+ and A-type K+ currents in dorsal root ganglion neurones innervating the rat urinary bladder. J Physiol, 1996. 494 (Pt 1): p. 1-16.
30. Abrams, P.H., Detrusor instability and bladder outlet obstruction. Neurourol Urodyn, 1985. 4: p. 317.
31. Gosling, J.A., et al., Decrease in the autonomic innervation of human detrusor muscle in outflow obstruction. J Urol, 1986. 136(2): p. 501-4.
32. Harrison, S.C., et al., Bladder instability and denervation in patients with bladder outflow obstruction. Br J Urol, 1987. 60(6): p. 519-22.
33. Sibley, G.N., The physiological response of the detrusor muscle to experimental bladder outflow obstruction in the pig. Br J Urol, 1987. 60(4): p. 332-6.
34. Speakman, M.J., et al., Bladder outflow obstruction—a cause of denervation supersensitivity. J Urol, 1987. 138(6): p. 1461-6.
35. Harrison, S.C., D.R. Ferguson, and P.T. Doyle, Effect of bladder outflow obstruction on the innervation of the rabbit urinary bladder. Br J Urol, 1990. 66(4): p. 372-9.
36. Azadzoi, K.M., et al., Canine bladder blood flow and oxygenation: changes induced by filling, contraction and outlet obstruction. J Urol, 1996. 155(4): p. 1459-65.
37. Lemack, G.E., et al., Altered response to partial bladder outlet obstruction in mice lacking inducible nitric oxide synthase. J Urol, 2000. 163(6): p. 1981-7.
38. van Koeveringe, G.A., et al., Effect of partial urethral obstruction on force development of the guinea pig bladder. Neurourol Urodyn, 1993. 12(6): p. 555-66; discussion 566-71.
39. Seki, N., O.M. Karim, and J.L. Mostwin, The effect of experimental urethral obstruction and its reversal on changes in passive electrical properties of detrusor muscle. J Urol, 1992. 148(6): p. 1957-61.
40. Sjogren, C., et al., Atropine resistance of transmurally stimulated isolated human bladder muscle. J Urol, 1982. 128(6): p. 1368-71.
41. Steers, W.D. and W.C. De Groat, Effect of bladder outlet obstruction on micturition reflex pathways in the rat. J Urol, 1988. 140(4): p. 864-71.
42. Steers, W.D., et al., Alterations in afferent pathways from the urinary bladder of the rat in response to partial urethral obstruction. J Comp Neurol, 1991. 310(3): p. 401-10.
43. Ishizuka, O., et al., Role of intrathecal tachykinins for micturition in unanaesthetized rats with and without bladder outlet obstruction. Br J Pharmacol, 1994. 113(1): p. 111-6.
44. Gu, B.J., et al., Role of supraspinal tachykinins for micturition in conscious rats with and without bladder outlet obstruction. Naunyn Schmiedebergs Arch Pharmacol, 2000. 361(5): p. 543-8.
45. Lepor, H. and G. Machi, Comparison of AUA symptom index in unselected males and females between fifty-five and seventy-nine years of age. Urology, 1993. 42(1): p. 36-40; discussion 40-1.
46. Resnick, N.M., S.V. Yalla, and E. Laurino, The pathophysiology of urinary incontinence among institutionalized elderly persons. N Engl J Med, 1989. 320(1): p. 1-7.
47. Griffiths, D.J.e.a., Geriatric urge incontinence : basic dysfunction and contributory factors. Neurourol Urodyn, 1990. 9: p. 406.
48. Kitada, S., et al., Bladder function in elderly men with subclinical brain magnetic resonance imaging lesions. J Urol, 1992. 147(6): p. 1507-9.
49. Elbadawi, A., S.V. Yalla, and N.M. Resnick, Structural basis of geriatric voiding dysfunction. II. Aging detrusor: normal versus impaired contractility. J Urol, 1993. 150(5 Pt 2): p. 1657-67.
50. Elbadawi, A., S.V. Yalla, and N.M. Resnick, Structural basis of geriatric voiding dysfunction. III. Detrusor overactivity. J Urol, 1993. 150(5 Pt 2): p. 1668-80.
51. Elbadawi, A., S.V. Yalla, and N.M. Resnick, Structural basis of geriatric voiding dysfunction. IV. Bladder outlet obstruction. J Urol, 1993. 150(5 Pt 2): p. 1681-95.
52. Resnick, N.M. and S.V. Yalla, Detrusor hyperactivity with impaired contractile function. An unrecognized but common cause of incontinence in elderly patients. Jama, 1987. 257(22): p. 3076-81.
53. Kohan, A.D., et al., Effect of aging on bladder function and the response to outlet obstruction in female rats. Urol Res, 2000. 28(1): p. 33-7.
54. Nishimoto, T., et al., Age-dependent alterations in beta-adrenergic responsiveness of rat detrusor smooth muscle. J Urol, 1995. 153(5): p. 1701-5.
55. Yoshida, M.e.a., Age-related changes in achetylcholine and adenosine triphosphate release from human bladder smooth muscles. Neurourol Urodyn, 1999. 18(4): p. 346.
56. Yoshida, M., et al., Age-related changes in cholinergic and purinergic neurotransmission in human isolated bladder smooth muscles. Exp Gerontol, 2001. 36(1): p. 99-109.
57. Sand, P.K., et al., The effect of retropubic urethropexy on detrusor stability. Obstet Gynecol, 1988. 71(6 Pt 1): p. 818-22.
58. Plevnik, S.e.a., Short-term electrical stimulation : home treatment for urinary incontinence. World J Urol, 1986. 4: p. 24.

59. Ohlsson, B.L., M. Fall, and S. Frankenberg-Sommar, Effects of external and direct pudendal nerve maximal electrical stimulation in the treatment of the uninhibited overactive bladder. Br J Urol, 1989. 64(4): p. 374-80.
60. Artibani, W., Diagnosis and significance of idiopathic overactive bladder. Urology, 1997. 50(6A Suppl): p. 25-32; discussion 33-5.
61. Maggi, C.A., Tachykinins and calcitonin gene-related peptide (CGRP) as co-transmitters released from peripheral endings of sensory nerves. Prog Neurobiol, 1995. 45(1): p. 1-98.
62. Wakabayashi, Y., et al., Substance P-containing axon terminals in the mucosa of the human urinary bladder: pre-embedding immunohistochemistry using cryostat sections for electron microscopy. Histochemistry, 1993. 100(6): p. 401-7.
63. Ferguson, D.R., I. Kennedy, and T.J. Burton, ATP is released from rabbit urinary bladder epithelial cells by hydrostatic pressure changes—a possible sensory mechanism? J Physiol, 1997. 505 (Pt 2): p. 503-11.
64. Chen, C.C., et al., A P2X purinoceptor expressed by a subset of sensory neurons. Nature, 1995. 377(6548): p. 428-31.
65. Dunn, P.M., Y. Zhong, and G. Burnstock, P2X receptors in peripheral neurons. Prog Neurobiol, 2001. 65(2): p. 107-34.
66. Vlaskovska, M., et al., P2X3 knock-out mice reveal a major sensory role for urothelially released ATP. J Neurosci, 2001. 21(15): p. 5670-7.
67. Cockayne, D.A., et al., Urinary bladder hyporeflexia and reduced pain-related behaviour in P2X3-deficient mice. Nature, 2000. 407(6807): p. 1011-5.
68. Elneil, S., et al., Distribution of P2X(1) and P2X(3) receptors in the rat and human urinary bladder. Pharmacology, 2001. 63(2): p. 120-8.
69. Wiseman, O.J., C.J. Fowler, and D.N. Landon, The role of the human bladder lamina propria myofibroblast. BJU Int, 2003. 91(1): p. 89-93.
70. Fry, C.H., et al., Control of bladder function by peripheral nerves: avenues for novel drug targets. Urology, 2004. 63(3 Suppl 1): p. 24-31.
71. Maggi, C.A., Prostanoids as local modulators of reflex micturition. Pharmacol Res, 1992. 25(1): p. 13-20.
72. Anderson, K.E., Pharmacology of lower urinary tract smooth muscles and penile erectile tissues. Pharmacol Rev, 1993. 45(3): p. 253-308.
73. Birder, L.A., et al., Adrenergic- and capsaicin-evoked nitric oxide release from urothelium and afferent nerves in urinary bladder. Am J Physiol, 1998. 275(2 Pt 2): p. F226-9.
74. Pandita, R.K., H. Mizusawa, and K.E. Andersson, Intravesical oxyhemoglobin initiates bladder overactivity in conscious, normal rats. J Urol, 2000. 164(2): p. 545-50.
75. Andersson, K.E., Bladder activation: afferent mechanisms. Urology, 2002. 59(5 Suppl 1): p. 43-50.
76. Smet, P.J., K.H. Moore, and J. Jonavicius, Distribution and colocalization of calcitonin gene-related peptide, tachykinins, and vasoactive intestinal peptide in normal and idiopathic unstable human urinary bladder. Lab Invest, 1997. 77(1): p. 37-49.
77. Maggi, C.A., et al., Cystometric evidence that capsaicin-sensitive nerves modulate the afferent branch of micturition reflex in humans. J Urol, 1989. 142(1): p. 150-4.
78. Lazzeri, M., et al., Intravesical resiniferatoxin for the treatment of hypersensitive disorder: a randomized placebo controlled study. J Urol, 2000. 164(3 Pt 1): p. 676-9.
79. Silva, C., M.J. Ribeiro, and F. Cruz, The effect of intravesical resiniferatoxin in patients with idiopathic detrusor instability suggests that involuntary detrusor contractions are triggered by C-fiber input. J Urol, 2002. 168(2): p. 575-9.
80. Brading, A.F. and W.H. Turner, The unstable bladder: towards a common mechanism. Br J Urol, 1994. 73(1): p. 3-8.
81. Brading, A.F., A myogenic basis for the overactive bladder. Urology, 1997. 50(6A Suppl): p. 57-67; discussion 68-73.
82. Mills, I.W., et al., Studies of the pathophysiology of idiopathic detrusor instability: the physiological properties of the detrusor smooth muscle and its pattern of innervation. J Urol, 2000. 163(2): p. 646-51.
83. Sui, G.P., et al., Impedance measurements and connexin expression in human detrusor muscle from stable and unstable bladders. BJU Int, 2003. 92(3): p. 297-305.
84. Yoshida, M., et al., Effects of age and muscle stretching on acetylcholine release in isolated human bladder smooth muscle. J Urol, 2002. 167: p. 40.
85. Yossepowitch, O., et al., The effect of cholinergic enhancement during filling cystometry: can edrophonium chloride be used as a provocative test for overactive bladder? J Urol, 2001. 165(5): p. 1441-5.
86. Wall, L.L. and J.O. DeLancey, The politics of prolapse: a revisionist approach to disorders of the pelvic floor in women. Perspect Biol Med, 1991. 34(4): p. 486-96.
87. Cutner, A. and L.D. Cardozo, The lower urinary tract in pregnancy and the puerperium. International Urogynecology Journal, 1992. 3(312-23).
88. Francis, W.J.A., Disturbances of bladder function in relation to pregnancy. Journal of Obstetrics and Gynecology of the British Empire, 1960. 67: p. 353-66.
89. Stanton, S.L., R. Kerr-Wilson, and V.G. Harris, The incidence of urological symptoms in normal pregnancy. Br J Obstet Gynaecol, 1980. 87: p. 897-900.
90. Hong, P.L., M. Leong, and V. Selzer, Uroflowmetric observation in pregnancy. Neurourol Urodynam, 1988. 7(61-70).
91. Parboosingh, J. and A. Doig, Studies in nocturia in normal pregnancy. J Obstet Gynaecol Br Comw, 1873. 80: p. 888-895.
92. Nemir, A. and R.P. Middleton, Stress incontinence in young nulliparous women. American Journal of Obstetrics and Gynecology, 1954. 68: p. 1166-8.
93. Wolin, L.H., Stress incontinence in young healthy nulliparous subjects. Journal of Urology, 1969. 101: p. 545-549.
94. Hojberg, K.E., et al., Urinary incontinence: prevalence and risk factors at 16 weeks of gestation. British Journal of Obstetrics andGynaecology, 1999. 106: p. 842-850.
95. Iosif, S., L. Henriksson, and U. Ulmsten, Postpartum incontinence. Urol Int, 1981. 36(1): p. 53-8.
96. Iosif, S., Stress incontinence during pregnancy and in puerperium. Int J Gynaecol Obstet, 1981. 19(1): p. 13-20.
97. Viktup, L., et al., The symptom of stress incontinence caused by pregnancy or delivery in primiparas. Obstet Gynecol, 1992. 79: p. 945-499.
98. Groutz, A., et al., Stress urinary incontinence: prevalence among nulliparous compared with primiparous and grand multiparous premenopausal women. Neurourol Urodyn, 1999. 18(5): p. 419-25.
99. Allen, R.E., et al., Pelvic floor damage and childbirth: a neurophysiological study. Br J Obstet Gynaecol, 1990. 97: p. 770-779.
100. Snooks, S.J., et al., Risk factors in childbirth causing damage to the pelvic floor innervation. Int J Colorectal Dis, 1986. 1: p. 20-24.
101. Brown, S. and J. Lumley, Maternal health after childbirth: results of an Australian population based survey. Br J Obstet Gynaecol, 1998. 105: p. 156-161.
102. Handa, V.L., T.A. Harris, and D.R. Ostergard, Protecting the pelvic floor: obstetric management to prevent incontinence and

pelvic organ prolapse. [Review] [46 refs]. Obstetrics & Gynecology, 1996. 88(3): p. 470-8.

103. Rortveit, G., et al., Vaginal dellivery pparameters and urinary incontinence; the Norwegian EPICONT study. Am J Obstet Gynecol, 2003. 189: p. 1268-1274.
104. Peschers, U.M., et al., Levator ani function before and after childbirth. 1997. 104: p. 1004-1008.
105. Tunn, R., et al., MR imaging of levator ani muscle recovery following vaginal delivery. Int-Urogynecol-J-Pelvic-Floor-Dysfunct., 1999. 10(300-307).
106. Persson, J., -.H.P. Wolner, and H. Rydhstroem, Obstetric risk factors for stress urinary incontinence: a population-based study. Obstet Gynecol, 2000. 96(3): p. 440-5.
107. Johanson, R.B., et al., Maternal and child health after assisted vaginal delivery: five-year follow up of a randomised controlled study comparing forceps and ventouse. Br J Obstet Gynaecol, 1999. 106(6): p. 544-549.
108. Meyer, S., O. Bachelard, and G.P. De, Do bladder neck mobility and urethral sphincter function differ during pregnancy compared with during the non-pregnant state? Int Urogynecol J Pelvic Floor Dysfunct, 1998. 9(6): p. 397-404.
109. King, J. and R. Freeman, Is antenatal bladder neck mobility a risk factor for postpartum stress incontinence? Br J Obstet Gynaecol, 1998. 105(12): p. 1300-7.
110. Abitbol, M.M., Birth and human evolution: anatomical and obstetrical mechanics in primates. 1997, Westport, CT.: Bergin and Garvey.
111. Moerman, M.L., Growth of the birth canal in adolescent girls. Am J Obstet Gynecol, 1982. 143: p. 528-532.
112. Robinson, J.N., et al., Epidural analgesia and third- or fourth-degree lacerations in nulliparas. Obstet Gynecol, 1999. 94(2): p. 259-62.
113. Francis, W.J.A., The onset of stress incontinence. Journal of Obstetrics and Gynecology of the British Empire, 1960. 67: p. 899-903.
114. Signorello, L.B., et al., Midline episiotomy and anal incontinence: retrospective cohort study. Bmj, 2000. 320(7227): p. 86-90.
115. Fortney, J.A. and S.J. B., The Base of the Iceberg: Prevalence and Perceptions of Maternal Morbidity in Four Developing Countries. 1996, Research Triange Park NC: Family Health International.
116. Carroli, P.R. and B. J., Episiotomy for Vaginal Birth. 2000: Cochrane-Database-Syst-Rev.
117. Angioli, R., et al., Severe perineal lacerations during vaginal delivery: the University of Miami experience. Am J Obstet Gynecol, 2000. 182(5): p. 1083-5.
118. Klein, M.C., et al., Relationship of episiotomy to perineal trauma and morbidity, sexual dysfunction, and pelvic floor relaxation. Am J Obstet Gynecol, 1994. 171(3): p. 591-8.
119. Olayinka Oyelese, K., A. Porter, and C. Wai, Midline episiotomy and anal incontinence. Is episiotomy ethically acceptable? Bmj, 2000. 320(7249): p. 1602.
120. Mills, M.S. and D.J. Murphy, Midline episiotomy and anal incontinence. Results should be interpreted with caution in British context. Bmj, 2000. 320(7249): p. 1601-2.
121. Chaliha, C. and A.H. Sultan, Midline episiotomy and anal incontinence. Training is needed in the recognition and repair of perineal trauma. Bmj, 2000. 320(7249): p. 1601.
122. Sampselle, C.M., et al., Effect of pelvic muscle exercise on transient incontinence during pregnancy and after birth. Obstet Gynecol, 1998. 91(3): p. 406-12.
123. Morkved, S. and K. Bo, Prevalence of urinary incontinence during pregnancy and postpartum. Int Urogynecol J Pelvic Floor Dysfunct, 1999. 10(6): p. 394-8.
124. Miller, K., et al., Pelvic floor electrical stimulation for genuine stress incontinence: who will benefit and when? Int Urogynecol J Pelvic Floor Dysfunct, 1998. 9(5): p. 265-70.
125. Cockshott, W.P., Public changes associated with obstetric vesico vaginal fistulae. Clin Radiol, 1973. 24(2): p. 241-7.
126. Flynn, P., et al., How can second-stage management prevent perineal trauma? Critical review. Can Fam Physician, 1997. 43: p. 73-84.
127. Klein, M.C., et al., Determinants of vaginal-perineal integrity and pelvic floor functioning in childbirth. Am J Obstet Gynecol, 1997. 176(2): p. 403-10.
128. Eason, E., et al., Preventing perineal trauma during childbirth: a systematic review. Obstet Gynecol, 2000. 95(3): p. 464-71.
129. Kelly, H. and C. Burnham, Disease of the Kidneys, Ureters and Bladder, with Special Reference to Women. Vol. 2. 1922, New York and London: D. Appleton and Company.
130. Oelrich, T.M., The striated urogenital sphincter muscle in the female. Anat Rec, 1983. 205(2): p. 223-32.
131. DeLancey, J.O., Functional anatomy of the female lower urinary tract and pelvic floor. Ciba Found Symp, 1990. 151: p. 57-69.
132. DeLancey, J.O., Structural support of the urethra as it relates to stress urinary incontinence: the hammock hypothesis. Am J Obstet Gynecol, 1994. 170(6): p. 1713-20.
133. Athanassopoulos, A., et al., Stamey endoscopic vesical neck suspension in female urinary stress incontinence: results and changes in various urodynamic parameters. International Urology & Nephrology, 1994. 26(3): p. 293-9.
134. Bump, R.C., J.A. Fantl, and W.G. Hurt, Dynamic urethral pressure profilometry pressure transmission ratio determinations after continence surgery: understanding the mechanism of success, failure, and complications. Obstet Gynecol, 1988. 72(6): p. 870-4.
135. Bunne, G. and A. Obrink, Influence of pubococcygeal repair on urethral closure pressure at stress. Acta Obstet Gynecol Scand, 1978. 57(4): p. 355-9.
136. Hilton, P. and S.L. Stanton, Urethral pressure measurement by microtransducer: the results in symptom-free women and in those with genuine stress incontinence. Br J Obstet Gynaecol, 1983. 90(10): p. 919-33.
137. Masuda, H., et al., [Analysis of continence mechanisms by stress urethral pressure profiles]. [Japanese]. Nippon Hinyokika Gakkai Zasshi - Japanese Journal of Urology, 1994. 85(3): p. 434-9.
138. Obrink, A., G. Bunne, and A. Ingelman-Sundberg, Pressure transmission to the pre-urethral space in stress incontinence. Urol Res, 1978. 6(3): p. 135-40.
139. Penttinen, J., et al., Successful colposuspension in stress urinary incontinence reduces bladder neck mobility and increases pressure transmission to the urethra. Arch Gynecol Obstet, 1989. 244(4): p. 233-8.
140. Penttinen, J., K. Kaar, and A. Kauppila, Effect of suprapubic operation on urethral closure. Evaluation by single cough urethrocystometry. Br J Urol, 1989. 63(4): p. 389-91.
141. Rottenberg, R.D., et al., Urodynamic and clinical assessment of the Lyodura sling operation for urinary stress incontinence. Br J Obstet Gynaecol, 1985. 92(8): p. 829-34.
142. van-Geelen, J.M., et al., The clinical and urodynamic effects of anterior vaginal repair and Burch colposuspension. Am J Obstet Gynecol, 1988. 159(1): p. 137-44.
143. Martan, A., et al., [Ultrasonic evaluation of paravaginal defects before and after surgical treatment in women with urinary stress incontinence]. Ceska Gynekol, 2000. 65(3): p. 152-6.
144. Jeffcoate, T.N.A. and H. Roberts, Observations on stress incontinence of urine. Am J Obstet Gynecol, 1952. 64: p. 721.

145. Pregazzi, R., et al., Perineal ultrasound evaluation of urethral angle and bladder neck mobility in women with stress urinary incontinence. Bjog, 2002. 109(7): p. 821-7.

146. Hodgkinson, C.P., Relationship of the female bladder and urethra in urinary stress incontinence. Am J Obstet Gynecol, 1953. 65(3): p. 560-573.

147. Hodgkinson, C.P., Stress urinary incontinence—1970. Am J Obstet Gynecol, 1970. 108(7): p. 1141-68.

148. Wall, L.L., et al., Bladder neck mobility and the outcome of surgery for genuine stress urinary incontinence. A logistic regression analysis of lateral bead-chain cystourethrograms. Journal of Reproductive Medicine, 1994. 39(6): p. 429-35.

149. Blaivas, J.G. and C.A. Olsson, Stress incontinence: classification and surgical approach. J Urol, 1988. 139(4): p. 727-31.

150. McGuire, E.J., R.D. Cespedes, and H.E. O'Connell, Leak-point pressures. [Review] [12 refs]. Urologic Clinics of North America, 1996. 23(2): p. 253-62.

151. McGuire, E.J., Diagnosis and treatment of intrinsic sphincter deficiency. International Journal of Urology, 1995. 2(Suppl 1): p. 7-10; discussion 16-8.

152. Leach, G.E., et al., Female stress urinary incontinence clinical guidelines panel summary report on surgical management of female stress urinary incontinence. Journal of Urology, 1997. 158: p. 875-880.

153. Horbach, N.S. and D.R. Ostergard, Predicting intrinsic urethral sphincter dysfunction in women with stress urinary incontinence. Obstet Gynecol, 1994. 84(2): p. 188-92.

154. Kayigil, O., A.S. Iftekhar, and A. Metin, The coexistence of intrinsic sphincter deficiency with type II stress incontinence. J Urol, 1999. 162(4): p. 1365-6.

155. Chaikin, D., J. Rosenthal, and J. Blaivas, Pubovaginal fascial sling for all types of stress urinary incontinence: long-term analysis. J Urol, 1998. 160(4): p. 1312-6.

156. Bemelmans, B.L. and C.R. Chapple, Are slings now the gold standard treatment for the management of female urinary stress incontinence and if so which technique? Curr Opin Urol, 2003. 13(4): p. 301-7.

157. Kiilholma, P.J., et al., Perineal ultrasound: an alternative for radiography for evaluating stress urinary incontinence in females. Annales Chirurgiae et Gynaecologiae - Supplementum, 1994. 208: p. 43-5.

158. Karan, A., et al., Hypermobility syndrome in 105 women with pure urinary stress incontinence and in 105 controls. Arch Gynecol Obstet, 2004. 269(2): p. 89-90.

159. Meyer, S., et al., The assessment of bladder neck position and mobility in continent nullipara, mulitpara, forceps-delivered and incontinent women using perineal ultrasound: a future office procedure? International Urogynecology Journal and Pelvic Floor Dysfunction, 1996. 7(3): p. 138-46.

160. Heit, M., Intraurethral ultrasonography: correlation of urethral anatomy with functional urodynamic parameters in stress incontinent women. Int Urogynecol J Pelvic Floor Dysfunct, 2000. 11(4): p. 204-11.

161. Masuda, H., et al., [Analysis of continence mechanisms by stress urethral pressure profiles]. Nippon Hinyokika Gakkai Zasshi, 1994. 85(3): p. 434-9.

162. Kauppila, A., J. Penttinen, and V.M. Haggman, Six-microtransducer catheter connected to computer in evaluation of urethral closure function of women. Urology, 1989. 33(2): p. 159-64.

163. Behr, J., M. Winkler, and U. Schwiersch, [Urodynamic observations on the Marshall-Marchetti-Krantz operation]. Geburtshilfe Frauenheilkd, 1986. 46(9): p. 649-53.

164. Vanderschot, E.L., M.L. Chafik, and F.M. Debruyne, Has the suprapubic suspension operation any influence on the urethral pressure profile? Br J Urol, 1979. 51(2): p. 140-3.

165. Langer, R., et al., Continence mechanism after colpo-needle suspension for stress urinary incontinence. Journal of Reproductive Medicine, 1995. 40(10): p. 699-702.

166. Hertogs, K. and S.L. Stanton, Lateral bead-chain urethrocystography after successful and unsuccessful colposuspension. Br J Obstet Gynaecol, 1985. 92(11): p. 1179-83.

167. Snooks, S.J., P.R. Barnes, and M. Swash, Damage to the innervation of the voluntary anal and periurethral sphincter musculature in incontinence: an electrophysiological study. J Neurol Neurosurg Psychiatry, 1984. 47(12): p. 1269-73.

168. Swash, M., S.J. Snooks, and M.M. Henry, Unifying concept of pelvic floor disorders an incontinence. J Roy Soc Med, 1985. 78: p. 906-933.

169. Ismael, S., et al., Postpartum lumbosacral plexopathy limited to autonomic and perineal manifestations: clinical and electrophysiological study of 19 patients. J Neurol Neurosurg Psychiatry, 2000. 68(6): p. 771-3.

170. Takahashi, S., et al., Electromyographic study of the striated urethral sphincter in type 3 stress incontinence: evidence of myogenic-dominant damages. Urology, 2000. 56(6): p. 946-50.

171. Weidner, A., et al., Pelvic muscle electromyography of levator ani and external anal sphincter in nulliparous women and women with pelvic floor dysfunction. Am J Obstet Gynecol, 2000. 183(6): p. 1390-9; discussion 1399-401.

172. Gunnarsson, M. and A. Mattiasson, Female stress, urge, and mixed urinary incontinence are associated with a chronic and progressive pelvic floor/vaginal neuromuscular disorder: An investigation of 317 healthy and incontinent women using vaginal surface electromyography. Neurourol Urodyn, 1999. 18(6): p. 613-21.

173. Bakas, P., et al., Pudendal nerve terminal motor latency in women with genuine stress incontinence and prolapse. Gynecol Obstet Invest, 2001. 51(3): p. 187-90.

174. Pieber, D., F. Zivkovic, and K. Tamussino, Timing of urethral pressure pulses before and after continence surgery. Neurourol Urodyn, 1998. 17(1): p. 19-23.

175. Thor, K.B., Serotonin and norepinephrine involvement in efferent pathways to the urethral rhabdosphincter: implications for treating stress urinary incontinence. Urology, 2003. 62(4 Suppl 1): p. 3-9.

176. Yang, A., et al., Dynamic evaluation of pelvic floor descent using fastscan MRI and cinematic display. Radiology, 1991. 179: p. 25-33.

177. Gufler, H., et al., Comparison of cystourethrography and dynamic MRI in bladder neck descent. J Comput Assist Tomogr, 2000. 24(3): p. 382-8.

178. Yang, A., et al., Patterns of prolapse demonstrated with dynamic fastscan MRI; re-assesment of conventional concepts of pelvic floor weakness. Neurourology and Urodynamics, 1993. 12: p. 310.

179. Kim, J.K., et al., The urethra and its supporting structures in women with stress urinary incontinence: MR imaging using an endovaginal coil. AJR Am J Roentgenol, 2003. 180(4): p. 1037-44.

180. Yang, A., et al., High resoluton magnetic resonance imaging of urethra and periurethral structures using intravaginal surface coil and quadrature phased array surface coil. Neurourology and Urodynamics, 1993. 12: p. 329.

181. Perez, N., et al., Dynamic magnetic resonance imaging of the female pelvis: radio-anatomy and pathologic applications. Preliminary results. Surg Radiol Anat, 1999. 21(2): p. 133-8.

182. Sanders, R.C., et al., Imaging the female urethra. Ultrasound Quarterly, 1994. 12(3): p. 167-183.

183. Masata, J., et al., [Ultrasonography of the funneling of the urethra]. Ceska Gynekol, 2000. 65(2): p. 87-90.

184. Schaer, G.N., et al., Improvement of perineal sonographic bladder neck imaging with ultrasound contrast medium. Obstetrics & Gynecology, 1995. 86(6): p. 950-4.

185. Siracusano, S., et al., The feasibility of urethral color ultrasound imaging in the diagnosis of female intrinsic sphincter deficiency: preliminary results. Spinal Cord, 2002. 40(4): p. 192-5.

186. Huang, W.C. and J.M. Yang, Bladder neck funneling on ultrasound cystourethrography in primary stress urinary incontinence: a sign associated with urethral hypermobility and intrinsic sphincter deficiency. Urology, 2003. 61(5): p. 936-41.

187. Ghoniem, G.M., et al., Grades of intrinsic sphincteric deficiency (ISD) associated with female stress urinary incontinence. Int Urogynecol J Pelvic Floor Dysfunct, 2002. 13(2): p. 99-105; discussion 105.

188. Martan, A., et al., Ultrasound imaging of paravaginal defects in women with stress incontinence before and after paravaginal defect repair. Ultrasound Obstet Gynecol, 2002. 19(5): p. 496-500.

189. Nichols, D.H. and C.L. Randall, Vaginal Surgery. 1989, Baltimore: Williams and Wilkins. 463.

190. Mostwin, J.L., et al., Radiography, sonography, and magnetic resonance imaging for stress incontinence. Contributions, uses, and limitations. Urologic Clinics of North America, 1995. 22(3): p. 539-49.

191. Milley, P.S. and D.H. Nichols, The relationship between the pubo-urethral ligaments and the urogenital diaphragm in the human female. Anat Rec, 1971. 170: p. 281.

192. Zacharin, R.A., The suspensory mechanism of the female urethra. J Anatom, 1961. 97: p. 423.

193. Zacharin, R.F., The anatomic supports of the female urethra. Obstet Gynecol, 1968. 32(6): p. 754-9.

194. Mostwin, J.L., et al., Evaluation of stress incontinence by ultrasonography and MRI. Scan J Urol Nephrol, 2000.

195. O'Boyle, A.L., et al., The natural history of pelvic organ support in pregnancy. Int Urogynecol J Pelvic Floor Dysfunct, 2003. 14(1): p. 46-9; discussion 49.

196. Bump, R.C., et al., The standardization of terminology of female pelvic organ prolapse and pelvic floor dysfunction. Am J Obstet Gynecol, 1996. 175(1): p. 10-7.

197. Sze, E.H., G.B. Sherard, 3rd, and J.M. Dolezal, Pregnancy, labor, delivery, and pelvic organ prolapse. Obstet Gynecol, 2002. 100(5 Pt 1): p. 981-6.

198. Uustal, F.E., G. Wingren, and P. Kjolhede, Factors associated with pelvic floor dysfunction with emphasis on urinary and fecal incontinence and genital prolapse: an epidemiological study. Acta Obstet Gynecol Scand, 2004: p. 383-389.

199. Mant, J., R. Painter, and M. Vessey, Epidemiology of genital prolapse: observations from the Oxford Family Planning Association Study. Br J Obstet Gynaecol, 1997. 104(5): p. 579-85.

200. Samuelsson, E.C., et al., Signs of genital prolapse in a Swedish population of women 20 to 59 years of age and possible related factors. Am J Obstet Gynecol, 1999. 180(2 Pt 1): p. 299-305.

201. Rinne, K.M. and P.P. Kirkinen, What predisposes young women to genital prolapse? Eur J Obstet Gynecol Reprod Biol, 1999. 84(1): p. 23-5.

202. Swift, S.E., The distribution of pelvic organ support in a population of female subjects seen for routine gynecologic health care. Am J Obstet Gynecol, 2000. 183(2): p. 277-85.

203. Group, P.M.I.S., Risk factors for genital prolapse in non-hysterectomized women around menopause results from a large cross-sectional study in menopausal clinics in Italy. Eur J Obstet Gynecol Reprod Biol, 2000: p. 125-40.

204. Klein, M.C., et al., Relationship of episiotomy to perineal trauma and morbidity, sexual dysfunction, and pelvic floor relaxation. Am J Obstet Gynecol, 1994. 171(3): p. 591-8.

205. Taskin, O., et al., The effects of episiotomy and Kegel exercises on postpartum pelvic relaxation: a prospective controlled study. J Gynecol Surg, 1996: p. 123-7.

206. Sartore, A., et al., The effects of mediolateral episiotomy on pelvic floor function after vaginal delivery. Obstet Gynecol, 2004. 103(4): p. 669-73.

207. Swift, S.E., T. Pound, and J.K. Dias, Case-control study of etiologic factors in the development of severe pelvic organ prolapse. Int Urogynecol J Pelvic Floor Dysfunct, 2001. 12(3): p. 187-92.

208. Olsen, A.L., et al., Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence. Obstet Gynecol, 1997. 89(4): p. 501-6.

209. Versi, E., et al., Urogenital prolapse and atrophy at menopause: a prevalence study. Int Urogynecol J Pelvic Floor Dysfunct, 2001. 12(2): p. 107-10.

210. Goepel, C., et al., Periurethral connective tissue status of postmenopausal women with genital prolapse with and without stress incontinence. Acta Obstet Gynecol Scand, 2003. 82(7): p. 659-64.

211. Snooks, S.J., et al., Risk factors in childbirth causing damage to the pelvic floor innervation. Int J Colorectal Dis, 1986. 1(1): p. 20-4.

212. Lubowski, D.Z., et al., Increase in pudendal nerve terminal motor latency with defaecation straining. Br J Surg, 1988. 75(11): p. 1095-7.

213. Spence-Jones, C., et al., Bowel dysfunction: a pathogenic factor in uterovaginal prolapse and urinary stress incontinence. Br J Obstet Gynaecol, 1994. 101(2): p. 147-52.

214. Fialkow, M.F., et al., Posterior vaginal wall defects and their relation to measures of pelvic floor neuromuscular function and posterior compartment symptoms. Am J Obstet Gynecol, 2002. 187(6): p. 1443-8; discussion 1448-9.

215. DeLancey, J., et al., Levator ani muscle structure and function in women with prolapse compared to women with normal support. Neurourol Urodyn, 2003: p. 542-3 Abstract.

216. Busacchi, P., et al., Abnormalities of somatic peptide-containing nerves supplying the pelvic floor of women with genitourinary prolapse and stress urinary incontinence. Urology, 2004. 63(3): p. 591-5.

217. Davis, G.D., Uterine prolapse after laparoscopic uterosacral transection in nulliparous airborne trainees. A report of three cases. J Reprod Med, 1996. 41(4): p. 279-82.

218. Jorgensen, S., H.O. Hein, and F. Gyntelberg, Heavy lifting at work and risk of genital prolapse and herniated lumbar disc in assistant nurses. Occup Med (Lond), 1994. 44(1): p. 47-9.

219. Bump, R.C., et al., Obesity and lower urinary tract function in women: effect of surgically induced weight loss. Am J Obstet Gynecol, 1992. 167(2): p. 392-7; discussion 397-9.

220. Deeb, M.E., et al., Prevalence of reproductive tract infections, genital prolapse, and obesity in a rural community in Lebanon. Bull World Health Organ, 2003. 81(9): p. 639-45.

221. Strinic, T., et al., Pulmonary ventilatory function in premenopausal women with and without genital descensus. Coll Antropol, 2002. 26 Suppl: p. 139-42.

222. Marchionni, M., et al., True incidence of vaginal vault prolapse. Thirteen years of experience. J Reprod Med, 1999. 44(8): p. 679-84.

223. Gimbel, H., et al., Randomised controlled trial of total compared with subtotal hysterectomy with one-year follow up results. Bjog, 2003. 110(12): p. 1088-98.

224. Thakar, R., et al., Outcomes after total versus subtotal abdominal hysterectomy. N Engl J Med, 2002. 347(17): p. 1318-25.

225. Wiskind, A.K., S.M. Creighton, and S.L. Stanton, The incidence of genital prolapse after the Burch colposuspension. Am J Obstet Gynecol, 1992. 167(2): p. 399-404; discussion 404-5.

226. Holley, R.L., et al., Recurrent pelvic support defects after sacrospinous ligament fixation for vaginal vault prolapse. J Am Coll Surg, 1995. 180(4): p. 444-8.

227. Bump, R.C., et al., Randomized prospective comparison of needle colposuspension versus endopelvic fascia plication for potential stress incontinence prophylaxis in women undergoing vaginal reconstruction for stage III or IV pelvic organ prolapse. The Continence Program for Women Research Group. Am J Obstet Gynecol, 1996. 175(2): p. 326-33; discussion 333-5.

228. Langer, R., et al., Long-Term (10-15 years) follow-up after Burch colposuspension for urinary stress incontinence. Int Urogynecol J Pelvic Floor Dysfunct, 2001. 12(5): p. 323-6; discussion 326-7.

229. Demirci, F., et al., Long-term results of Burch colposuspension. Gynecol Obstet Invest, 2001. 51(4): p. 243-7.

230. Kwon, C.H., et al., The development of pelvic organ prolapse following isolated Burch retropubic urethropexy. Int Urogynecol J Pelvic Floor Dysfunct, 2003. 14(5): p. 321-5; discussion 325.

231. Langer, R., et al., Prevention of genital prolapse following Burch colposuspension: comparison between two surgical procedures. Int Urogynecol J Pelvic Floor Dysfunct, 2003. 14(1): p. 13-6; discussion 16.

232. Nieminen, K., H. Huhtala, and P.K. Heinonen, Anatomic and functional assessment and risk factors of recurrent prolapse after vaginal sacrospinous fixation. Acta Obstet Gynecol Scand, 2003. 82(5): p. 471-8.

233. Benson, J.T. and E. McClellan, The effect of vaginal dissection on the pudendal nerve. Obstet Gynecol, 1993. 82(3): p. 387-9.

234. Benson, J.T., V. Lucente, and E. McClellan, Vaginal versus abdominal reconstructive surgery for the treatment of pelvic support defects: a prospective randomized study with long-term outcome evaluation. Am J Obstet Gynecol, 1996. 175(6): p. 1418-21; discussion 1421-2.

235. Roovers, J.P., et al., A randomised controlled trial comparing abdominal and vaginal prolapse surgery: effects on urogenital function. Bjog, 2004. 111(1): p. 50-6.

236. Good, M.C., P.R. Copas, and M.C. Doody, Uterine prolapse after laparoscopic uterosacral transection. J Reprod Med, 1993: p. 995-6.

237. Al-Rawizs, S. and T. Al-Rawizs, Joint hypermobility in women with genital prolapse. Lancet., 1982: p. 1439-41.

238. Carley, M.E. and J. Schaffer, Urinary incontinence and pelvic organ prolapse in women with Marfan or Ehlers Danlos syndrome. Am J Obstet Gynecol, 2000. 182(5): p. 1021-3.

239. Visco, A.G. and L. Yuan, Differential gene expression in pubococcygeus muscle from patients with pelvic organ prolapse. Am J Obstet Gynecol, 2003. 189(1): p. 102-12.

240. Boreham, M.K., et al., Morphometric analysis of smooth muscle in the anterior vaginal wall of women with pelvic organ prolapse. Am J Obstet Gynecol, 2002. 187(1): p. 56-63.

241. Boreham, M.K., et al., Morphometric properties of the posterior vaginal wall in women with pelvic organ prolapse. Am J Obstet Gynecol, 2002. 187(6): p. 1501-8; discussion 1508-9.

242. Takano, C.C., et al., Analysis of collagen in parametrium and vaginal apex of women with and without uterine prolapse. Int Urogynecol J Pelvic Floor Dysfunct, 2002. 13(6): p. 342-5; discussion 345.

243. Barbiero, E.C., et al., Analysis of type I collagen in the parametrium of women with and without uterine prolapse, according to hormonal status. Int Urogynecol J Pelvic Floor Dysfunct, 2003. 14(5): p. 331-4; discussion 334.

244. Lind, L.R., V. Lucente, and N. Kohn, Thoracic kyphosis and the prevalence of advanced uterine prolapse. Obstet Gynecol, 1996. 87(4): p. 605-9.

245. Nguyen, J.K., et al., Lumbosacral spine and pelvic inlet changes associated with pelvic organ prolapse. Obstet Gynecol, 2000. 95(3): p. 332-6.

246. Sze, E.H., et al., A retrospective comparison of abdominal sacrocolpopexy with Burch colposuspension versus sacrospinous fixation with transvaginal needle suspension for the management of vaginal vault prolapse and coexisting stress incontinence. Int Urogynecol J Pelvic Floor Dysfunct, 1999. 10(6): p. 390-3.

247. Handa, V.L., et al., Architectural differences in the bony pelvis of women with and without pelvic floor disorders. Obstet Gynecol, 2003. 102(6): p. 1283-90.

248. Blakely, C. and W. Mills, The obstetric and gynaecological compliations of bladder exstrophy and epispadias. Br J Obstet Gynaecol, 1981: p. 167-73.

249. Kahn, M.A. and S.L. Stanton, Posterior colporrhaphy: its effects on bowel and sexual function. Br J Obstet Gynaecol, 1997. 104(1): p. 82-6.

250. Barrington, J.W. and G. Edwards, Posthysterectomy vault prolapse. Int Urogynecol J Pelvic Floor Dysfunct, 2000. 11(4): p. 241-5.

251. Barrington, F.J.F., The nervous mechanism of micturition. Quarterly Journal of Experimental Physiology, 1915. 8: p. 33-71.

252. Barrington, F.J.F., The component reflexes of micturiton in the cat. Parts I & II. Brain, 1931. 54: p. 177-188.

253. Barrington, F.J.F., The component reflexes of micturiton in the cat. Part III. Brain, 1941. 64: p. 239-243.

254. Schick, E., et al., Observations on the function of the female urethra: III: An overview with special reference to the relation between urethral hypermobility and urethral incompetence. Neurourol Urodyn, 2004. 23(1): p. 22-6.

255. Richardson, D.A., A.E. Bent, and D.R. Ostergard, The effect of uterovaginal prolapse on urethrovesical pressure dynamics. Am J Obstet Gynecol, 1983. 146(8): p. 901-5.

256. Bergman, A., P.P. Koonings, and C.A. Ballard, Predicting postoperative urinary incontinence development in women undergoing operation for genitourinary prolapse. Am J Obstet Gynecol, 1988. 158(5): p. 1171-5.

257. Zivkovic, F., et al., Urethral profilometry in women with uterovaginal prolapse. Int Urogynecol J Pelvic Floor Dysfunct, 1995: p. 10-13.

258. Chaikin, D.C., A. Groutz, and J.G. Blaivas, Predicting the need for anti-incontinence surgery in continent women undergoing repair of severe urogenital prolapse. J Urol, 2000. 163(2): p. 531-4.

259. Gallentine, M.L. and R.D. Cespedes, Occult stress urinary incontinence and the effect of vaginal vault prolapse on abdominal leak point pressures. Urology, 2001. 57(1): p. 40-4.

260. Versi, E., D.J. Lyell, and D.J. Griffiths, Videourodynamic diagnosis of occult genuine stress incontinence in patients with anterior vaginal wall relaxation. J Soc Gynecol Investig, 1998. 5(6): p. 327-30.

261. Bai, S.W., et al., Relationship between stress urinary incontinence and pelvic organ prolapse. Int Urogynecol J Pelvic Floor Dysfunct, 2002. 13(4): p. 256-60; discussion 260.

262. Klutke, J.J., et al., Urodynamic outcome after surgery for severe prolapse and potential stress incontinence. Am J Obstet Gynecol, 2000: p. 1378-1381.

263. Karram, M.M., What is the optimal anti-incontinence procedure in women with advanced prolapse and 'potential' stress incontinence? Int Urogynecol J Pelvic Floor Dysfunct, 1999. 10(1): p. 1-2.

264. Marinkovic, S.P. and S.L. Stanton, Incontinence and voiding difficulties associated with prolapse. J Urol, 2004. 171(3): p. 1021-8.

265. Coates, K.W., et al., Uroflowmetry in women with urinary incontinence and pelvic organ prolapse. Br J Urol, 1997. 80(2): p. 217-21.

266. Dietz, H.P., B.T. Haylen, and T.G. Vancaillie, Female pelvic organ prolapse and voiding function. Int Urogynecol J Pelvic Floor Dysfunct, 2002. 13(5): p. 284-8.

267. Fitzgerald, M.P., N. Kulkarni, and D. Fenner, Postoperative resolution of urinary retention in patients with advanced pelvic organ prolapse. Am J Obstet Gynecol, 2000. 183(6): p. 1361-3; discussion 1363-4.

268. Yanik, F.F., T. Akpolat, and I. Kocak, Acute renal failure—an unusual consequence of uterine prolapse. Nephrol Dial Transplant, 1998. 13(10): p. 2648-50.

269. Sudhakar, A.S., et al., Bilateral hydroureter and hydronephrosis causing renal failure due to a procidentia uteri: a case report. Int Surg, 2001. 86(3): p. 173-5.

270. Gomes, C.M., et al., Simultaneous upper and lower urinary tract obstruction associated with severe genital prolapse: diagnosis and evaluation with magnetic resonance imaging. Int Urogynecol J Pelvic Floor Dysfunct, 2001. 12(2): p. 144-6.

271. Chuang, F.R., et al., Bilateral moderate hydroureteronephrosis due to uterine prolapse: two case reports and review of the literature. Ren Fail, 2003. 25(5): p. 879-84.

272. Redding, M.D., The Relaxed Perineum and Anorectal Disease. Dis Colon Rectum, 1965. 49: p. 279-82.

273. Altringer, W.E., et al., Four-contrast defecography: pelvic "floorscopy". Dis Colon Rectum, 1995. 38(7): p. 695-9.

274. Kelvin, F.M., et al., Female pelvic organ prolapse: diagnostic contribution of dynamic cystoproctography and comparison with physical examination. AJR Am J Roentgenol, 1999. 173(1): p. 31-7.

275. Agachan, F., J. Pfeifer, and S.D. Wexner, Defecography and proctography. Results of 744 patients. Dis Colon Rectum, 1996. 39(8): p. 899-905.

276. Fenner, D.E., Diagnosis and assessment of sigmoidoceles. Am J Obstet Gynecol, 1996. 175(6): p. 1438-41; discussion 1441-2.

277. Lopez, A., et al., Cystodefecoperitoneography in patients with genital prolapse. Int Urogynecol J Pelvic Floor Dysfunct, 2002. 13(1): p. 22-9.

278. Karasick, S. and S.M. Ehrlich, Is constipation a disorder of defecation or impaired motility?: distinction based on defecography and colonic transit studies. AJR Am J Roentgenol, 1996. 166(1): p. 63-6.

279. van Dam, J.H., W.C. Hop, and W.R. Schouten, Analysis of patients with poor outcome of rectocele repair. Dis Colon Rectum, 2000. 43(11): p. 1556-60.

280. Karlbom, U., et al., Does surgical repair of a rectocele improve rectal emptying? Dis Colon Rectum, 1996. 39(11): p. 1296-302.

281. Mellgren, A., et al., Results of rectocele repair. A prospective study. Dis Colon Rectum, 1995. 38(1): p. 7-13.

282. Goh, J.T., J.J. Tjandra, and M.P. Carey, How could management of rectoceles be optimized? ANZ J Surg, 2002. 72(12): p. 896-901.

283. Jackson, S.L., et al., Fecal incontinence in women with urinary incontinence and pelvic organ prolapse. Obstet Gynecol, 1997. 89(3): p. 423-7.

284. Khullar, V., et al., Prevalence of faecal incontinence among women with urinary incontinence. Br J Obstet Gynaecol, 1998. 105(11): p. 1211-3.

285. Meschia, M., et al., Prevalence of anal incontinence in women with symptoms of urinary incontinence and genital prolapse. Obstet Gynecol, 2002. 100(4): p. 719-23.

286. Soligo, M., et al., Double incontinence in urogynecologic practice: a new insight. Am J Obstet Gynecol, 2003. 189(2): p. 438-43.

287. Gordon, D., et al., Anal incontinence: prevalence among female patients attending a urogynecologic clinic. Neurourol Urodyn, 1999. 18(3): p. 199-204.

288. Brubaker, L. and P. Norton, Current clinical nomenclature for description of prolapse. J Pelvic Surg, 1996: p. 256-9.

289. Ho, Y.H., et al., Transanal approach to rectocele repair may compromise anal sphincter pressures. Dis Colon Rectum, 1998. 41(3): p. 354-8.

290. van Dam, J.H., et al., Fecal continence after rectocele repair: a prospective study. Int J Colorectal Dis, 2000. 15(1): p. 54-7.

291. Rao, S.S. and R.S. Patel, How useful are manometric tests of anorectal function in the management of defecation disorders? Am J Gastroenterol, 1997. 92(3): p. 469-75.

292. Rao, S.S., Fecal Incontinence. Clinical Perspectives in Gastroenterology. Gastroenterology, 1999. 2: p. 277-288.

293. Matzel, K.E., R.A. Schmidt, and E.A. Tanagho, Neuroanatomy of the striated muscular anal continence mechanism. Implications for the use of neurostimulation. Dis Colon Rectum, 1990. 33(8): p. 666-73.

294. Salmons, S. and G. Vrobva, The influence of activity on some contractile characteristics of mammalian fast and slow muscles. Journal of Physiology, 1969. 201: p. 535-49.

295. Johnson, M.A., et al., Data on the distribution of fibre types in thirty-six human muscles. An autopsy study. J Neurol Sci, 1973. 18(1): p. 111-29.

296. Kerremans, R., Electrical activity and motility of the internal anal sphincter: an "in vivo" electrophysiological study in man. Acta Gastroenterol Belg, 1968. 31(7): p. 465-82.

297. Wankling, W.J., et al., Basal electrical activity in the anal canal in man. Gut, 1968. 9(4): p. 457-60.

298. Schouten, W.R. and J.D. Blankensteijn, Ultra slow wave pressure variations in the anal canal before and after lateral internal sphincterotomy. Int J Colorectal Dis, 1992. 7(3): p. 115-8.

299. Hancock, B.D. and K. Smith, The internal sphincter and Lord's procedure for haemorrhoids. Br J Surg, 1975. 62(10): p. 833-6.

300. Rao, S.S., et al., Anorectal contractility under basal conditions and during rectal infusion of saline in ulcerative colitis. Gut, 1988. 29(6): p. 769-77.

301. Frenckner, B. and C. Von Euler, Influence of pudendal block on the function of the anal sphincter. Gut, 1975. 16: p. 482-489.

302. Gibbons, C.P., et al., An analysis of anal sphincter pressure and anal compliance in normal subjects. Int J Colorectal Dis, 1986. 1(4): p. 231-7.

303. Gibbons, C.P., et al., Role of anal cushions in maintaining continence. Lancet, 1986. 1(8486): p. 886-8.

304. Parks, A.G., N.H. Porter, and J. Hardcastle, The syndrome of the descending perineum. Proc R Soc Med, 1966. 59(6): p. 477-82.

305. Gunterberg, B., et al., Anorectal function after major resections of the sacrum with bilateral or unilateral sacrifice of sacral nerves. Br J Surg, 1976. 63(7): p. 546-54.

306. Duthie, H.L. and F.W. Gairns, Sensory nerve-endings and sensation in the anal region of man. Br J Surg, 1960. 47: p. 585-95.

307. Goligher, J.C. and E.S. Hughes, Sensibility of the rectum and colon. Its role in the mechanism of anal continence. Lancet, 1951. 1(10): p. 543-7.

308. Read, M.G. and N.W. Read, Role of anorectal sensation in preserving continence. Gut, 1982. 23(4): p. 345-7.

309. Sun, W.M., N.W. Read, and T.C. Donnelly, Anorectal function in incontinent patients with cerebrospinal disease. Gastroenterology, 1990. 99(5): p. 1372-9.

310. Rao, S.S., K.D. Welcher, and J. Happel, Can biofeedback therapy improve anorectal function in fecal incontinence? Am J Gastroenterol, 1996. 91(11): p. 2360-6.

311. Wald, A. and A.K. Tunuguntla, Anorectal sensorimotor dysfunction in fecal incontinence and diabetes mellitus. Modification with biofeedback therapy. N Engl J Med, 1984. 310(20): p. 1282-7.

312. Mohanty, S., et al., Behavioral therapy for rectal hypersensitivity. Am J Gastroenterol, 2001. 96: p. A955.

313. Collet, L., et al., Cerebral evoked potentials after endorectal mechanical stimulation in humans. Am J Physiol, 1988. 254(4 Pt 1): p. G477-82.

314. Rogers, J., Chapt 12: Anal and Rectal Sensation, in Bailliere's Clinical Gastroentereology, M. Henry, Editor. 1992, Bailliere Tindall: London. p. 179-181.

315. Bharucha, A.E., et al., Viscoelastic properties of the human colon. Am J Physiol Gastrointest Liver Physiol, 2001. 281(2): p. G459-66.

316. Devroede, G. and J. Lamarche, Functional importance of extrinsic parasympathetic innervation to the distal colon and rectum in man. Gastroenterology, 1974. 66(2): p. 273-80.

317. Frenckner, B., Function of the anal sphincters in spinal man. Gut, 1975. 16(8): p. 638-44.

318. Duthie, H.L. and R.C. Bennett, The relation of sensation in the anal canal to the functional anal sphincter: a possible factor in anal continence. Gut, 1963. 4: p. 179-82.

319. Miller, R., et al., Anorectal sampling: a comparison of normal and incontinent patients. Br J Surg, 1988. 75(1): p. 44-7.

320. Miller, R., et al., Anorectal temperature sensation: a comparison of normal and incontinent patients. Br J Surg, 1987. 74(6): p. 511-5.

321. Rogers, J., et al., Temperature gradient between the rectum and the anal canal: evidence against the role of temperature sensation as a sensory modality in the anal canal of normal subjects. Br J Surg, 1988. 75: p. 1083-1085.

322. Miller, R., et al., Sensory discrimination and dynamic activity in the anorectum: evidence using a new ambulatory technique. Br J Surg, 1988. 75(10): p. 1003-7.

323. Martelli, H., et al., Some parameters of large bowel motility in normal man. Gastroenterology, 1978. 75(4): p. 612-8.

324. Finlay, I.G., K. Carter, and I. McCleod, A comparison of intrarectal function of gas and mass on anorectal angle and anal canal pressure (Abstract). Br J Surg, 1986. 73: p. A1025.

325. Garry, R.C., Responses to stimulation of caudal end of large bowel in cat. J Physiol (Lond), 1933. 78: p. 208-224.

326. Gaston, E.A., The physiology of fecal continence. Surg Gynecol Obstet. 148: p. 280-290.

327. Kumar, D., et al., Prolonged anorectal manometry and external anal sphincter electromyography in ambulant human subjects. Dig Dis Sci, 1990. 35(5): p. 641-8.

328. Duthie, H.L. and J.M. Watts, Contribution of the External Anal Sphincter to the Pressure Zone in the Anal Canal. Gut, 1965. 28: p. 64-8.

329. Dubrovsky, B., Effects of rectal distension on the sphincter ani externus and levator ani muscles in cats. Am J Physiol, 1988. 254(1 Pt 1): p. G100-6.

330. Lestar, B., et al., The internal anal sphincter can not close the anal canal completely. Int J Colorectal Dis, 1992. 7(3): p. 159-61.

331. Lestar, B., F. Penninckx, and R. Kerremans, The composition of anal basal pressure. An in vivo and in vitro study in man. Int J Colorectal Dis, 1989. 4(2): p. 118-22.

332. Sun, W.M., T.C. Donnelly, and N.W. Read, Utility of a combined test of anorectal manometry, electromyography, and sensation in determining the mechanism of 'idiopathic' faecal incontinence. Gut, 1992. 33(6): p. 807-13.

333. Kamm, M.A., Obstetric damage and faecal incontinence. Lancet, 1994. 344(8924): p. 730-3.

334. Sultan, A.H., et al., Anal-sphincter disruption during vaginal delivery. N Engl J Med, 1993. 329: p. 1905-1911.

335. Engel, A.F., et al., Relationship of symptoms in faecal incontinence to specific sphincter abnormalities. Int J Colorectal Dis, 1995. 10(3): p. 152-5.

336. Sultan, A.H., et al., Third degree obstetric anal sphincter tears: risk factors and outcome of primary repair. Bmj, 1994. 308(6933): p. 887-91.

337. Green, J.R. and S.L. Soohoo, Factors associated with rectal injury in spontaneous deliveries. Obstet Gynecol, 1989. 73(5 Pt 1): p. 732-8.

338. Nygaard, I.E., S.S. Rao, and J.D. Dawson, Anal incontinence after anal sphincter disruption: a 30-year retrospective cohort study. Obstet Gynecol, 1997. 89(6): p. 896-901.

339. Loening-Baucke, V. and S. Anuras, Effects of age and sex on anorectal manometry. Am J Gastroenterol, 1985. 80(1): p. 50-3.

340. Loening-Baucke, V. and S. Anuras, Anorectal manometry in healthy elderly subjects. J Am Geriatr Soc, 1984. 32(9): p. 636-9.

341. Laurberg, S. and M. Swash, Effects of aging on the anorectal sphincters and their innervation. Dis Colon Rectum, 1989. 32(9): p. 737-42.

342. Bannister, J.J., L. Abouzekry, and N.W. Read, Effect of aging on anorectal function. Gut, 1987. 28(3): p. 353-7.

343. Rao, S.S., et al., Manometric tests of anorectal function in healthy humans. Am J Gastroenterol, 1999. 94: p. 773-783.

344. McHugh, S.M. and N.E. Diamant, Effect of age, gender, and parity on anal canal pressures. Contribution of impaired anal sphincter function to fecal incontinence. Dig Dis Sci, 1987. 32(7): p. 726-36.

345. Haadem, K., J.A. Dahlstrom, and L. Ling, Anal sphincter competence in healthy women: clinical implications of age and other factors. Obstet Gynecol, 1991. 78(5 Pt 1): p. 823-7.

346. Haadem, K., et al., Estrogen receptors in the external anal sphincter. Am J Obstet Gynecol, 1991. 164(2): p. 609-10.

347. Knudsen, U.B., S. Laurberg, and C.C. Danielsen, Age-related changes in the striated anal sphincter in female rats. A quantitative morphometric study. Scand J Gastroenterol, 1991. 26(3): p. 347-52.

348. Knudsen, U.B., S. Laurberg, and C.C. Danielsen, Influence of bilateral oophorectomy and estrogen substitution on the striated anal sphincter in adult female rats. Scand J Gastroenterol, 1991. 26(7): p. 731-6.

349. Olsen, A.L. and S.S. Rao, Clinical neurophysiology and electrodiagnostic testing of the pelvic floor. Gastroenterol Clin North Am, 2001. 30(1): p. 33-54, v-vi.

350. Snooks, S.J., et al., Injury to innervation of pelvic floor sphincter musculature in childbirth. Lancet, 1984. 2(8402): p. 546-50.

351. Burnett, S.J. and C.I. Bartram, Endosonographic variations in the normal internal anal sphincter. Int J Colorectal Dis, 1991. 6(1): p. 2-4.

352. Snooks, S., M.M. Henry, and M. Swash, Faecal incontinence after anal dilatation. Br J Surg, 1984. 71(8): p. 617-8.

353. Speakman, C.T., et al., Sphincter injury after anal dilatation demonstrated by anal endosonography. Br J Surg, 1991. 78(12): p. 1429-30.

354. Abbsakoor, F., et al., Anal endosonography in patients with anorectal symptoms after haemorrhoidectomy. Br J Surg, 1998. 85: p. 1522-1524.

355. Chun, A.B., et al., Anal sphincter structure and function in homosexual males engaging in anoreceptive intercourse. Am J Gastroenterol, 1997. 92(3): p. 465-8.

356. Engel, A.F., M.A. Kamm, and I.C. Talbot, Progressive systemic sclerosis of the internal anal sphincter leading to passive faecal incontinence. Gut, 1994. 35(6): p. 857-9.

357. Vaizey, C.J., M.A. Kamm, and C.I. Bartram, Primary degeneration of the internal anal sphincter as a cause of passive faecal incontinence. Lancet, 1997. 349(9052): p. 612-5.

358. Varma, J.S., A.N. Smith, and A. Busuttil, Function of the anal sphincters after chronic radiation injury. Gut, 1986. 27(5): p. 528-33.

359. Sood, A., et al., Anorectal dysfunction after surgical treatment for cervical cancer. J Am Coll of Surg, 2002 (In press).

360. Parks, A.G., Anorectal incontinence. Proc R Soc Med, 1975. 68: p. 681-690.

361. Bartolo, D.C., et al., Flap-valve theory of anorectal continence. Br J Surg, 1986. 73(12): p. 1012-4.

362. Bannister, J.J., C. Gibbons, and N.W. Read, Preservation of faecal continence during rises in intra-abdominal pressure: is there a role for the flap valve? Gut, 1987. 28(10): p. 1242-5.

363. Womack, N.R., J.F. Morrison, and N.S. Williams, Prospective study of the effects of postanal repair in neurogenic faecal incontinence. Br J Surg, 1988. 75(1): p. 48-52.

364. Percy, J.P., et al., Electrophysiological study of motor nerve supply of pelvic floor. Lancet, 1981. 1(8210): p. 16-7.

365. Milligan, E. and C.N. Morgan, Surgical anatomy of the anal canal with special reference to anorectal fistulae. Lancet, 1934. 2: p. 1150-1156.

366. Barnes, P.R., et al., Experience of posterior division of the puborectalis muscle in the management of chronic constipation. Br J Surg, 1985. 72(6): p. 475-7.

367. Snooks, S., M.M. Henry, and M. Swash, Fecal incontinence due to external sphincter division in childbirth is associated with damage to the innervation of the pelvic floor musculature: a double pathology. Br J Obstet Gynae, 1985. 92: p. 824-828.

368. Snooks, S.J., M. Swash, and M.M. Henry, Abnormalities in central and peripheral nerve conduction in patients with anorectal incontinence. J R Soc Med, 1985. 78(4): p. 294-300.

369. Lubowski, D.Z., et al., Asymmetrical pudendal nerve damage in pelvic floor disorders. Int J Colorectal Dis, 1988. 3(3): p. 158-60.

370. Tetzschner, T., et al., Anal and urinary incontinence in women with obstetric anal sphincter rupture. Br J Obstet Gynaecol, 1996. 103(10): p. 1034-40.

371. Fasth, S., L. Hulten, and S. Nordgren, Evidence for a dual pelvic nerve influence on large bowel motility in the cat. J Physiol, 1980. 298: p. 159-69.

372. Akervall, S., et al., Manovolumetry: a new method for investigation of anorectal function. Gut, 1988. 29(5): p. 614-23.

373. Shepherd, J.J. and P.G. Wright, The response of the internal anal sphincter in man to stimulation of the presacral nerve. Am J Dig Dis, 1968. 13(5): p. 421-7.

374. Lubowski, D.Z., et al., Neural control of internal anal sphincter function. Br J Surg, 1987. 74(8): p. 668-70.

375. Rogers, J., M.M. Henry, and J.J. Misiewicz, Combined sensory and motor deficit in primary neuropathic fecal incontinence. Gut, 1986. 29: p. 5-9.

376. Roe, A.M., D.C. Bartolo, and N.J. Mortensen, New method for assessment of anal sensation in various anorectal disorders. Br J Surg, 1986. 73(4): p. 310-2.

377. Kiff, E.S. and M. Swash, Normal proximal and delayed distal conduction in the pudendal nerves of patients with idiopathic (neurogenic) faecal incontinence. J Neurol Neurosurg Psychiatry, 1984. 47(8): p. 820-3.

378. Swash, M. and S.J. Snooks, Slowed motor conduction in lumbosacral nerve roots in cauda equina lesions: a new diagnostic technique. J Neurol Neurosurg Psychiatry, 1986. 49(7): p. 808-16.

379. Swash, M., S.J. Snooks, and D.H. Chalmers, Parity as a factor in incontinence in multiple sclerosis. Arch Neurol, 1987. 44(5): p. 504-8.

380. Andrews, J. and P. Nathan, Lesions of the anterior frontal lobes and disturbances of micturition and defecation. Brain, 1964. 87: p. 233-62.

381. Swash, M. and S. Mathers, Sphincter disorders and the nervous system., in Neurology and general medicine, M. Aminoff, Editor. 1989, Churchill-Livingstone: New York. p. 449-70.

382. Caruana, B.J., et al., Anorectal sensory and motor function in neurogenic fecal incontinence. Comparison between multiple sclerosis and diabetes mellitus. Gastroenterology, 1991. 100(2): p. 465-70.

383. Sun, W.M., et al., Disturbances in anorectal function in patients with diabetes mellitus and faecal incontinence. Eur J Gastroenterol Hepatol, 1996. 8(10): p. 1007-12.

384. Schiller, L.R., et al., Pathogenesis of fecal incontinence in diabetes mellitus: evidence for internal-anal-sphincter dysfunction. N Engl J Med, 1982. 307(27): p. 1666-71.

385. Rao, S.S., Practice guidelines for fecal incontinence. Am J Gastroenterol, 2002 (in press).

386. Wald, A., Colonic and anorectal motility testing in clinical practice. Am J Gastroenterol, 1994. 89(12): p. 2109-15.

387. Rao, S.S., et al., Anorectal sensitivity and responses to rectal distention in patients with ulcerative colitis. Gastroenterology, 1987. 93(6): p. 1270-5.

388. Farthing, M.J. and J.E. Lennard-jones, Sensibility of the rectum to distension and the anorectal distension reflex in ulcerative colitis. Gut, 1978. 19(1): p. 64-9.

389. Berger, A., et al., Excision of the rectum with colonic J pouch-anal anastomosis for adenocarcinoma of the low and mid rectum. World J Surg, 1992. 16(3): p. 470-7.

390. Glickman, S. and M.A. Kamm, Bowel dysfunction in spinal-cord-injury patients. Lancet, 1996. 347(9016): p. 1651-3.

391. Brittain, K.R., S.M. Peet, and C.M. Castleden, Stroke and incontinence. Stroke, 1998. 29(2): p. 524-8.

392. Read, N.W., et al., Anorectal function in elderly patients with fecal impaction. Gastroenterology, 1985. 89(5): p. 959-66.

393. Loening-Baucke, V.A. and B.M. Cruikshank, Abnormal defecation dynamics in chronically constipated children with encopresis. J Pediatr, 1986. 108(4): p. 562-6.

394. Goligher, J.C., The functional results after sphincter-saving resections of the rectum. Ann R Coll Surg Engl, 1951. 8(6): p. 421-38.

395. Scharli, A.F. and W.B. Kiesewetter, Defecation and continence: some new concepts. Dis Colon Rectum, 1970. 13(2): p. 81-107.

396. Rao, S.S., J. Kempf, and M. Stessman, Anal seepage: Sphincter dysfunction or incomplete evacuation? Gastroenterology, 1998. 114: p. A824.

397. Rao, S.S., M. Stessman, and M. Kempf, Is biofeedback therapy (BT) useful in patients with anal seepage? Gastroenterology, 1999. 116: p. G4636.

398. Williams, J.G., et al., Incontinence and rectal prolapse: a prospective manometric study. Dis Colon Rectum, 1991. 34(3): p. 209-16.

399. Leung, F. and S.S. Rao, Treatment of fecal incontinence in the elderly., in The Encyclopedia of Elder Care: The Comprehensive Resource on Geriatric and Social Care. 2001, Springer Publishing Company: New York. p. 261-4.

400. Glazener, C.M., et al., Postnatal maternal morbidity: extent, causes, prevention and treatment. Br J Obstet Gynaecol, 1995. 102(4): p. 282-7.

401. Beersiek, F., A.G. Parks, and M. Swash, Pathogenesis of ano-rectal incontinence. A histometric study of the anal sphincter musculature. J Neurol Sci, 1979. 42(1): p. 111-27.

402. Neill, M.E. and M. Swash, Increased motor unit fibre density in the external anal sphincter muscle in ano-rectal incontinence: a single fibre EMG study. J Neurol Neurosurg Psychiatry, 1980. 43(4): p. 343-7.

403. Kiff, E.S. and M. Swash, Slowed conduction in the pudendal nerves in idiopathic (neurogenic) faecal incontinence. Br J Surg, 1984. 71(8): p. 614-6.

404. Snooks, S.J., et al., Effect of vaginal delivery on the pelvic floor: a 5-year follow-up. Br J Surg, 1990. 77(12): p. 1358-60.

405. Allen, R.E., et al., Pelvic floor damage and childbirth: a neurophysiological study. Br J Obstet Gynaecol, 1990. 97(9): p. 770-9.

406. Mallett, V., et al., Pelvic floor damage and childbirth: a neuropysiologic follow up study. Neurourol Urodyn, 1994. 13: p. 357-8.

407. Small, K.A. and J.M. Wynne, Evaluating the pelvic floor in obstetric patients. Aust N Z J Obstet Gynaecol, 1990. 30(1): p. 41-4, 45.

408. Cornes, H., D.C. Bartolo, and G.M. Stirrat, Changes in anal canal sensation after childbirth. Br J Surg, 1991. 78(1): p. 74-7.

409. Chaliha, C., et al., Anal function: effect of pregnancy and delivery. Am J Obstet Gynecol, 2001. 185(2): p. 427-32.

410. Law, P.J., M.A. Kamm, and C.I. Bartram, Anal endosonography in the investigation of faecal incontinence. Br J Surg, 1991. 78(3): p. 312-4.

411. Sultan, A.H., et al., Anal endosonography: Precision of identifying sphincter defects confirmed histologically. Br J Surg, 1994. 81: p. 466-9.

412. Sultan, A.H., et al., Internal anal sphincter division during lateral sphincterotomy. Prospective ultrasound study. Dis Colon Rectrum, 1994. 37: p. 1031-33.

413. Sultan, A.H., et al., Anal-sphincter disruption during vaginal delivery. N Engl J Med, 1993. 329(26): p. 1905-11.

414. Donnelly, V., et al., Obstetric events leading to anal sphincter damage. Obstet Gynecol, 1998. 92(6): p. 955-61.

415. Fynes, M., et al., Cesarean delivery and anal sphincter injury. Obstet Gynecol, 1988. 92: p. 496-500.

416. Abramowitz, L., et al., Are sphincter defects the cause of anal incontinence after vaginal delivery? Results of a prospective study. Dis Colon Rectum, 2000. 43(5): p. 590-6; discussion 596-8.

417. DeLeeuw, J.W., et al., Risk factors for third degree perineal ruptures during delivery. Br J Obstet, 2001. 108: p. 383-7.

418. Buchhave, P., et al., Risk factors for rupture of the anal sphincter. Eur J Obstet Gynecol Reprod Biol, 1999. 87: p. 129-32.

419. Fynes, M., et al., Effect of second vaginal delivery on anorectal physiology and faecal continence: a prospective study. Lancet, 1999. 354(9183): p. 983-6.

420. Willis, S., et al., Childbirth and incontinence: a prospective study on anal sphincter morphology and function before and early after vaginal delivery. Langenbecks Arch Surg, 2002. 387(2): p. 101-7.

421. Nazir, M., E. Carlsen, and B. Nesheim, Do occult anal sphincter injuries, vector volume manometry and delivery variables have any predictive value for bowel symptoms after first time vaginal delivery without third and fourth degree rupture? A prospective study. Acta Obstet Gynecol Scand, 2002. 81: p. 720-726.

422. Belmonte-Montes, C., et al., Anal sphincter injury after vaginal delivery in primiparous females. Dis Colon Rectum, 2001. 44(9): p. 1244-8.

423. Varma, A., et al., Obstetric anal sphincter injury: prospective evaluation of incidence. Dis Colon Rectum, 1999. 42(12): p. 1537-43.

424. Rieger, N., et al., A prospective study of anal sphincter injury due to childbirth. Scand J Gastroenterol, 1998. 33(9): p. 950-5.

425. Zetterstrom, J., et al., Effect of delivery on anal sphincter morphology and function. Dis Colon Rectum, 1999. 42(10): p. 1253-60.

426. Groom, K.M. and S. Paterson-Brown, Third degree tears: are they clinically underdiagnosed? Gastroenterology International, 2000. 13: p. 76-7.

427. Sultan, A.H., M.A. Kamm, and C.N. Hudson, Obstetric perineal tears: an audit of training. Journal of Obstetrics and Gynaecology, 1995. 15: p. 19-23.

428. Sultan, A.H. and R. Thakar, Lower genital tract and anal sphincter trauma. Best Pract Res Clin Obstet Gynaecol, 2002. 16(1): p. 99-115.

429. Sultan, A.H., Editorial: Obstetric perineal injury and anal incontinence. Clinical Risk, 1999: p. 193-6.

430. Gynaecologists, R.C.o.O.a., Management of Third and Fourth Degree Perineal Tears Following Vaginal Delivery., in RCOG Guideline No. 29. 2001, RCOG Press: London.

431. Sangalli, M.R., L. Floris, and A. Weil, Anal incontinence in women with third or fourth degree perineal tears and subsequent vaginal deliveries. Aust N Z J Obstet Gynaecol, 2000. 40: p. 244-8.

432. Fitzpatrick, M., et al., A randomized clinical trial comparing primary overlap with approximation repair of third degree obstetric tears. Am J Obstet Gynecol, 2000: p. 1220-4.

433. Poen, A.C., et al., Third-degree obstetric perineal tear: long-term clinical and functional results after primary repair. Br J Surg, 1998. 85: p. 1433-8.

434. Sultan, A.H., et al., Primary repair of obstetric anal sphincter rupture using the overlap technique. Br J Obstet Gynaecol, 1999. 106(4): p. 318-23.

435. Malouf, A.J., et al., Long-term results of overlapping anterior anal-sphincter repair for obstetric trauma. Lancet, 2000. 355(9200): p. 260-5.

436. Fernando, R.J., et al., Obstetric anal sphincter injury - Does repair technique affects outcome? Blair Bell Society. BJOG, 2004 (in press).

437. Sultan, A.H. and M.A. Abulafi, Anal incontinence - the role of the obstetrician and gynaecologist., in The Yearbook of Obstetrics and Gynaecology, D. Sturdee, K. Olah, and D.e. Keane, Editors. 2001, RCOG Press: London. p. 170-187.

438. Nichols, D.H., Gynecolgic and Obstetric Surgery. 1993, Boston: Mosby. 1053-4.

439. Sultan, A.H. and S.L. Stanton, Preserving the pelvic floor and perineum during childbirth—elective caesarean section? Br J Obstet Gynaecol, 1996. 103(8): p. 731-4.

440. DeLeeuw, J.W., et al., Anal sphincter damage after vaginal delivery: functional outcome and risk factors for fecal incontinence. Acta Obstet Gynecol Scand, 2001. 80: p. 830-834.

441. Johanson, R.B., et al., Maternal and child health after assisted vaginal delivery: five-year follow up of a randomised controlled study comparing forceps and ventouse. Br J Obstet Gynaecol, 1999. 106(6): p. 544-9.

442. Bofill, J.A., et al., A randomized prospective trial of the obstetric forceps versus the M-cup vacuum extractor. Am J Obstet Gynecol, 1996. 175(5): p. 1325-30.

443. Johanson, R.B. and V. Menon, Vacuum extraction versus forceps for assisted vaginal delivery., in The Cochrane Library, Issue 2, C. Review, Editor. 2004, John Wiley & Sons, Ltd.: Chichester, UK.

444. Sultan, A.H., R.B. Johanson, and J.E. Carter, Occult anal sphincter trauma following randomized forceps and vacuum delivery. Int J Gynaecol Obstet, 1998. 61(2): p. 113-9.

445. Johanson, R.B. and B.K.V. Menon, Soft versus rigid vacuum extractor cups for assisted vaginal delivery; Vacuum extraction versus forceps for assisted vaginal delivery., in The Cochrane Library, Issue 1. 2001, Update Software: Oxford.

446. Farrell, S.A., V.M. Allen, and T.F. Baskett, Anal incontinence in primaparas. J Soc Obstet Gynaecol Can, 2001. 23: p. 321-6.

447. MacArthur, C., et al., Obstetric practice and faecal incontinence three months after delivery. Br J Obstet Gynaecol, 2001. 108: p. 678-83.

448. RCOG, Effective procedures in obstetrics suitable for audit., in Audit Committee. 1993, RCOG Medical Audit Unit: Manchester.

449. Woolley, R.J., Benefits and risks of episiotomy: A review of the English language literature since 1980. Obstet Gynecol Surv, 1995. 50: p. 806-35.

450. Carroli, G. and J. Belizan, Episiotomy for vaginal birth, in The Cochrane Library, Issue 2, C. Review, Editor. 2004, John Wiley & Sons, Ltd.: Chichester, UK.

451. Henriksen, T.B., et al., Methods and consequences of changes in use of episiotomy. Bmj, 1994. 309(6964): p. 1255-8.

452. Henriksen, T.B., et al., Episiotomy and perineal lesions in spontaneous vaginal deliveries. Br J Obstet Gynaecol, 1992. 99(12): p. 950-4.

453. Coats, P.M., et al., A comparison between midline and mediolateral episiotomies. Br J Obstet Gynaecol, 1980. 87(5): p. 408-12.

454. Pirhonen, J.P., et al., Frequency of anal sphincter rupture at delivery in Sweden and Finland—result of difference in manual help to the baby's head. Acta Obstet Gynecol Scand, 1998. 77(10): p. 974-7.

455. Thakar, R., et al., Can workshops on obstetric anal sphincter rupture change practice? Int Urogynecol J, 2001: p. 252.

456. Donnelly, V.S., et al., Postpartum fecal incontinence is more common in women with irritable bowel syndrome. Dis Colon Rectum, 1998. 41(5): p. 586-9.

457. Yalla, S.V., et al., Neurourology and Urodynamics: Principles and Practice. 1988, New York: MacMillan. 533.

458. Oelrich, T.M., The urethral sphincter muscle in the male. American Journal of Anatomy, 1980. 158(2): p. 229-46.

459. Myers, R.P., J.R. Goellner, and D.R. Cahill, Prostate shape, external striated urethral sphincter and radical prostatectomy: the apical dissection. Journal of Urology, 1987. 138(3): p. 543-50.

460. Myers, R., et al., Puboperineales: muscular boundaries of the male urogenital hiatus in 3D from magnetic resonance imaging. J Urol, 2000. 164(4): p. 1412-5.

461. Yucel, S. and L.S. Baskin, An anatomical description of the male and female urethral sphincter complex. J Urol, 2004. 171(5): p. 1890-7.

462. U.S.DepartmentofHealthandHumanServices, Benign Prostatic Hyperplasia: Diagnosis and Treatment. Vol. N94-0582. 1994: Agency for Health Care Policy and Research.

463. Warwick, R.T., et al., A urodynamic view of prostatic obstruction and the results of prostatectomy. British Journal of Urology, 1973. 45(6): p. 631-45.

464. Brading, A.F., A myogenic basis for the overactive bladder. [Review] [52 refs]. Urology, 1997. 50(6A Suppl): p. 57-67; discussion 68-73.

465. Speakman, M.J., et al., Bladder outflow obstruction—a cause of denervation supersensitivity. Journal of Urology, 1987. 138(6): p. 1461-6.

466. Brading, A.F., et al., The role of smooth muscle and its possible involvement in diseases of the lower urinary tract. [Review] [15 refs]. Clinical Science, 1986. 70(Suppl 14): p. 7s-13s.

467. Murakumo, M., et al., Three-dimensional arrangement of collagen and elastin fibers in the human urinary bladder: a scanning electron microscopic study. J Urol, 1995. 154(1): p. 251-6.

468. Steers, W.D. and W.C. De Groat, Effect of bladder outlet obstruction on micturition reflex pathways in the rat. Journal of Urology, 1988. 140(4): p. 864-71.

469. Steers, W.D., et al., Alterations in afferent pathways from the urinary bladder of the rat in response to partial urethral obstruction. Journal of Comparative Neurology, 1991. 310(3): p. 401-10.

470. Seki, N., O. Karim, and J. Mostwin, The effect of experimental urethral obstruction and its reversal on changes in passive electrical properties of detrusor muscle. J Urol, 1992. 148(6): p. 1957-61.

471. Seaman, E.K., et al., Persistence or recurrence of symptoms after transurethral resection of the prostate: a urodynamic assessment. Journal of Urology, 1994. 152(3): p. 935-7.

472. Murphy, G.P., et al., National patterns of prostate cancer treatment by radical prostatectomy: results of a survey by the American College of Surgeons Commission on Cancer. Journal or Urology, 1993. 152: p. 1817-1819.

473. Fowler, F.J., Jr., et al., Patient-reported complications and follow-up treatment after radical prostatectomy. The National Medicare Experience: 1988-1990 (updated June 1993). Urology, 1993. 42(6): p. 622-9.

474. Walsh, P.C., Editorial: the status of radical prostatectomy in the United States in 1993: where do we go from here. Journal of Urology, 1994. 152: p. 1816.

475. Morten, J., et al., Urinary incontinence in patients undergoing radical prostatectomy. Journal of Urology, 1995. 153: p. 506A.

476. Litweiler, S.E., et al., Radical retropubic prostatectomy in a community practice setting: analysis of long-term outcomes, continence and potency rates, and retreatment rates. Journal of Urology, 1995. 193: p. 252A.

477. Catalona, W., et al., Potency, continence and complication rates in 1,870 consecutive radical retropubic prostatectomies. J Urol, 1999. 162(2): p. 433-8.

478. Walsh, P., et al., Patient-reported urinary continence and sexual function after anatomic radical prostatectomy. Urology, 2000. 55(1): p. 58-61.

479. de Leval, J., A. Chantraine, and L. Penders, [The striated sphincter of the urethra. 1: Recall of knowledge on the striated sphincter of the urethra]. [French]. Journal d Urologie, 1984. 90(7): p. 439-54.

480. Myers, R.P., Male urethral sphincter anatomy and radical prostatectomy. Urological Clinics of North America, 1991. 18(2): p. 211-225.

481. Coakley, F.V., et al., Urinary continence after radical retropubic prostatectomy: relationship with membranous urethral length on preoperative endorectal magnetic resonance imaging. J Urol, 2002. 168(3): p. 1032-5.

482. Zvara, P., et al., The detailed neuroanatomy of the human striated urethral sphincter [see comments]. British Journal of Urology, 1994. 74(2): p. 182-7.

483. Narayan, P., et al., Neuroanatomy of the external urethral sphincter: implications for urinary continence preservation during radical prostate surgery [see comments]. Journal of Urology, 1995. 153(2): p. 337-41.

484. Hollabaugh, R., et al., Preservation of putative continence nerves

during radical retropubic prostatectomy leads to more rapid return of urinary continence. Urology, 1998. 51(6): p. 960-7.

485. Kaye, K., et al., Urinary continence after radical retropubic prostatectomy. Analysis and synthesis of contributing factors: a unified concept. Br J Urol, 1997. 80(3): p. 444-501.

486. John, H., et al., Evidence of trigonal denervation and reinnervation after radical retropubic prostatectomy. J Urol, 2001. 165(1): p. 111-3.

487. Soloway, M. and E. Neulander, Bladder-neck preservation during radical retropubic prostatectomy. Semin Urol Oncol, 2000. 18(1): p. 51-6.

488. Poon, M., et al., Radical retropubic prostatectomy: bladder neck preservation versus reconstruction. J Urol, 2000. 163(1): p. 194-8.

489. Shelfo, S., C. Obek, and M. Soloway, Update on bladder neck preservation during radical retropubic prostatectomy: impact on pathologic outcome, anastomotic strictures, and continence. Urology, 1998. 51(1): p. 73-8.

490. John, H. and D. Hauri, Seminal vesicle-sparing radical prostatectomy: a novel concept to restore early urinary continence. Urology, 2000. 55(6): p. 820-4.

491. Jarow, J., Puboprostatic ligament sparing radical retropubic prostatectomy. Semin Urol Oncol, 2000. 18(1): p. 28-32.

492. Poore, R., D. McCullough, and J. Jarow, Puboprostatic ligament sparing improves urinary continence after radical retropubic prostatectomy. Urology, 1998. 51(1): p. 67-72.

493. Jorion, J., [Aponeurotic suspension of a vesico-urethral anastomosis after radical prostatectomy]. Acta Urol Belg, 1998. 66(2): p. 1-4.

494. Gray, M., G. Petroni, and D. Theodorescu, Urinary function after radical prostatectomy: a comparison of the retropubic and perineal approaches. Urology, 1999. 53(5): p. 881-90; discussion 890-1.

495. Walsh, P.C., A.W. Partin, and J.I. Epstein, Cancer control and quality of life following anatomical radical retropubic prostatectomy: results at ten years. Journal of Urolgy, 1994. 152: p. 1831-1836.

496. Chao, R. and M.E. Mayo, Incontinence after radical prostatectomy: detrusor or sphincter causes [see comments]. Journal of Urology, 1995. 154(1): p. 16-8.

497. Prieto Chaparro, L., et al., [Radical prostatectomy: usefulness of selective electromyography of the periurethral sphincter in the assessment of urinary continence]. [Spanish]. Archivos Espanoles de Urologia, 1994. 47(5): p. 483-7.

498. Aanestad, O., et al., Interference pattern in the urethral sphincter: a quantitative electromyographic study in patients before and after radical retropubic prostatectomy. Scand J Urol Nephrol, 1998. 32(6): p. 378-82.

499. Hammerer, P., et al., Urodynamic parameters before and after radical prostatectomy. Journal of Urology, 1993. 149: p. 235A.

500. Ficazzola, M. and V. Nitti, The etiology of post-radical prostatectomy incontinence and correlation of symptoms with urodynamic findings. J Urol, 1998. 160(4): p. 1317-20.

501. Kleinhans, B., et al., Changes of urodynamic findings after radical retropubic prostatectomy. Eur Urol, 1999. 35(3): p. 217-21; discussion 221-2.

502. Winters, J., R. Appell, and R. Rackley, Urodynamic findings in postprostatectomy incontinence. Neurourol Urodyn, 1998. 17(5): p. 493-8.

503. Groutz, A., et al., The pathophysiology of post-radical prostatectomy incontinence: a clinical and video urodynamic study. J Urol, 2000. 163(6): p. 1767-70.

504. Hu, K. and K. Wallner, Urinary incontinence in patients who have a TURP/TUIP following prostate brachytherapy. Int J Radiat Oncol Biol Phys, 1998. 40(4): p. 783-6.

505. Goluboff, E.T., et al., Urodynamics and the etiology of post-prostatectomy urinary incontinence: the initial Columbia experience [see comments]. Journal of Urology, 1995. 153(3 Pt 2): p. 1034-7.

506. Leach, G.E., Post-prostatectomy incontinence: the importance of bladder dysfunction [editorial; comment]. Journal of Urology, 1995. 153(3 Pt 2): p. 1038.

507. Leach, G.E., C.M. Yip, and B.J. Donovan, Post-prostatectomy incontinence: the influence of bladder dysfunction. Journal of Urology, 1987. 138(3): p. 574-8.

508. Foote, J., S.K. Yun, and G.E. Leach, Post-prostatectomy incontinence: pathophysiology, evaluation and management. Urological Clinics of North America, 1991. 18: p. 229.

509. Aboseif, S.R., et al., Preoperative urodynamic evaluation: does it predict the degree of urinary continence after radical retropubic prostatectomy? Urologia Internationalis, 1994. 53(2): p. 68-73.

510. Furlow, W.L. and D.M. Barrett, Recurrent or persistent urinary incontinence in patients with the artificial urinary sphincter: diagnostic considerations and management. Journal of Urology, 1985. 133(5): p. 792-5.

511. Diokno, A.C., L.P. Sonda, and R.J. MacGregor, Long-term followup of the artificial urinary sphincter. Journal of Urology, 1984. 131(6): p. 1084-6.

512. Fishman, I.J., R. Shabsigh, and F.B. Scott, Experience with the artificial urinary sphincter model AS800 in 148 patients. Journal of Urology, 1989. 141(2): p. 307-10.

513. Gundian, J.C., D.M. Barrett, and B.G. Parulkar, Mayo Clinic experience with use of the AMS800 artificial urinary sphincter for urinary incontinence following radical prostatectomy. Journal of Urology, 1989. 142(6): p. 1459-61.

514. Kil, P.J., et al., Factors determining the outcome following implantation of the AMS 800 artificial urinary sphincter. British Journal of Urology, 1989. 64(6): p. 586-9.

515. Malloy, T.R., A.J. Wein, and V.L. Carpiniello, Surgical success with AMS M800 GU sphincter for male incontinence. Urology, 1989. 33(4): p. 274-6.

516. Webster, G.D. and S.A. Sihelnik, Troubleshooting the malfunctioning Scott artificial urinary sphincter. Journal of Urology, 1984. 131(2): p. 269-72.

517. Perez, L.M. and G.D. Webster, Successful outcome of artificial urinary sphincters in men with post-prostatectomy urinary incontinence despite adverse implantation features. Journal of Urology, 1992. 148(4): p. 1166-70.

518. Resnick, N.M., Voiding dysfunction in the elderly., in Neurourology and Urodynamics: Principles and Practice., M.E. Yalla SV, Elbadawi A, Blaivas JG,, Editor. 1988, MacMillan Publising Company: New York. p. 303-330.

519. Ouslander, J.G., Urinary incontinence in nursing homes: incidence, remission and associated factors. J Am Geriatr Soc, 1993. 41: p. 1083-1089.

520. Brandeis, G.B., et al., The prevalence of potentially remediable urinary incontinence in frail elderly people: A study using the Minimum Data Set. J Am Geriatr Soc, 1997. 45: p. 179-184.

521. Diokno, A.C., M.B. Brown, and A.R. Herzog, Relationship between use of diuretics and continence status in the elderly. Urology, 1991. 38: p. 39-42.

522. Fantl, J.A., et al., Diuretics and urinary incontinence in community-dwelling women. Neurourol Urodyn, 1990. 9: p. 25-34.

523. Resnick, N.M., et al., Risk factors for incontinence in the nursing home: A multivariate study. Neurourol Urodyn, 1988. 7: p. 274-276.

524. Resnick, N.M., et al., Short-term variability of self report of incontinence in older persons. Journal of the American Geriatrics Society, 1994. 42(2): p. 202-7.

525. Resnick, N.M., Urinary incontinence in the elderly. Medical Grand Rounds, 1984. 3: p. 281-290.

526. Resnick, N. and M. Paillard, Natural history of nosocomial incontinence. Gerontologist, 1984. 24: p. 212A.

527. Boscia, J.A., et al., Lack of association between bacteriuria and symptoms in the elderly. Am J Med, 1986. 81: p. 979-982.

528. Ouslander, J.G. and J.F. Schnelle, Incontinence in the nursing home. Ann Int Med, 1995. 122: p. 438-449.

529. Holroyd-Leduc and S.E. Straus, Management of incontinence in women. JAMA, 2004. 291: p. 986-995.

530. Marshall, H.J. and D.G. Bevers, a-adrenoceptor blocking drugs and female urinary incontinence: prevalence and reversibility. Brit J Clin Pharmacol, 1996. 42: p. 507-509.

531. Hellstrom, P.M. and A. Sjoqvist, Involvement of opioid and nicotinic receptors in rectal and anal reflex inhibition of urinary bladder motility in cats. Acta Physiol Scand, 1988. 133: p. 559-562.

532. Damon, H., et al., Postdelivery anal function in primiparous females: ultrasound and manometric study. Dis Colon Rectum, 2000. 43(4): p. 472-7.

533. Faltin, D.L., et al., Diagnosis of anal sphincter tears by postpartum endosonography to predict fecal incontinence. Obstet Gynecol, 2000. 95(5): p. 643-7.

534. Wood, J., L. Amos, and N. Rieger, Third degree anal sphincter tears: risk factors and outcome. Aust N Z J Obstet Gynaecol, 1998. 38(4): p. 414-7.

535. Walsh, C.J., et al., Incidence of third-degree perineal tears in labour and outcome after primary repair. Br J Surg, 1996. 83(2): p. 218-21.

536. Sander, P., et al., Anal incontinence after third- /fourth degree laceration. One-year follow-up after pelvic floor exercises. Int J Urogynecol, 1999. 10: p. 177-81.

537. Crawford, L.A., et al., Incontinence following rupture of the anal sphincter during delivery. Obstet Gynecol, 1993. 82(4 Pt 1): p. 527-31.

538. Sorensen, M., et al., Sphincter rupture in childbirth. Br J Surg, 1993. 80(3): p. 392-4.

539. Nielsen, M.B., et al., Anal endosonographic findings in the follow-up of primarily sutured sphincteric ruptures. Br J Surg, 1992. 79(2): p. 104-6.

540. Go, P.M. and G.A. Dunselman, Anatomic and functional results of surgical repair after total perineal rupture at delivery. Surg Gynecol Obstet, 1988. 166(2): p. 121-4.

541. Fenner, D.E., et al., Fecal and urinary incontinence after vaginal delivery with anal sphincter disruption in an obstetrics unit in the United States. Am J Obstet Gynecol, 2003. 189(6): p. 1543-9; discussion 1549-50.

542. Wagenius, J. and J. Laurin, Clinical symptoms after anal sphincter rupture: a retrospective study. Acta Obstet Gynecol Scand, 2003. 82(3): p. 246-50.

543. Fornell, E.K., et al., Clinical consequences of anal sphincter rupture during vaginal delivery. J Am Coll Surg, 1996. 183(6): p. 553-8.

544. Zetterstrom, J., et al., Anal sphincter tears at vaginal delivery: risk factors and clinical outcome of primary repair. Obstet Gynecol, 1999. 94(1): p. 21-8.

545. Sorensen, S.M., et al., Perineal rupture following vaginal delivery. Acta Obstet Gynecol Scand, 1988. 67: p. 315-8.

546. Williams, A., et al., Effect of new guideline on outcome following third degree perineal tears: results of a three-year audit. Int Urogynecol J, 2003. 14: p. 385-389.

547. Kammerer-Doak, D.N., et al., A prospective cohort study of women after primary repair of obstetric anal sphincter laceration. Am J Obstet Gynecol, 1999. 181(6): p. 1317-22; discussion 1322-3.

548. Haadem, K., S. Ohrlander, and G. Lingman, Long-term ailments due to anal sphincter rupture caused by delivery—a hidden problem. Eur J Obstet Gynecol Reprod Biol, 1988. 27(1): p. 27-32.

549. Bek, K.M. and S. Laurberg, Risks of anal incontinence from subsequent vaginal delivery after a complete obstetric anal sphincter tear. Br J Obstet Gynaecol, 1992. 99(9): p. 724-6.

550. Davis, K., et al., Symptoms and anal sphincter morphology following primary repair of third-degree tears. Br J Surg, 2003. 90(12): p. 1573-9.

551. Nazir, M., et al., Early evaluation of bowel symptoms after primary repair of obstetric perineal rupture. Dis Colon Rectrum, 2003. 46: p. 1245-1250.

552. Gjessing, H., B. Backe, and Y. Sahlin, Third degree obstetric tears; outcome after primary repair. Acta Obstet Gynecol Scand, 1998. 77(7): p. 736-40.

553. Goffeng, A.R., et al., Objective methods cannot predict anal incontinence after primary repair of extensive anal tears. Acta Obstet Gynecol Scand, 1988. 77: p. 439-43.

554. Kelly, W. and E. Burnham, Disease of the Kidneys, Ureters and Bladder, With Special reference to Women. Vol. 2. 1922.