Continued from front page

usually not curative, continued treatment is necessary.

Reports of various outcomes with drug therapy must be considered in the light that about 30% of trials reported in the literature declare pharmaceutical support, hence may be biased.

Anticholinergic drugs

Anticholinergic drugs are better than placebo. The most common drugs used to treat detrusor overactivity are Oxybutinin (Ditropan), Tolterodine (Detrusitol) and more recently Solfenacin succinate (Vesicare). It has been established that oxybutinin and Tolterodine demonstrate similar efficacy, but those taking Tolterodine have less risk of withdrawal due to adverse events and less risk of dry mouth. There are insufficient trials to draw conclusions about the efficacy of solfenacin versus tolterodine. There is less risk of dry mouth with extended release preparations regardless of which drug was used. There is less risk of dry mouth with lower doses. There is insufficient data to reach conclusions about the relative efficacy of different doses of oxybutinin and solfenacin. It has been established that with tolterodine, the lowest doses are less effective.

Extended release preparations have been developed to reduce the side effects, particularly dry mouth. For oxybutinin dry mouth is between 9% and 34% less likely with extended preparation (Oxytrol), Extended release preparation of tolterodine has a 6% to 38% less risk of dry mouth. Unfortunately this is not yet available in Australia.

Practice points

- anticholinergic drugs are effective
- oxybutinin and Tolterodine appear to have similar effects of cure
- tolterodine has lesser risk of withdrawal due to dry mouth
- if Tolterodine is being prescribed, the clinical effects are similar with 1 mg and 2 mg dose but dry mouth is less likely with the 1 mg dose
- when extended preparations are prescribed this results in a lower risk of dry mouth but no loss of efficacy.[1]

Botox (Botulinum toxin) injections

The injection of botox into the bladder has been recently advocated in refractory cases of detrusor overactivity. The rationale of using botox is that detrusor paralysis should reduce the symptoms of bladder overactivity. Botox is injected into the detrusor walls via cystoscopy, usually avoiding the trigone.

Only a small number of randomised controlled trials are currently available. Intravesical botox does appear to reduce incontinence when compared with placebo. A significant increase in cystometric capacity and decrease in detrusor pressure has been reported after botox injection. Additionally quality of life measures have been shown to improve after botox injection. Few adverse side effects have been reported. Increase in residual volumes has been reported. It must be recognised that the therapeutic use of botox is recent and that rare adverse effects may yet to declare themselves.

It appears from the published literature that significant improvement lasts for 1 year to 18 months, after which time, repeat injection is required.

Most of the studies have been used for neurogenic overactive bladder, hence results may not be the same with idiopathic detrusor overactivity.

Practice points

- botox injections show promise
- as yet little data exists on safety and efficacy
- most of the evidence to support its use is anecdotal
- the difference in response of neurogenic and idiopathic detrusor overactivity is as yet unclear
- no long-term follow up has been published
- the optimal dose has not as yet been established
- botox increases post-void residual volume and cystometric capacity[2]

1 Hay-Smith J Herbison P Ellis G Morris A "Which anticholinergic drug for overactive bladder symptoms in adults" *Cochrane Database of Systematic Reviews* (3) CD005429, 2005

2 Duthie J Wilson DI Herbison GP Wilson D " Botulinum toxin injections for adults with overactive bladder syndrome (Review)" *Cochrane Database of Systematic Reviews* (3) CD005493, 2007

Vesica

SYDNEY urodynamic CENTRES

Who are 'Sydney Urodynamic Centres'?

Sydney Urodynamic Centres has been providing the women of New South Wales and their doctors with a comprehensive urodynamic service for the past 20 years. They are able to scientifically assess female urinary incontinence and lower urinary tract dysfunction, provide an accurate diagnosis to the referring doctor and advise on clinical management.

The service is run by three urogynaecologists, trained and accredited in this sub-specialty by the Royal Australian and New Zealand College of Obstetricians and Gynaecologist (RANZCOG). These partners are assisted by a group of highly trained nurses who are adept at making the experience more pleasant for the women. There are seven centres around Sydney where studies can be performed in order to facilitate easy access to the service for most women.

These locations are:

SYDNEY
Sydney Urodymanic Centre
Level 3, 139 Macquarie Street, Sydney

CHATSWOOD
North Shore Urodynamic Centre
Suite 70, Chatswood Village
47 Neridah Street, Chatswood

CAMPERDOWN
Camperdown Urodynamic Centre
Suite 404, RPAH Medical Centre
100 Carillon Avenue, Newtown

CONCORD
Concord Urodynamic Centre
Level 2, Concord Hospital Medical Centre
209 Hospital Road, Concord West

BANKSTOWN
Bankstown Urodynamic Centre
Suite 2, Level 1, 56 Kitchener Parade, Bankstown

LIVERPOOL
Liverpool Urodynamic Centre
Suite 20, 2nd Floor, 17 Moore Street, Liverpool

PENRITH
Penrith Urodynamic Centre
Nepean Private Specialist Centre
Suite 1, 1A Barber Avenue, Penrith

For all appointments call (02) 9790 6969

If you don't want to receive this newsletter or the details we have for you are incorrect please contact us at pracman@urodynamic.com.au or fax (02) 9790 6441.

Associate Professor Hans Peter Dietz

MD PhD FRANZCOG DDU CU

Associate Professor Dietz graduated from Heidelberg University, Germany, in 1988. After first emigrating to New Zealand, he arrived in Australia in 1997 and completed his FRANZCOG training in 1998. Between 1999 and 2002, Associate Professor Dietz undertook urogynaecology subspecialty training in Sydney, in addition to presenting a PhD thesis at the University of NSW. His major research interests include the interaction between pelvic floor biomechanics and childbirth, pelvic floor imaging, as well as the effects of anti-incontinence surgery on anatomy and voiding function. Today, he is employed as Associate Professor of Obstetrics and Gynaecology at the Nepean Campus of the University of Sydney, as well as a specialist in urogynaecology at the Sydney Urodynamic Centres.

Associate Professor Christopher Benness

MBBS MD FRCOG FRANZCOG CU

Following graduation from Sydney University, Associate Professor Benness did his specialty and sub-specialty training in both Sydney and London. An accredited sub-specialist in urogynaecology with the RANZCOG, he is a trainer and examiner in this field. He is a senior specialist in gynaecology at the Royal Prince Alfred Hospital, where he is also Head of the Department of Urogynaecology and a past Chairman of the Medical Board. He is the current Chairman of the NSW State Committee of RANZCOG. He is active in both teaching and research, and is a Clinical Associate Professor at the University of Sydney. His main research interests are improving surgical procedures for stress incontinence and prolapse.

Dr Andrew Korda

MA MHL MB BS FRCOG FRANZCOG CU FACLM

Following graduation from the University of Sydney, Dr Korda did his speciality training at the Royal Prince Alfred Hospital in Sydney, with further training in Oxford and New York. He is an accredited sub-specialist in urogynaecology, pelvic floor disorders, and reconstructive pelvic surgery. Dr Korda is also a senior specialist in gynaecology at the Royal Prince Alfred Hospital, where he is Chairman of the Pelvic Floor Unit. He is a clinical lecturer in gynaecology at the University of Sydney, and is involved in both teaching and research. Dr Korda was Chief Examiner in Urogynaecology and past Chairman of the Urogynaecology Sub-specialty Committee of the RANZCOG. He is also trustee of the Australian Bladder Foundation.

Vesica

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SYDNEY urodynamic CENTRES

Sydney Urodynamic Centres newsletter for medical practitioners

Practice point

The major portion of the neurohormonal stimulus for physiological bladder contraction is acetylcholine induced stimulation of postganglionic parasympathetic muscarinic cholinergic receptor sites on bladder smooth muscle.

Anticholinergic drugs depress normal bladder contractions and involuntary detrusor contractions. When using anticholinergic drugs, the normal bladder contractions are depressed, involuntary detrusor contractions are diminished and maximum bladder capacity is increased. It is therefore difficult to evaluate urodynamic studies when a patient is taking anticholinergic drugs.

It is important to stop anticholinergic drugs for a week prior to a urodynamic study.

The aetiology of prolapse

by Hans Peter Dietz

Female pelvic organ prolapse is a common condition. It conveys a significant burden on individuals and society, even if it rarely threatens the general health and/ or life of the patient. In the US alone, pelvic organ prolapse is thought to lead to over 250,000 surgical procedures per year, with about 30% being re-operations(1). In a population study performed in the Pacific Northwest, the lifetime risk of undergoing a single operation for prolapse or incontinence by age 80 was found to be 11.1% in 1997(2). Female pelvic organ prolapse may give rise to symptoms of vaginal fullness and dragging, with the patient eventually noticing a protrusion from the vagina. Certain forms of prolapse are associated with bladder and bowel dysfunction(3, 4), although the exact nature and magnitude of such associations are not well defined at present.

Another issue that until recently was very poorly defined is aetiology. When one checks recent textbooks on the causation of female pelvic organ prolapse one finds more waffle than fact. Childbirth of course is the prime suspect, and this link is well established in epidemiological studies(5, 6). Until very recently however nobody knew why. Obesity is also blamed, as is ageing and chronic conditions such as asthma and constipation, again without any particular insight into causative mechanisms. And then there are 'genetic factors', usually blamed on collagen subtypes or metabolism. Research into this aspect of the aetiology of prolapse is very fashionable. To date, unfortunately it has generated nothing but hot air. And even the previously mentioned accepted risk factors may not be as cut- and- dried as one would accept.

Let's look at the most obvious of all- ageing. Just about everyone seems to agree that age is an established risk factor(7). Experimental findings of unexpectedly high rates of mild/ moderate prolapse in young and/or asymptomatic women(8, 9) and increased tissue stiffness after menopause(10) haven't shaken the consensus. It's very odd then that, in a study on 971 women, we've recently found that cystocele and rectocele are NEGATIVELY associated with age in women after menopause. In essence, our findings suggest that things get worse for the anterior and central compartment until about the age of 55. After that, the chance of improvement is slightly higher than the likelihood of deterioration (see Figure 1). So maybe age isn't such an important factor after all- except for uterine prolapse, which shows a near- linear association with age.

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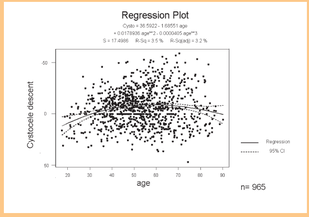

Figure 1: The relationship between age and cystocele descent.

What about pregnancy and childbirth? For quite a few years now the debate has been over whether it's pregnancy itself or the delivery that predisposes to prolapse. Both epidemiological and observational cohort studies have now shown that the main factor in the causation of prolapse is vaginal childbirth, and it seems we've recently worked out how it happens.

The levator ani muscle has to stretch enormously in childbirth, by a factor of anywhere by between 25 and 250%, depending on the distensibility of the muscle in a given individual. Skeletal muscle is supposed to rupture once it is stretched beyond a factor of 1.6, but in pregnancy other rules apply. Amazingly, most women in fact don't do major damage. Some overstretch the levator which causes excessive distensibility ('ballooning'), and this is associated with symptoms and signs of prolapse of all three compartments(11). We call this 'microtrauma'. Others

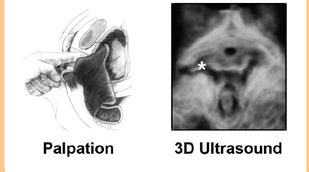

Figure 2: Levator defects can be palpated. The defect visible on ultrasound (right image) is evident as a widened gap between the urethra and the insertion of the puborectalis muscle on the pelvic sidewall on vaginal examination as illustrated on the left. A full avulsion is defined as a complete absence of muscle fibres on the inferior pubic ramus- that is, there is no muscle palpable over the bony surface of the inferior pubic ramus.

suffer 'macrotrauma', that is, the lowermost part of the levator muscle, the puborectalis, is shorn off the pelvic sidewall during crowning of the baby's head. We've shown that this trauma is the result of childbirth(12), that it can be detected in Labour Ward(13), and that the risk is strongly associated with age at first delivery and vaginal operative delivery(14). This kind of trauma can be palpated(15), although confirmation by imaging is preferable.

While there clearly are lots of other factors, levator tears ('avulsion injury') are the most substantial risk factor for female pelvic organ prolapse that we've found so far. This applies mainly to prolapse of the bladder and uterus (see Table).

	Cystocele (n=781)	Uterine prolapse (n=681)*	Rectocele (n=781)
Unilateral avulsion	2.2 (1.9-2.7)	2.0 (1.0-4.1)	1.2 (0.9-1.7)
Bilateral avulsion	2.5 (2.1-3.0)	7.1 (4.3-11.6)	1.6 (1.2-2.1)
Any levator avulsion	2.3 (2.0-2.7)	4.0 (2.5-6.5)	1.4 (1.1-1.7)

Table 1: Relative Risks of significant prolapse (stage 2 and higher) in women with levator avulsion relative to women with intact levator ani. The figures in parentheses signify confidence intervals.

Patients with unilateral avulsion are 2-4 times more likely to have a stage 2 or higher prolapse of the bladder and uterus. For bilateral avulsion this relationship is even stronger, with a sevenfold increase in the risk of uterine prolapse. Our findings are consistent with results recently obtained by magnetic resonance imaging(16). It is very likely that delivery-related major levator trauma ('avulsion injury') represents a significant part of the 'missing link' between vaginal childbirth and prolapse.

I have little doubt that we will soon learn how to predict and prevent such trauma, but of course all such efforts come too late for those who see us with prolapse. To benefit those women we will have to focus on developing secondary repair techniques, or at least surgical techniques that focus on compensating for levator trauma. And of course we'll have to learn how to diagnose levator avulsion, whether it be on imaging or on clinical examination. If you're interested in this topic we'll hold a course on 'Pelvic Floor Assessment' in July 2008 at Nepean Hospital. For further information email me at hpdietz@bigpond.com.

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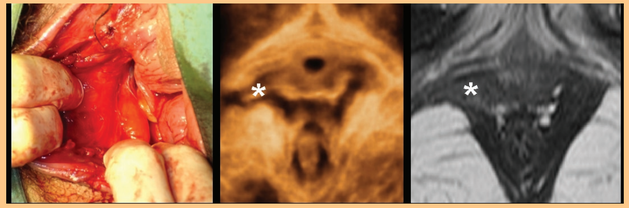

Figure 1: Typical right- sided levator avulsion injury as diagnosed in Delivery Suite (left) after a normal vaginal delivery at term, on 3D ultrasound (center) and on magnetic resonance imaging (right) three months postpartum. This patient was asymptomatic apart from deep dyspareunia. The defect is indicated by a *.

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DETRUSOR OVERACTIVITY

by Andrew Korda

The normal bladder is a compliant reservoir that only contracts under voluntary control during micturition. An unstable bladder is one that contracts involuntarily or can be provoked to do so.

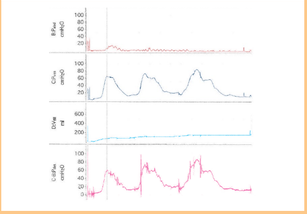
The motor nerve supply to the detrusor muscle is via the parasympathetic nerve fibres, specifically to the pelvic nerve (S2-4). Its effects are mediated by the transmission of acetylcholine on muscarinic receptors. Sympathetic innervation is derived from the hypogastric nerve and acts predominantly on beta-adrenoreceptors to cause relaxation of the detrusor.

A detrusor contraction is initiated at the rostral pons. Efferent pathways emerge from the sacral spinal cord as the pelvic parasympathetic nerves and run forwards to the bladder. Acetylcholine is released at the neuromuscular junction, which results in a co-ordinated bladder contraction. In order to achieve normal detrusor function a balance between parasympathetic and sympathetic stimulation is needed.

Detrusor overactivity is defined as a condition in which the detrusor contracts objectively on urodynamic testing either spontaneously or on provocation, during bladder filling.

The uninhibited contractions give rise to frequency, nocturia, urgency, urge incontinence and nocturnal enuresis. Most commonly patients have a multitude of these symptoms.

The pathophysiology of this condition is not fully understood. In a minority of women there is a detectable underlying neurological cause for their symptoms, but this is unusual. Detrusor overactivity may arise from poorly learnt bladder control as an infant. There is a strong association between childhood enuresis and the development of detrusor overactivity in adult life. Many women with detrusor overactivity show evidence of abnormal psychoneurotic state.



An example of phasic detrusor contractions of an overactive bladder during the filling phase of urodynamic studies

Increased sensitivity of nerve endings in the bladder to local stimuli may result in abnormal reflex responses that result in frequency and urgency. It is thought that there is a change in the properties of smooth muscle of the detrusor, which predisposes to unstable contractions. This change is caused by long-term reduction in the functional innervation of the bladder wall.

Although detrusor overactivity has no known aetiological factor, it is more common in women who have had vaginal deliveries. It has been well established that there is a relationship between incontinence and the number of children. The first child and pregnancy virtually doubles the prevalence of incontinence in women from 20% to about 40%.[1]

Clinical presentation is usually:

- frequency,
- nocturia,
- urgency,
- urge incontinence
- stress incontinence
- nocturnal enuresis
- coital incontinence.

The main therapies are:

- drug therapy;
- behaviour therapy;
- maximal electrical stimulation;
- botox injection;
- augmentation cystoplasty;
- urinary diversion.

The last two therapies are used in extreme cases only, when there is severe compromise in the patient's quality of life.

Overactive bladder is a chronic condition and treatment is

1 Millard RJ "Epidemiology (Australia) in Cardozo L & Staskin D (eds) *Textbook of Female Urology and Urogynaecology* (Isis Medical Media Ltd: London; 2001) 40