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29th September – 3rd October 2009

"We broke our records"

Never before have there been so many excellent abstract submissions

SAN FRANCISCO – With the 39th meeting, the Congress of the International Continence Society (ICS) finally returns to the U.S.A. The ICS Congress News talked to the president of the current congress, Mr. Anthony Stone.

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1st Edition

CN: Mr. Stone, the 39th meeting of the International Continence Society will take place in San Francisco. How important was it to bring the congress to the U.S.A.?

Stone: The last time the ICS was in the United States was ten years ago, in Denver, Colorado. The ICS is obviously an international society, but in terms of membership numbers I believe there is a little more emphasis on European members. This is why we were very keen in bringing the ICS to the U.S.A. It is a tremendous opportunity to involve and collaborate with U.S.-American clinicians and scientists.

CN: There are many topics in the scientific program. Which will be the highlights?

Stone: I would not be able to tell you until all presentations have been

heard. There was however a large increase in abstract submissions to the society this year. We broke our record of over 1,000, and the overall standard of the presentations that have been assessed by our scientific committee was excellent. Because of this, we increased the number of accepted papers by over 30 percent, thus we have a lot of parallel sessions. This way we will be able to hear a lot of highlights all across the board: basic science, epidemiology, medical and surgical therapy. It will be a bit of a change for the ICS though which was often limited. We felt that the excellence of the submissions were so good that we had to accept more papers.

Continence Society

CN: There will be four state of the art lectures. In one lecture, the pharmaceutical industry and medical education will be contrasted. How important is this relationship at all?

Stone: The pharmaceutical industry is very important in our practice. But I would have to say, the



ICS Congre

Anthony Stone

same goes for devices for the treatment of incontinence. The ICS has a role to promote education, research and improve patient care. Because of the tremendous number of drugs and devices, we really need a balanced relationship. We need balance in financial support, education, research and outcomes between the ICS and the pharmaceutical industry.

> CN: Has this relationship changed over the years? consider that until relatively recently

we had maybe one drug to treat the overactive bladder, now we have several drugs. In terms of overall incontinence treatment, we had no devices and now we have many. The ICS is of course the responsible body to oversee and promote research, so the relationship has become more important. It has become symbiotic. We need the pharmaceutical industry to develop the drugs and devices, and they need us to be able to evaluate and use them on our patients to improve patient care.

CN: *There are a lot of congresses* in the field of urology. Which role does the Congress of the International Continence Society play here?

Stone: Basically, the great difference with the ICS is that it is really focused on the management of incontinence, both urinary and fecal. Therefore this is a large focus in the areas of education, research and patient care.

> CN: What is the most important goal of the society in the future?

Stone: Overall, the goal of the A ICS is to be a forum for this diverse group of people to improve patient Stone: Yes. If you care in the field of incontinence. But what I think is very important is

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the education in the less developed places of the world, where incontinence may be a significant problem but they do not have the medical expertise or the facilities.

CN: Incontinence therapy is a field with a lot of options to cure patients: drug therapy, surgical therapy, continence training. Which field has been developing the fastest?

Stone: You cannot look at one area, this is a multi-faceted development. Drugs have become more effective and there has been a lot of improvement regarding side-effects, especially for the overactive bladder. We have now less invasive surgical procedures and there is a better understanding of conservative therapy. All these areas are developing at a similar pace.

CN: Which field seems to be the most promising in the future?

Stone: If you look at this multi-faceted development, there are many areas that show great promise. Especially in the prevention of incontinence, like birth injury and understanding the genetics of stress incontinence and overactive bladder or regeneration of the bladder and sphincter. There has also been improvement in the area of neuromodulation – there is some very exciting work on reinnervation of the bladder in patients with Spina bifuda or spinal cord injuries. But also improvements in diagnostic parameters such as functional MRI and pelvic ultrasound seem to be very promising.

CN: Incontinence is a very common disorder. Everywhere in the world there are people who are affected by it. How could the ICS face this challenge?

Stone: We always had challenges to deal with. This is not different to any of these other challenges. Currently, the way the ICS is dealing with this global problem is to facilitate dissemination of knowledge by education, workshops and courses, developing fellowships and promoting collaborative research. And as already mentioned, partnerships with the industry make sure that we get the right drugs and the right products to manage this problem.

CN: Which role could media play regarding educating people about the importance of incontinence therapy?

Stone: Incontinence is a common problem, but it is a difficult one to communicate to the general public. I think the media can be very helpful in identifying ways of educating people. It can always act as a conduit for both the good developments and certainly alert the public to bad developments such as a bad device or a bad drug. So it actually plays both ways.

CN: Mr. Stone, thank you for answering our questions.







ICS Notes

- If you are attending a course or a workshop, please ensure that you complete the evaluation form and return it to the hostess at the entrance on your way out of the room. In return for this, you will receive a certificate of attendance with CME accreditation. If you did not get chance to exchange your evaluation form please bring it along to the ICS booth and we would be happy to provide your certificate of attendance.
- If you have any questions or queries regarding your membership, ICS educational courses, or if you need any other information on the ICS then please visit the ICS exhibition booth where a member of ICS staff will be able to assist you.
- Visit the ICS booth to review and print abstracts and watch videos. Also renew your membership for 2010 or join the ICS! Also exchange your voucher (found in your delegate bag) for your ICS 2009 Abstract USB stick.
- ICS members will be able to vote on the Special Resolution at the AGM on Friday 2nd October*.
- * Please note the AGM is only open to ICS members who have renewed their membership for 2009. Members who have joined for 2010 may attend but will have no voting rights. We recommend that you make your way to the AGM during the coffee break to allow for attendees to be recorded on entry. This will allow the AGM to run to schedule.

Orthotopic neobladder diversion

Careful selection of patients is essential

NASHVILLE – For more than a century urologists have utilized intestinal segments for reconstruction of the urinary tract following extirpative surgeries. However, objectives have evolved from a simple diversion of urine with conservation of renal function to the anatomic and functional preservation of near normal volitional voiding without altered body image.

In fact, the desire to afford patients with a near normal state of voiding

reful and prudent patient selection. In women this implies that with regards to their bladder malignancy there is no concern for urethral involvement or posterior wall invasion into the vagina. In appropriately selected patients, prior studies with anatomic preservation of the anterior vaginal wall have demonstrated an acceptable complication rate and excellent oncologic control with regards to margin status. Several authors have proposed technical modifications, including creation of a posterior support platform, to minimize chronic voiding issues in women with neobladder diversions. However, the long-term voiding function of this female population is inadequately characterized as most large series are predominantly composed of male patients. Therefore, this study was designed to specifically address voiding function in a consecutive series of female patients that underwent radical cystectomy with orthotopic neobladder diversion. A retrospective review of electronic medical records from 1995 to 2008 of female patients with ileal neobladder urinary diversions was performed to evaluate demographics, preoperative and postoperative voiding function, surgical technique, postoperative urinary infection, need for further procedures, and diversion



ficant renal or hepatic dysfunction, comorbid conditions affecting overall life expectancy or functional status, or an inability or unwillingness to perform neobladder maintenance including self-catheterization. Anterior vaginal wall sparing radical cystectomy and bilateral pelvic lymph node dissection was performed. Briefly, this technique involves sharply developing the plane between the posterior bladder wall and anterior vagina (Fig. 1 panels A and B). If required, supracervical hysterectomy was performed. Elevating the bladder specimen from the pelvis, the posterior plane between the bladder and vagina was developed with a combination of sharp and blunt dissection. Hemostasis was maintained with selective use of electrocautery in conjunction with suture ligation. The anterior urethra was divided with electrocautery and the bladder specimen removed with special attention to preservation of the endopelvic fascia (Fig. 1, panels C and D). The posterior bed of the resection was carefully inspected and any defects in the vaginal wall repaired with absorbable suture. The neobladder was configured in accordance with surgeon preference, most frequently utilizing a Studer

by retaining the natural continence mechanism while eliminating a cutaneous stoma or absolute requirement for intermittent catheterization led to the development of orthotopic urinary diversion. However, healthrelated quality of life (HRQOL) analysis has failed to show a consistent pattern favoring continent diversion in bladder cancer patients. This dilemma is in part certainly due to the variety definitions utilized to measure HRQOL, but may additionally reflect patient expectations when compared to actual outcomes. Indeed, enthusiasm for the neobladder procedure must be tempered by the known complications with regards to both oncologic control and voiding function. The first premise of continent diversion remains ca-



Fig 1: Anterior vaginal sparing radical cystectomy technique. Panels A and C reprinted from Journal of Urology Vol. 168, S.S. Chang et al., "Preservation of the anterior vaginal wall during female radical cystectomy with orthotopic urinary diversion: Technique and results," pp. 1442-1445 (2002) with permission from Elsevier

related complications. Approval for conducting this retrospective analysis was provided by the Vanderbilt University Institutional Review Board. Women with muscle-invasive urothelial cancer or high risk superficial bladder malignancy without evidence of bladder neck or urethral involvement, and without extensive carcinoma in situ and/or invasive tumors involving the trigone were candidates for orthotopic diversion. Exclusion criteria for orthotopic diversion additionally included signi-

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or Hautmann technique to fashion the ileal reservoir. Prior to creation of the neobladder-urethral anastomosis, an omental or peritoneal flap was routinely positioned as a tissue bolster on the anterior vagina.

Forty-one female patients were identified who underwent cystectomy and orthotopic diversion with sufficient follow up for inclusion in the analysis. Mean patient age was 60.7 years (range 34 – 74 years) with the majority of women (92.7 %) able to undergo anterior vaginal wall sparing procedures (Table 1). Eight patients had concurrent hysterectomy (19.5 %). In those patients without vaginal sparing surgeries, all experienced some degree of postoperative incontinence or retention. For women with vaginal sparing surgery, but excluding patients with

	average	range
age	60.7 yrs	34 – 74 yrs
	# pts	% pts
vaginal sparing	38	92.7%
hysterectomy	8	19.5%

Table 1: Patient characteristics

neobladder-vaginal fistulas prior to repair, 6 patients reported diurnal

incontinence (15.8 %), 6 indicated daytime only incontinence (15.8 %), and 10 acknowledged nighttime only incontinence (26.3 %) (Table 2). Overall complete continence in patients with vaginal sparing was 42 Table 2: Continence %. Two patients with

preoperative stress incontinence both had significant post-diversion incontinence symptoms. Average number of pads per day was 3.7 for those with diurnal incontinence, 2.8 for daytime only, and 0.7 for nighttime only. These differences were significant for diurnal versus nighttime (p=0.002) and daytime versus nighttime (p=0.027). Twenty-nine women (76 %) were able to adequately empty with a mean postvoid residual (PVR) of 32 cc (Table 3). Twelve patients (24 %) experienced urinary retention necessitating self catheterization with a mean PVR of 326 cc (p = 0.0008).

With regards to complications, eight patients (19 %) reported urinary infections associated with fever or local symptoms (Table 4). Neobladder-vaginal fistulas were diagnosed in 3 patients (7.3 %). Nine women required further surgical interventions specifically related to their urinary diversion including six patients who underwent injection of urethral bulking agents (14.6 %). In this series of women undergoing orthotopic diversion, we revealed that a substantial portion of patients experience some degree of voiding dysfunction. Indeed, all of the patients who did not have vaginal sparing had postoperative voiding issues although the contribution of the wider resection to these results is uncertain. These data reinforce the necessity of preoperative voiding function evaluation and counseling to insure that patient expectations

match expected outcomes. A comparison of the severity and incidence

of voiding dysfunction amongst various surgical series is confounded by the variability in definitions, endpoints, surgical technique and length of follow-up. Additionally, symptoms have rarely been assessed using validated instruments, and we acknowledge this as a limitation to the global utility of this analysis.

The perceived improved quality of life of the orthotopic neobladder as compared to incontinent diversion may be significantly reduced or eliminated in patients with severe

voiding dysfunction. Daytime incontinence may range from mild stress incontinence to total incontinence in a small percentage, but complete continence was only achieved in 42 % of the women in our series of neobladder patients. It is worth noting that almost

half of these patients experienced some degree of nighttime inconti-

type	# pts	% pts	PPD	outcomes		
				versus diurnal	versus daytime	
diurnal	6	15.8%	3.7			
daytime only	6	15.8%	2.8	p=0966		
nighttime only	10	26.3%	0.7	p=0002	p=0.027	
total	22	57.9%				

nence. Alternatively, approximately one-third of this population develo-

ped hypercontinence or high post-void residuals requiring selfcatheterization. This is consistent with the findings of other similar series in women where 31 % required intermittent self-catheterization for neobladder emptying. Although not specifically assessed in our patient group, hypercontinence may

be particularly common following an episode of urinary retention where the neobladder may become silently overdistended and fails to recover its natural tonicity.

When indications for orthotopic diversion were initially extended to female patients there was appropriate concern over the rate of neobladder-to-vagina fistula. Fortunately, neobladder-vaginal fistula formation is relatively rare and reported at less than 5 % in multiple series, in concordance with the 7 % revealed in the current analysis. Surgical refinements that decrease fistula formation include avoidance of overlapping suture lines and inter-

> position of omentum in situations where the anterior vaginal wall has been incised or partially excised. Most fistulas that develop in the setting of a female neobladder will require surgi

cal intervention, and often are not amenable to a repair without complete mobilization and subsequent interposition a vascularized flap. With regards to techniques outside of vaginal sparing to enhance continence outcomes, it is critical that the neobladder be constructed such that it can accommodate a sufficient volume under low pressure. Intrinsic

SIC	# pts	% pts	mean PVR	outcomes
no	29	70.7%	32 cc	
yes	12	29.3%	326 cc	p=0.0008

Table 3: Voiding function

Complication	# pts	% pts
urinary tract infection	8	19.0%
neobladder-vaginal fistula	3	7.3%
anastomotic stricture	2	92.7%
neobladder stone	1	19.5%

Table 4: Neobladder complications

to the spheroid shape of the reservoir are mathematical principals that dictate the optimal length of bowel to achieve the desired capacity. If too small a segment is selected, the capacity will be low and risk unnecessary and avoidable incontinence and urinary frequency. Likewise, if too generous a segment of bowel is selected, poor emptying and urinary retention will ensue. Poor emptying can precipitate not only the need for life-long self catheterization but also distention with the rare but devastating complication of neobladder perforation.

During cystectomy, particular attention should be directed toward preserving the rhabdosphincter in order to protect the continence mechanism. In women, anterior vaginal wall preservation may spare damage to urethral innervation. It is equally important to gently handle and preserve the levator muscle and pelvic floor fascia. Lastly, positioning of the neobladder neck in the most dependent portion of the pelvis may help ensure proper funne-

> ling of the bladder outlet upon voiding. This study enforces the concept that orthotopic diversion in the carefully selected female patient should be offered only with suitable counseling that will realistically prepare the patient with regards to postoperative voiding dysfunction. Additionally, this analysis highlights the need for prospective studies, including thorough

preoperative functional evaluation and standardized quality of life assessment, to allow more accurate determination of women who may be optimal candidates for orthotopic urinary diversion.

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Session 31 (Poster) - Nocturia & Incontinence, Saturday 3rd October, 15:00-16:00, Hall E



INTERNATIONAL CONTINENCE SOCIETY • 39TH ANNUAL MEETING

Gala Dinner aboard the San Francisco Belle

Friday, 2 October, 2009

We are very excited to be hosting the ICS 2009 Gala Dinner Join us! aboard the beautifully renovated San Francisco Belle cruise ship. We will station at the dock whilst guests arrive and then take a cruise around San Francisco Bay to enjoy the breathtaking sites of the city from any one of the three enclosed decks, spacious sun deck or complete wrap around decks of the stern wheeler. The Belle evokes images of classic riverboat cruises down the Mississippi at the turn of the last century, when a river cruise was a relaxed and elegant affair.

Tickets to the Gala Dinner cost \$125 per person and are available from the Registration Desk until 17:00 on Thursday, 1 October. All participants who have purchased tickets must exchange the voucher they receive as part of their registration for a dinner ticket and choose their seating at the Gala Dinner Desk, which will be open at the following times:



Melissa R. Kaufman

The ICS Meeting Gala Dinner is always a very enjoyable event. In spectacular surroundings, our guests enjoy an evening of food, drink, laughter and dancing.

The programme for the evening includes:

- 18:30 Coaches will depart from the meeting hotels and the Moscone Center
- 19:30 Boarding the San Francisco Belle
- 20:30 Cruise, dinner and dancing to the 'City Beat Sextet'
- 22:30 Return to dock
- 23:00 Transfers will return guests to the hotels at 23:00

Vednesday, 30 September, 2009	15:30 - 18:45
hursday, 1 October, 2009	07:00 - 19:00
riday, 2 October, 2009	07:00 - 11:00



Are the effects of oxybutynin on cognition topical or oral?

A double-blind placebo-controlled study employing sensitive cognitive and psychomotor testing

WASHINGTON – Although orally administered oxybutynin has been shown to impair cognitive function in older adults, the effects of oxybutynin chloride topical gel (OTG) on the central nervous system (CNS) are not known. Thus, a study was designed to evaluate whether the cognitive effects of oxybutynin differ with different routes of administration.

xybutynin is an antimuscarinic agent that is widely used to treat patients with overactive bladder (OAB). It relaxes the detrusor muscle of the bladder by acting as a competitive antagonist of acetylcholine at muscarinic receptors. However, the anticholinergic action of oxybutynin is not limited to the bladder. Oral formulations are associated with frequent peripheral anticholinergic adverse effects, such as dry mouth. Oral forms also have been shown to impair cognitive function in older adults, most likely as the result of action on the central muscarinic receptors.

The potential of detrimental CNS effects

The potential for detrimental CNS effects is of particular concern in the elderly because they are more likely to have preexisting cognitive deficits or may already be receiving anticholinergics for comorbid medical conditions. OTG is a recently approved (FDA) transdermal gel formulation of oxybutynin chloride. A placebo-controlled phase 3 study has demonstrated that OTG is efficacious in improving OAB-related urinary symptoms and, importantly, that it has a low incidence of peripheral anticholinergic adverse effects. Moreover, clinical trials with another transdermally administered oxybutynin formulation have found a low incidence of selfreported CNS adverse events. These studies suggest that topical administration of OTG may have a more favorable CNS profile than oral administration of oxybutynin.

Comparisson of OTG-effects and oxybutynin tablets



Gary G. Kay

The HVLT-R offers a brief assessment of verbal learning (immediate recall) and memory (delayed recall) and has been shown to be sensitive to memory decline attributed to tolterodine, another antimuscarinic drug for OAB. Additional secondary outcome measures included other tests of Immediate Recall, Visual Attention, Information-Processing Speed, Psychomotor/Reaction Time, and Self-reported Memory Functioning.

Methods and study design

From 11th September, 2008 to 31st October, 2008, 152 heal-

thy adults aged 60-79 years who did not take any excluded concomitant medications were enrolled at 5 US centers. Participants were randomly assigned to receive OTG 1 g once daily (OTG gel plus placebo capsules), OXB-IR 5 mg 3 times daily (OXB-IR capsules plus placebo gel), or placebo (placebo gel plus placebo capsules) for 1 week. Topical gel was applied daily to rotating sites on the abdomen, upper arms/shoulders, or thighs. On day 8, participants returned to the clinic for observed dosing and

assessment of cognitive and psychomotor functioning and adverse events. Of 152 healthy participants, 49 received OTG, 52 received OXB-IR, and 51 received placebo. Mean age was 68.2 years (range 60.0 to 79.0). Three participants in the OXB-IR group discontinued early and were not evaluated for outcome variables. There was no significant treatment effect with respect to the primary end point (Table 1), delayed recall on the Name-Face Associa-

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A prospective study was used to compare the effects of OTG and of oxybutynin immediate-release tablets (OXB-IR) versus placebo on cognitive function in older, healthy adults. Sensitive cognitive testing measures were employed. Tests of Delayed Recall have demonstrated memory deterioration related to the use of oral oxybutynin. Three Delayed Recall tests were included as outcome measures: the Name-Face Association Test was the primary outcome measure, and the First-Last Name Association Test and the Misplaced Objects Test were secondary outcome measures. The Hopkins Verbal Learning Test-Revised (HVLT-R) was administered as a secondary outcome measure.

Date of preparation: September



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tion Test (P=0.2733); comparisons between each of the active treatment groups versus placebo also revealed no significant differences (OTG vs placebo, P=0.1551; OXB-IR vs placebo, P=0.1767). However, one of the secondary end points, delayed recall on the Misplaced Objects Test (Table 1), showed a significant treatment effect (P=0.0294), with OXB-IR having the lowest number of correct responses and OTG the greatest number of correct responses. In addition, results from an immediate recall test, analysis of Reliable Change scores in the HVLT-R Total Free Recall, indicate that substantially more subjects

	OTG (n = 49)	Placebo (n = 51)	OXB-IR (n = 49)		
Name-Face Association Test, mean (SD)	7.02 (3.17)	7.77 (3.71)	7.06 (3.68)		
OTG vs Placebo	P = .1551				
OXB-IR vs Placebo		P = .1767			
Overall	P = .2733				
Misplaced Objects Test, mean (SD)	13.64 (3.03)	13.16 (3.44)	12.38 (3.34)		
OTG vs Placebo	P = .3678				
OXB-IR vs Placebo	P = .0692				
Overall	P = .0294				

OTG = Oxybutynin chloride topical gel; OXB-IR = oxybutynin immediate-release tablet; SD, standard deviation. P value is from analysis of covariance.

Adverse Events, n (%)	OTG (n = 49)	Placebo (n = 51)	OXB-IR (n = 52)	Overall (n = 152)
Dry mouth	4 (7.8)	3 (6.1)	38 (73.1)	45 (29.6)
Headache	2 (3.9)	0 (0)	4 (7.7)	6 (3.9)
Nausea	0 (0)	0 (0)	4 (7.7)	4 (2.6)
Constipation	0 (0)	0 (0)	3 (5.8)	3 (2.0)
Cough	0 (0)	0 (0)	3 (5.8)	3 (2.0)
Dizziness	0 (0)	0 (0)	3 (5.8)	3 (2.0)
Nasal dryness	0 (0)	0 (0)	3 (5.8)	3 (2.0)
Urinary hesitation	0 (0)	0 (0)	3 (5.8)	3 (2.0)
Dry eye	0 (0)	0 (0)	2 (3.8)	2 (1.3)
Dry throat	0 (0)	0 (0)	2 (3.8)	2 (1.3)
Urine flow decreased	0 (0)	0 (0)	2 (3.8)	2 (1.3)
OTG = Oxybutynin chlorid	le topical gel; C)XB-IR = oxybuty	nin immediate-re	lease tablet.

Table 1: Effects of OTG, Placebo, and OXB-IR on Sensitive Measures of Delayed Recall at Study End

Table 2: Treatment-Emergent (Unsolicited) Adverse Events Reported by>2% of Subjects in Any Treatment Group

receiving OXB-IR (n=10) showed a significant decline (ie, a decline of ≥6 from baseline) than those receiving OTG (n=5) or placebo (n=6). No other treatment-related differences were demonstrated on the remaining secondary end points.

The safety profile of OTG was also better than that of OXB-IR (Table 2). The incidence of treatmentrelated peripheral anticholinergic adverse events was similarly low in the OTG and placebo groups, but more frequent in the OXB-IR group. The most common event, dry mouth, was reported in 3/49 (6.1 %) participants on OTG, 4/51 (7.8 %) on placebo, and 38/52 (73.1%) on OXB-IR. Three subjects from the OXB-IR treatment group prematurely discontinued participation in the study because of adverse events related to their treatment. No serious adverse events were reported during the study.

OTG without an effect on cognitive function

This study demonstrated that OTG does not have a clinically meaningful effect on cognitive function in older non-demented adults. The more favorable CNS anticholinergic adverse effect profile associated with topical administration of OTG may be due to the avoidance of high peak plasma concentrations of oxybutynin, which are observed following oral administration or due to the decreased first-pass metabolism of oxybutynin to N-desethyloxybutynin, which is believed to be the major cause of anticholinergic adverse effects. These findings highlight the potential of topical administration of OTG as a safer and more tolerable way of delivering oxybutynin than oral administration for the treatment of OAB in elderly patients.

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Session 11 (Poster) – Gerontology & BPH, Thursday 1st October, 16:00– 17:30, Hall E A question of pressure



Historical theories about pelvic organ support directly conflict with what is seen during clinical examination or what can be seen as the results of surgery. The classical view of pelvic organ support suggests that there are "fascial layers" between the bladder vaginal and rectum that hold the organs in place.

Failure of the central fascia is presumed to be responsible for prolapse. However, observation reveals that re-suspension of the va-



Fig. 1: The levator ani muscle acts to close the pelvic floor while the apical supports hold the pelvic organs in proper alignment so that the do not prolapse downward.

ginal apex with sacrocolpopexy without anything else being done

to the anterior fascia corrects cystocele. Similarly the emerging role of pelvic muscle injury in the cause of prolapse must be considered as well. The advent of soft tissuce imaging (MRI and ultrasound) with the creation of 3-D models from anatomy in living women without pelvic floor disorders allows us to see what is wrong. In addition, computer based functional biomechanical models enable hypotheses concerning the effects of specific anatomical defects. A re-examination of our theories and observations concerning pelvic organ support, therefore, seems appropriate.

The pelvic organs are supported in their positions by the levator ani muscles and various connective tissue attachments (Fig. 1). The levator ani muscles have a constant activity that closes the pelvis. This constant "resting" activity is increased during events such as coughing or jumping. The pubic portion of the levator ani muscles are frequently injured during vaginal birth, especially when forceps are used. 56 % of women



Fig. 3: 3D volume-rendered model of anterior support system based on MR images (left) and geometrically simplified finite element biomechanical model (right); AVW: anterior vaginal wall; CL: cardinal ligament; US: uterosacral ligament; ATFP: arcus tendineus fascia pelvis

refer to these connections as fascias and ligaments they resemble mesenteries more than skeletal ligaments. In the upper portion of the genital tract, the cervix and upper vagina are attached to the pelvic walls by the cardinal and uterosacral ligaments. The cardinal ligaments are primarily vascular in composition



Fig. 2: The magnitude of differences between women with and without stress urinary incontinence in measures of pelvic floor parameters as assessed by effect size. MUCP, maximal urethral closure pressure; Aa, location of POP-Q anterio4r vaginal wall point 3 cm above the hymen during Valsalva; GH, genital hiatus diameter; Levator, levator hiatus.

who have pelvic organ prolapse are found to have this type of injury involving more than half of the muscle while only 16 % of women with normal support of similar age and parity have this type of injury. This results in 40 % reduction in muscle force exerted on an instrumented vaginal speculum during a maximal voluntary contraction. This injury is NOT more common in women who seek care for stress incontinence than asymptomatic women of similar age and parity although it is more common in primiparous women 9 months after their first birth. Stress incontinence is primarily associated with loss of urethral closure pressure and not loss of urethral support as previously thought Fig. 4. Because this levator injury occurs during childbirth, an improved understanding of muscle injury mechanisms and rehabilitation are important to minimizing the consequences of this injury later in life.



cross section) reveal an extensive network of connective tissue below the peritoneum that has variously been called the rectal pillars, pararectal fascia and other names. In contrast to the vertical cardinal ligaments, these structures are more horizontal in orientation and pull the upper vaginal dorsally into the hollow of the sacrum. The middle of the vagina is attached laterally to the arcus tendineus fascia pelvis ventrally, and to the posterior arcus dorsally. Distally, the vagina is fused with the levator ani muscles laterally and the perineal body dorsally.

Pelvic organ support is provided by the interactions between the connective tissues and muscles (Figs. 3 and 4). When normal muscle function is present, the muscles hold the genital hiatus closed. In this situation, increases in abdominal pressure are balanced so that rises in bladder and rectal pressure are equal, canceling one another out. However, if the muscles are not strong enough to maintain closure during pressure increases, the some portions of the vagina descend to become exposed at the introitus. In this configuration, there is not a balance of pressures. The high pressures in the bladder, for example are on one side of the vaginal wall while the other side of the wall is exposed to atmospheric pressure. The force that results from this pressure differential forces the pelvic organs downward; placing tension on the supportive tissues. If the tissues are very strong they can resist this force, but if they are marginal, then they may fail. This can happen either acutely as described by some women who experience a sudden occurrence of prolapsed while lifting something heavy or may progress slowly over time.



at 18:45 to City Hall and return to the meeting hotels at 21:00. Reception at City Hall will begin at 19:00

All ICS Annual Meeting registered participants are invited to the Welcome Reception at the magnificent

San Francisco City Hall (only a short distance from the Moscone Center).

This is an informal event that offers participants the opportunity to mingle and relax with a drink in a beautiful setting away from the meeting and sessions.

The main city hall will be open for guests to walk around and see all the intricate details of the building's design.

San Francisco - Culinary mixing pot!

The Welcome Reception will offer participants a taste of the many and diverse cultures in San Francisco. With food stations depicting different neighbourhoods and culinary flavours such as Californian fish and seafood, Chinese Dim





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Sum, Japanese Sushi, Napa Valley wine and cheese.

City Hall Facts:

- The current city hall was built in 1915 and is in fact a replacement of an earlier City Hall that was destroyed during the 1906 Earthquake.
- The building is so vast that it occupies two full blocks of San Francisco
- · Has the fifth largest dome in the world
- Marilyn Monroe married Jo Di Maggio here in 1954
- George Moscone (then mayor of San Francisco) and famous gay politician and activist Harvey Milk were both assassinated here on 27 November, 1978



Connective tissue supports attach the vagina to the pelvic walls. The vaginal is a fibro-muscular tube that is attached to the pelvic walls on either side. Although it is traditional to



Fig. 4: Finite element model subjected to increase in abdominal pressure (100 cm H2O). shows the anterior vaginal wall bulging downward below the levator ani muscle. Color spectrum reveals stresses seen in the anterior vaginal wall and the proximal levator ani muscles tissues. Modified from Chen 2009.

and are relatively vertical in the standing position. Separate from the vertical cardinal ligaments, there is a complex of connective tissue that is more horizontal passing between the upper genital tract and the sacrum. The superficial portion of this complex is visible from above and is typically called the uterosacral ligament. MR imaging (and anatomical

Authors:

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State of the Art 1: Pelvic Floor Biomechanics: Imaging, Modelling, Insight and Change, Thursday 1st October, 11:00-11:30, Hall A

Promising area for further research

Bladder reinnervation: can new nerves improve the function of the neurogenic bladder?

PITTSBURGH – Surgical procedures which have been developed to promote the growth of new nerves into the urinary bladder (termed nerve rerouting) are being used to improve lower urinary tract (LUT) function in patients with neural injuries or congenital abnormalities of the spinal cord (spina bifida).

Studies in animals and humans indicate that the normal cholinergic innervation of the bladder that arises in the sacral spinal cord can be replaced by lumbar cholinergic motor axons that innervate striated muscle (Figs. 1 & 2). The new axons provide excitatory inputs to

the bladder that can be activated reflexly to induce bladder contractions and voiding. This article will focus on the basic neurobiology of nerve rerouting and the results of clinical studies indicating that new nerves can improve neurogenic LUT dysfunction.

The basic principles of

nerve rerouting are: (1) following peripheral nerve injury axons distal to the injury degenerate and the surviving central axon terminals produce growth cones that extend along the degenerated nerve trunks back to their original targets or to new targets that were also denervated by the injury, (2) denervated target cells express neurotrophic factors that attract regenerating axons and induce sprouting of adjacent uninjured axons and thereby promote the formation of new synaptic connections, (3) cholinergic motor axons can innervate decentralized autonomic ganglion cells in the bladder and may directly innervate bladder smooth muscle to establish new excitatory pathways between the spinal cord and the bladder.

Reinnervation of the bladder with lumbar motor axons was first proposed in 1907 by Kilvington and since then many animal studies have provided evidence that excitatory connections between new nerves and the bladder can be produced by rerouting of lumbar spinal ventral roots or peripheral motor nerves (obturator, genitofemoral or intercostal nerves) into the bladder.

Studies by Xiao and coworkers revealed that when a lumbar ventral root containing motor axons projecting to the hindlimb (Fig. 1) was grafted to a transected sacral ventral root carrying the efferent axons to the bladder, a new reflex pathway was established that could _______ evoke bladder contrac-

William C. de Groat

humans. The new reflex pathway was activated by electrical or tactile stimulation of cutaneous afferent axons that normally excite motoneurons in the lumbar spinal cord (Fig. 2). Axonal tracing studies in animals showed that after spinal root anastomosis lumbar motoneurons that normally innervate limb striated muscles send axons to the bladder.

tions in rats, cats and

send axons to the bladder. Pharmacological experiments showed that the Skin-CNS-Bladder Reflex was suppressed by a ganglionic blocking agent or by atropine indicating that the motor axons established cholinergic synapses with bladder parasympathetic ganglion cells that release acetylcholine which then activates muscarinic receptors in bladder smooth muscle.

The Skin-CNS-Bladder-Reflex was demonstrated after unilateral anastomosis of the lumbar-5 and sacral-2/3 spinal ventral roots in adult male patients with upper motoneuron lesions and in children with spina bifida. Voiding can be elicited in these patients by electri-





cal or tactile stimulation of the cutaneous receptors in the leg ipsilateral to the spinal root anastomosis (Fig. 1). Patients with neurogenic detrusor overactivity, detrusorsphincter-dyssynergia and high post-void residual volumes exhibited considerable improvement in these parameters 12-18 months after surgery. In children with spina bifida, bladder capacity increased and incontinence was reduced. Some of these children who lacked bladder sensation before surgery sensed bladder filling after the surgery. The major adverse effect was partial loss of lumbar-4-5 motor function on one side.

In summary, the effects of bladder nerve rerouting in animal experiments have been confirmed in clinical studies in patients with neurogenic storage and voiding symptoms. However most of the clinical studies have been performed by one research group in China and only a few papers have been published. More detailed urodynamic and neurological studies with long term follow up are needed. In addition, the findings of the Chinese group need to be confirmed in other medical centers using the same surgical techniques and simi-



lar patient populations. Unexpected results also need further study. For example the emergence of bladder sensations after rerouting motor nerves to the bladder is difficult to explain but may reflect plasticity in central neural pathways that is driven by rewiring of bladder nerves. Reorganization of circuitry in the sensorimotor cerebral cortex has been detected with brain imaging techniques after rerouting of nerves to striated muscles. A similar mechanism may underlie the changes in bladder sensory pathways. The conversion of dyssynergic voiding to synergic voiding after unilateral nerve rerouting is also unexpected because the normal innervation of the LUT is intact on the contralateral side of the spinal cord and should continue to induce dyssynergia. Partial denervation of the sphincter after unilateral transection of the sacral roots may contribute to a reduction in dyssynergia, but plasticity in spinal pathways may also be an important factor. Thus bladder nerve rerouting is a promising area for future research. Many questions remain to be answered.

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State of the Art 2: Bladder Reinnervation: Can New Nerves Improve the Function of the Neurogenic Bladder?, Friday, 2nd october, 14:30-15:00, Hall A

Essential role in the pathophysiology of the disease

Defective spinal modulation of nociceptive processing in patients with painful bladder syndrome

ROME – Painful Bladder Syndrome-Interstitial Cystitis (PBS/ IC) usually presents with suprapubic pain related to bladder filling, accompanied by other symptoms, such as increased daytime and night-time frequency, in the absence of proven urinary infection or other obvious pathology.

Sensation depends on neurophysiologic mechanisms in several different nerves, receptors, and transmitters. Different stimuli can elicit sensations in the lower urinary tract, such as bladder filling, micturition, noxious stimuli, and external stimuli. In chronic inflammatory bladder diseases such as Painful Bladder Syndrome-Interstitial Cystitis and Irritable Bowel Syndrome (IBS)¹ hypersensitivity to both visceral and somatic stimuli due to hyperexcitability of C-fiber afferent pathways, which are silent in the normal state during bladder filling, has been proposed as mechanism for bladder pain and urgency.

In patients with IBS,

this sensitivity has been documented throughout the gastrointestinal tract. In humans with PBS/IC, awareness of bladder filling occurs at smaller volumes than in normal individuals, an observation confirmed by urodynamic studies.

There appears to be a hyperresponsiveness of central stress circuits, mediating altered autonomic regulation and altered perceptual responses to visceral stimuli.

Visceral hypersensitivity can be influenced by peripheral and central mechanisms affecting pain perception.

Studies using electrical Silvia Malaguti stimulation and the RI-II lower limb reflex have locumen- further confirmed enhanced visceintestinal ral perception in other chronic pain /IC, awa- disease (e.g. Irritable Bowel Synpoccurs at drome).

> Abnormal central pain processing may play an important role in the initiation and maintenance PBS/IC suggesting a central sensitization of pain pathways, which takes place in the Central Nervous System,

triggered by the massive afferent visceral barrage upon convergent viscero-somatic neurons. The visceral barrage, however, is also likely to activate a reflex arc towards the periphery (afferent branch: visceral afferent fibers, efferent branch: somatic efferences towards the muscle) resulting in sustained muscle contraction and subsequent local sensitization of nociceptors. (Fig.1)

Objectives

The aim of this study was to evaluate the function of pain modulating systems sub serving diffuse noxious inhibitory controls (DNIC) in PBS/IC. DNIC is the phenomenon by which the perception of painful stimulus at a local area of the body (test stimulus) is inhibited by a second painful stimulus administered at a distal body site (conditioning stimulus) or, simply, pain is inhibited by pain. In subjects that do not suffer from chronic pain disorders, pain administered by the test stimulus is decreased or inhibited upon introduction of the conditioning stimulus at a distal body site. To our knowledge this is the only study that aims to test the effects of DNIC in individuals with PBS/IC.

Methods

We investigated the spinal transmission of nociceptive signals and the DNIC in 14 PBS/IC patients and

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continued from page 7

in 10 healthy subjects by means of Nociceptive Flexion Reflex RIII (NFR) as test stimulus, and the Cold Pressor Test (CPT) as heterotopic noxious conditioning stimulus.

Experimental procedure

Neurophysiological measurements were recorded in the following two conditions (Fig. 2): 1. baseline (measurement of baseline values):

2. painful session (immersing the hand in water at 2-4° C)^{2,3}

Results

The subjective pain thresholds and the RIII reflex threshold were significantly lower in PBS/IC vs. controls (Fig. 3). In controls a significant inhibition of the RIII reflex was observed during the CPT (-39%,P<0.05). PBS/IC patients showed facilitation (+35%,P<0.05) of the RIII reflex during CPT

Conclusions:

This is the first study to investigate endogenous pain mechanisms in individuals with PBS/IC by comparing their DNIC response to that of normal control individual: in the present study, significant differences were found between



ectric stimulation of sural nerve **Nociceptive Flexion** Reflex RIII (NFR) Cold Pressor Test (CPT)

normal controls and individuals with PBS/IC. Our study reveales that subjects with PBS/IC modulated pain differently from those in

Fig. 1: Central sensitization in PBS/IC (modified from Galer B, Gammaitoni A. Alvarez NA: XIV Pain. 11 Neurology. WebMD Scientific American® Medicine Online. Dale DC. Federman DD, Eds. WebMD Corporation, New York, 2002.)

Fig. 2: Experimental procedures: electric stmulation of sural nerve, NFR, CPT

the normal control group. Subjects in the PBS/IC group did not experience a decrease in pain

when the conditioning stimulus was applied, as is seen in normal control individuals. interpret We

our findings as the result of significant differences in pain modulation between normal controls and individuals with PBS/IC. Our results give di-



Fig. 3: results in controls and in PBS/IC patients.

rect evidence that a hyper excitability of spinal nociceptive processes is present in PBS/IC patients and demonstrate a dysfunction in systems sub serving DNIC in PBS/IC patients. Impairment of endogenous supraspinal pain modulation systems may contribute to the development and/or maintenance of central sensitization in PBS/IC.

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Session 29 (Poster) - Painful Bladder Syndrome / IC, Saturday 3rd October, 15:00-16:00, Haal C

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LONDON - The

provision of Continuing Medical Education (CME) by the pharmaceutical industry has evolved over the past 40 years. Content of the material provided has varied from factual data from clinical trials to more promotional material, and the variable nature of such information results in suspicion of all the material that is provided.

ll the content of industry pro-Avided material is governed by the Association of the British Pharmaceutical Industry's Code of

Kate Llovd

"Things ain't what they used to be"

Medical education and the pharmaceutical industry

carer network, to examine some of the issues concerning the relationships between industry, academia and the NHS. The working party's report entitled 'Innovating for Health - Patients, physicians and the pharmaceutical industry' was published in February 2009.³ One clear recommendation of the report is that in future industry should not be involved in the provision of education to 'doctors in training'.

"The goal should be to wean the education of doctors in training off pharmaceutical industry support over a time bound period, such as five years"

students, including food and travel should be prohibited.

Does this affect ICS and its membership?

3. Educational funds donated by industry should be disbursed by a centralised administrative unit, not by a company directly to a department or individual.

What does that look like in practice? Who makes up such a unit? Where is it based? What does it cover - all specialties, all conferences, all educational activities? How does it work? What criteria inform their decisions? How does an individual doctor make his/her NHS depend on the pharmaceutical industry for its pens, notepads, calculators, tissues and such items? Do such transactions impact the value the NHS places on industry? What is the benefit to industry? Does this activity demean both giver and recipient Whether over the next 5 years or sooner it remains unclear who will take over funding this important activity, if not physicians themselves? Fundamentally who will pay?

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Practice.1

As CME/CPD gains in importance with the advent of Revalidation, the objective quality standards

> of these activities invite closer scrutiny. The history of working relations between Industry and Health Care

> > NNOVATING FOR HEALTH Patients, physicians, the pharmaceutical industry and the NHS

edifying. A memorable issue of the British Medical Journal laid the blame on both parties. The issue formally entitled "Time to untangle doctors from drug companies" has become generally known by industry physicians as "the pigs and lizards issue" of the BMJ.² The industry is accused in this issue and elsewhere, and sometimes fairly, of using education (and specifically CME) as promotion, leading to suspicion of all

from the RCP patient and

Professionals has not always been

industry educational initiatives. In 2007 the Royal College of Physicians convened a working party consisting of academics, NHS physicians, industry physicians and representation

Other recommendations in the RCP report refer to education more broadly. Several of these relate to who should provide CME when, in the future, industry does not. I'll focus on four which refer to the current situation, and specifically to the funding of various activities by industry. All have the objective of reducing the influence of industry. Each recommendation is followed by some questions for you to consider.

1. There should be clear guidance to remove any uncertainties about students' interactions with industry

Where are the uncertainties? What interactions are taking place? Or are we clear already?

2. All gifts from industry to

case for receipt of such funds? Will it be slow and bureaucratic? Are those who decide completely free of bias? Can that be proven? Why would industry continue to provide funds given no chance to select the recipients of funds?

4. All gifts to doctors in training, including food and travel should end.

Is this a bit different? Is it more closely to conference attendance? How do you define 'doctor in training'? What gifts do you feel are appropriate and why? Do you receive gifts from companies in other fields? If so what type of gifts are they? Is it appropriate for an innovative industry which provides prescription medicines to be compared with those companies? Should the State of the Art 4: Medical Education and the Pharmaceutical Industry - Things ain't what they used to be, Saturday 3rd October, 13:00-13:30, Hall A

References:

1. Association of the British Pharmaceutical Industry. Code of Practice for the pharmaceutical industry 2008. www.abpi.org.uk/publications/pdfs/ pmcpa_code2008.pdf 2. KAMRANABBASSI AND RICHARD SMITH Volume 326 1155-1156 BMJ 2003

3. Innovating for Health. Patients, physicians, the pharmaceutical industry and the NHS. Report of a working party. RCP London Feb 2009.

Unknown etiology

Treatment of extensive BXO involving the whole pendulous urethra with bilateral buccal mucosa grafts

CAIRO – BXO (Balanitis xerotica obliterans) is a chronic dermatitis of unknown etiology that occurs on the penile skin.

It was first described in 1928 by Stuhmer in 9 adult patients.¹

Terminology

In accordance with the current recommendations, we will the use the term LS instead of BXO in this article.

Aetiology

The exact cause of LS is still unknown. A chronic bacterial infection by a spirochete called borrelia burgdorferi has been suggested.² However it is now generally accepted that LS is an autoimmune disease that could affect various parts of the body (e.g. breast, back and both male and female genitalia) (Fig. 1).



To our knowledge there is no report on LS involving the prostatic urethra or the bladder mucosa.

Presentations

Accidental discovery of LS during genital examination for unrelated causes is not unusual in early and mild cases.

Obstruction: Variable degrees of obstructed outlet symptoms up to retention are expected presentations.

UTI: Infection and irritative voiding symptoms are common presentations of LS involving the urethra.

Phimosis and Paraphimotic rings: These are possible presentations of LS in uncircumcised boys. The reason for this is thickening and toughness of the foreskin if affected by LS.

Diagnosis

Clinically: Classic LS appears as whitish plaques. The plaque may appear as blotches or give the glans a diffuse whitish tethered dry appearance (Fig. 3). The external meatus is often stenotic, inverted and difficult to open between your thumbs. The characteristic plaques of LS may also involve the penile shaft skin as well as the foreskin of uncircumcised patients.

Radiologically: ACUG (Ascending and micturating cystourethrography) is essential in all cases of LS to diagnose urethral involvement and evaluate the degree of urethral stricture disease. ACUG commonly discloses stricture of the fossa navicularis fig 4. However, involvement of variable degrees of the anterior urethra is not uncommon (Fig 5).

Histopathologic examination: Biopsy of the suspected lesion and histopathologic examination is the definite diagnostic method for LS. The classical histopathologic appearance is described above (see pathology)

Treatment

Conservative treatment: Topical steroids, topical antibiotics (tetracycline). These may have a role in mild cases. Testosterone (systemic and local treatment) has been proposed to improve the outcome of surgery for LS. This might be applicable to patients who have actual deficiency of the hormone.³

Surgical Treatment: The aim of surgery is to treat the complication of the sclerotic process, namely the urethral stricture disease or the foreskin involvement.

Conservative surgery

Circumcision: This is done when the disease involves the prepuce of uncircumcised boys to avoid phimosis and paraphimosis.

Simple maneuvers for meatal stenosis: Meatal dilation, meatotomy and meatoplasty are usually not sufficient for complete cure since the process usually involves the whole fossa navicula-



Fig. 3: Typical appearance of the glans involved with LS.

ris. Urethrotomy: Optical or Ottis (blind) urethrotomy may be a temporary solution for anterior urethral stricture. The



Fig. 6: Isolation of the corpus urethra and dorsal urethrotomy.





Fig. 7a & b: Application of the buccal grafts on the dorsum of the urethra.

ras that are affected by LS.⁵ Buccal mucosa is currently the best tissue used for augmentation Urethroplasty in cases of LS. The nature of the buccal mucosa and the easiness of its excision make it an ideal choice. *2. Tube or onlay flap?*

Most urethral reconstrutive surgeons use onlay urethroplasty instead of tube urethroplasty. The comparison between these two techniques is beyond the scope of this article.

3. Onlay on the Ventrum or Dorsum?

Ventral augmentation has a higher rate of diverticulation, sacculation and stricture recurrence than dorsal augmentation.^{6,7} Therefore, we prefer dorsal over ventral augmentation in cases of LS.

4. One or two stages?

Currently, one stage augmentation urethroplasty is generally recommended.⁸

A two stage procedure is indica-

an additional segment was harvested from the inner lip. The average length of the buccal grafts per patient was 15 cm (range: 11 – 19 cm). The harvested mucosa is sutured to the roof of the opened urethral strip (fig.7). None of our patient had noteworthy donor site complications. 5. How to manage the meatus?

In our experience, attempting reconstruction of the fossa navicularis during the main pendulous urethra repair often produce unsatisfactory results, probably due to impairment of the blood supply of the distal urethra which comes from the glans and flows proximally. For this reason we roof the FN with buccal mucosa and then postpone reconstruction of the FN for a 2nd stage not before 6 months using Duplay technique, or more commonly the Jordan ventral flap.

Not surprisingly many of our patients (5 of 13) refused the second stage for the FN closure and were satisfied with a hypospadic meatus.

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Session 16 (Poster) – Lower Urinary Tract, Physiology & Treatment, Friday 2nd October, 11:00–12:30, Hall E

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ris. Uret or Ottis tomy m

The principal lesion of LS is the developement of a whitish plaque on the affected skin area resulting in tethering, whiteness, thickening, and loss of elasticity. Histopathologically, there is evident hyperkeratosis, homogenization of collagen and edema of the stroma and marked lymphocytic infiltrate (Fig. 2).

This sclerotic process may involve the corpus urethra and hence produce urethral stricture that usually begins with stenosis of the meatus. Proximal extension and aggravation of the sclerotic process can occur if diagnosis is overlooked, with 2ry infection or/and with repeated instrumentation. Frequently the disease involves the distal pendulous urethra. Pan anterior urethral stricture disease 2ry to LS are not uncommon.



Fig. 4: LS involvement of the fossa navicularis.



Fig. 5: LS involving the pendulous urethra.

disease almost always recurs following these measures.

Perineal urethrotomy:⁴ This is an acceptable line of treatment in select advanced cases, particularly in poor surgical candidates.

Reconstruction: Urethroplasty for LS disease involves augmentation or replacement of the damaged urethra with healthy tissue. Five aspects should be considered in this regard: 1. What to use?

Since LS is a skin disease, it is agreed to avoid using skin for repair of urethted only if the urethra is non salvageable and extremely damaged. The scarred corpus urethra is completely excised and a buccal mucosa graft is placed on the tunica albuginea in the first stage and later in the second stage closure is performed 3-6 months later

Our preferred approach is a single stage buccal mucosa roofing urethroplasty. We report our results in 13 patients with extensive and pan anterior urethral strictures. We completely dissect the corpus urethra and perform the urethrotomy on the roof (Fig. 6). The urethrotomy should extend proximally until it overlaps with 1 cm of healthy "Non–LS" urethra. We measure the defect and harvest buccal mucosa grafts accordingly from both cheeks. In 2 cases ral stricture due to lichen sclerosus (balanitis xerotica obliterans) Urology vol 64, Issue 3, Pages 565-568 (September 2004).

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Exploring the gap between clinical trial and real world

The use of antimuscarinic medication in patients with OAB

LONDON – Antimuscarinic drug therapy is commonly prescribed as part of the multimodality treatment of overactive bladder (OAB). Newer longer acting preparations allow once daily dosing and in many cases selective dose escalation to maximize efficacy. Some patients may change from one medication to another if their first prescribed drug causes undue side effects or is not effective.

Door adherence to medication is **I** commonly encountered and associated with inadequate treatment. Open-label extension studies of tolterodine, solifenacin, darifenacin and fesoterodine have all reported >60 % persistence with medication at 12 months of treatment. Outside the rigors of a clinical trial where patients may not receive free medication, intensive investigation and regular follow-up; the persistence with antimuscarinic medication is substantially lower. Existing data comes mainly from short and medium term retrospective community based studies which have shown approximately 20 % persistence after 6 months of treatment (Kelleher et al 1997).

The effectiveness and frequency of medication switches and longterm use of antimuscarinic medication is unknown in clinical practice. The objectives of this study were to investigate health related quality of life and use of antimuscarinic medication in patients with OAB in a real world setting.

Women with symptoms of OAB referred from primary care to two tertiary Urogynaecology centres were recruited into a prospective study investigating the management of OAB in clinical practice.

The recruitment period of the study was between May 2006 and August 2007. After a baseline and 6 week visit, patients were followed at 3 monthly intervals for a minimum of 12 months.

All patients were given written and verbal information about the management of OAB and were offered long-acting once daily antimuscarinic medication; solifenacin, KHQ is a 33 item, multidimensional, lower urinary tract dysfunction questionnaire. The questionnaire measures 9 domains of health related quality of life (HRQL) and has been used extensively for the assessment of HRQL in patients with lower urinary tract dysfunction.

251 women consented to take part in the study. The mean age of participants was 55 years (age ranused in the two clinics were solifenacin and extended release tolterodine. 30 patients completing the minimum 12 month follow-up did not fill their prescription for antimuscarinic medication. Reasons given for not filling prescriptions were; not wanting to use medication, fear of potential side effects and interactions with concurrent medication. Figure 1 shows the percentage of



Fig. 1: Percentage of persons using antimuscarinic medication over a 24 months period

tolterodine, darifenacin, oxybutynin tablets or transdermal patches as part of a multimodality therapy. In addition to demographic data, details about medical co-morbidities and polypharmacy, the duration of use of antimuscarinic medication and periods without treatment were recorded. Patients also completed two validated questionnaires at each study visit; the Patient Perception of Bladder Condition scale (PPBC) and the Kings Health Questionnaire (KHQ/ICIQLUTSqol).

The PPBC is a single item questionnaire which provides a concise assessment of the patients' perception of their urinary symptoms. The ge 20-87 years). 133 patients (53 %) completed 12 months follow-up of which 68 patients (27 %) completed a further 12 month follow-up at the time of reporting this study. 118 patients (47 %) dropped out of the study within 6 months. The commonly cited reasons for non-completion of the study were unwillingness to complete study questionnaires at clinic appointments, resolution of symptoms, poor treatment efficacy and side effects from medication. Data from patients who completed the study were used in this analysis.

96 % of patients were prescribed an antimuscarinic during the study. The first line antimuscarinic agents patients using antimuscarinic medication over a 24 month period.

The mean duration of medication use was 17.5 weeks and 27.25 weeks in patients who completed twelve and 24 months follow-up, respectively. 28 % of patients using flexible dosing agents (solifenacin and darifenacin) chose to escalate the dose of their medication.

Greater severity of OAB symptoms as reported on the PPBC and KHQ was associated with use of a greater number of antimuscarinic agents, escalation of drug dose and a longer duration of medication use.

Patients who tried more than 3

antimuscarinic agents reported a longer duration of medication use than patients who used a single agent (mean duration 29.6 and 19.9 weeks respectively). Patients who required drug dose escalation used medication for longer periods than patients who continued using the lower dose.

Long-term use of antimuscarinic medication for OAB in clinical practice is poor. At twelve months of treatment 20 % of patients were using antimuscarinic medication, and all patients had ceased using medication by 24 months. Longer duration of medication use, use of multiple antimuscarinic medications and dose escalations are associated with a greater severity and health-related quality of life impact of OAB symptoms.

Long-term persistence with antimuscarinic medication in patients with OAB in clinical practice is lower than clinical studies would suggest. The percentage of patients requiring dose escalation in clinical practice is also significantly lower than that reported in clinical studies. A greater health-related quality of life impact from OAB is associated with the use of multiple antimuscarinic agents and a longer duration of medication use.

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Session 7 (Poster) - LUTS in Women I, Thursday, 1st October, 13:30-15:30, Hall D

Risk factors of de novo OAB and stress incontinence

BUCHEON – Incidence of urinary incontinence after surgical removal of urethral diverticulum is reported in a wide range from 1.7 % to 20.3 %. A few reports about evaluate urethral diverticulum and its surrounding structures, and also evaluated change of voiding symptom by Bristol female luts and occurrence of ly diagnosed with urethral diverticulum. Four patients had overactive bladder before surgery.In five of 24 patients (20.8 %) occurred de novo overactive bladder and 4 of 28 (14.3 %) patients de novo stress urinary incontinence occured after removal of urethral diverticulum. One of these patients had both stress incontinence and ovactive bladder. Incidence of stress incontinence and overactive bladder was significantly higher in patients with urethral diverticulum over 3 cm in diameter and located in proximal urethra on pelvic MR imaging. Among seven patients with diverticulum over 3 cm, stress incontinence occurred in three (P = 0.038) and overactive bladder in five patients (P = 0.000). Among eleven patients with diverticulum located in proximal urethra, stress incontinence occurred in four (P = 0.016) and overactive bladder in five patients (P = 0.011). In three of 28 patients, they had a large defect of urethra after removal of urethral diverticulum or weakened periurethral fascia by repeated inflammation. They simultaneously underwent Martius labial fat pad interposition (ML-FI) and none of them complained about any symptom of urinary incontinence or overactive bladder after surgery. In six of eight patients with urgency or frequency, symptoms improved and none presented with dysuria after surgery. Age, body mass index, number of delivery, and history of pelvic surgery did not statistically relate to occurrence of stress incontinence and overactive bladder.

moval of it are diverse, however in case of stress urinary incontinence following surgery, surgical correction of it is necessary. In this report, although diverticulum in the proximal urethra was high risk factor to develop stress urinary incontinence after surgery, it is hard to undergo combined preventive surgery of stress incontinence. In conclusion, size of urethral diverticulum over 3 cm and location in proximal urethra are significant risk factors of postoperative development of stress urinary incontinence and overactive bladder.

whether it is required or not to perform a preventive surgery in patients with high risk of stress incontinence following surgical removal of urethral diverticulum are present.

In this study, we would like to find risk factors related to de novo stress urinary incontinence and overactive bladder by retrospective review of past history, and findings of pelvic MR imaging of patients with urethral diverticulum.

Materials and Methods: We included 28 patients who underwent surgical removal of urethral diverticulum from November 2002 to December 2007. We obtained past medical history, physical examination, pelvic MR imaging to stress incontinence by the definition of stress urinary incontinence of ICS after surgery. We also analyzed risk factors of stress urinary incontinence and overactive bladder, including age, body mass index, number

of delivery, size and Young-Ho Kim location of diverticulum, and history of pelvic surgery Results: Patients age ranged from 20 to 59 years (mean age 38). an Patients presented with painful mass at anterior vaginal wall in 10 (26 %), dysuria in 5 (19 %), urgency in 4 (1 4%), frequency in 4 (14 %), in dyspareunia in 4 (14 %), and no symptom in 1 who was incidental-

Conclusion: Urethral diverticulum is very rare and difficult to diagnose. The results of surgical re-

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Session 16 (Poster) - Lower Urinary Tract, Physiology & Treatment, Friday 2nd October, 11:00-12:30, Hall E A viable alternative to sacral nerve stimulation for voiding dysfunction

ROYAL OAK - Sacral neuromodulation has been established as a safe and effective treatment for refractory urinary symptoms including frequency, urgency, incontinence, and idiopathic retention. However, up to a fourth of patients might not improve.

Ttimulating the pudendal nerve Odirectly provides increased afferent stimulation through the S2-S4 nerve routes. Therefore, placing a tined quadripolar lead at the pudendal nerve may help those who have failed to respond to sacral stimulation and perhaps other carefully

selected patient populations. In order to assess the safety and effectiveness of chronic pudendal neurostimulation (CPNS), we evaluated patients undergoing CPNS at our institution to determine changes in symptoms, complications, and treatment Kenneth M. Peters satisfaction.

All patients who had a staged procedure by a single surgeon were retrospectively reviewed after having a pudendal leaded placed using the ischial-rectal approach (Fig. 1). During the first procedure (Stage I), needle electrodes were placed in the anal sphincter to measure compound muscle action potentials (C-MAP). A foramen needle was then passed medial to the ischial



Fig. 1: Needle approach to pudendal localization.

tuberosity towards the ischial spine under fluoroscopy. Once pudendal nerve stimulation was confirmed by

tive survey was also developed and mailed to those who continued on CPNS. On the survey, patients rated changes in symptoms on a 7-point scale (markedly

Results

had a pudendal lead placed.

Most were female (79 %) and mean

age was 51.8 ± 16.9 years. Primary

urologic diagnoses and indications

for treatment were symptoms as-

sociated with interstitial cystitis/

painful bladder syndrome (IC/PBS),

and urinary urgency/frequency or

urge incontinence, retention, chro-

nic pelvic pain without IC/PBS, and

tethered sacral nerve. Three patients

also had pudendal nerve pathology

and 44 (52 %) had previously failed sacral neuromodulation. Overall, 71 % (60/84) improved on CPNS, however 5 of these who were also testing a sacral lead ultimately chose sacral and had their pudendal lead removed. Therefore, 55/84 continued on CPNS and almost all (93 %) who had previously failed sacral neuromodulation

responded to CPNS (41/44). Over 12 months after im-

plant, frequency, voided

volume, incontinence episodes, and

ICSI-PI scores improved (p < 0.0001

for all). Urgency also improved (p

A total of 84 patients

of patients reported improvements in all symptoms since implant (Fig. 3) except for bowel function (21 %) and sexual function (9 %). Although only 44 % were satisfied or extreme-

still recommend the treatment to a

friend. This finding suggests that

patients' personal satisfaction with

treatment had little effect on their

overall view of its' potential to pro-

Improvements in voiding, pelvic

pain, and fecal incontinence have

vide symptom relief.

been described in the few studies complications and revisions and/or reporting outcomes of CPNS. In our prospective, single-blinded, randomized, crossover trial comparing sacral and pudendal neuromodulati-



Fig. 3: Patients reporting improvements* in symptoms after CPNS. (* markedly, moderately or slightly improved)

ly satisfied with CPNS, 84 % would on, 79 % of patients preferred pudendal stimulation and rated CPNS as superior for improving pelvic pain, urinary urgency and frequency, and bowel function.

> Even though this current observational study's sample was heterogeneous and represented some of the most complex patients in our clinic,

re-operations were comparable to those associated with sacral neuromodulation. Our experience has been that using neurophysiologic parameters to guide lead placement is essential to improve success rates and minimize complications.

This study demonstrates the safety and efficacy of CPNS in a complex, refractory patient population. Adapting sacral neuromodulation principles and techniques to achieve pudendal stimulation is logical. Based on our experience, CPNS is a safe alternative particularly in those who have previously failed sacral stimulation.

Authors:

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i Contact author for references

Session 3 (Podium) - Neurourology I, Thursday 1st October, 11:30-12:30, Hall B



The Single Incision TOT system Sling



C-MAP, a quadripolar tined lead (InterStim®, Medtronic, Inc., Minneapolis, MN) was positioned and the tines deployed (Fig. 2). Patients then tested the lead for two weeks on an outpatient basis. If symptoms improved ³ 50 %, an implantable pulse generator (IPG) was connected to the pudendal lead during a second procedure (Stage II).

Baseline demographics, history, three-day voiding diaries and validated Interstitial Cystitis Symptom and Problem indices (ICSI-PI) were collected. Voiding diary parameters were again assessed at two weeks after lead placement (Stage I). During follow-up, voiding diaries and ICSI-PI questionnaires were collected at 3 and 6 months, and 1, 2, 3, and 4 years. A prospec= 0.0019), however pelvic pain did not change. When two, three, and four year observations were included, improvements were still seen over time in frequency, voided volume, incontinence episodes (p = 0.0002 for all), urgency (p = 0.0051), and ICSI-PI scores (p < 0.0001) even though fewer cases were available for analysis.

During follow-up (median 24.1 months), three lead migrations and two pain related events resulted in lead and/or IPG revision. Another two patients had minor complications that resolved with treatment and/or reprogramming. Mailed survey response rate was 73 %, and 88 % reported that they still had a device implanted and 83 % had it turned on all the time. The majority

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TURP improves long-term outcomes

Patients with LUTS by prostatic enlargement show better results for up to twelve years after surgery

SAPPORO – Transurethral resection of the prostate (TURP) is an effective surgical procedure for treatment of lower urinary tract symptoms (LUTS) by prostatic enlargement, especially for patients with bladder outlet obstruction (BOO).

Towever, whether TURP should The avoided for patients without BOO or those with detrusor underactivity (DUA) is controversial. Previously, we reported the urodynamic characteristics of 92 patients with LUTS by prostatic enlargement who underwent TURP and the short-term efficacy of TURP compared to the preoperative urodynamic findings.1 Although the overall treatment efficacy of TURP was better for patients with BOO than for those without it, neither the presence of detrusor overactivity (DO) nor status of detrusor contractility affected the efficacy at three months after surgery. Thus, we suggested that TURP might not be contraindicated for patients with DUA, at least to achieve a favorable short-term outcome. However, our previous study did not demonstrate the long-term outcome of TURP. In the present study, we investigated whether the efficacy of TURP lasted for more than 10 years in comparison to the preoperative urodynamic findings.

Ninety-two patients with LUTS by prostatic enlargement aged 50 or older underwent TURP between July 1995 and March 1997. Before TURP, the patients underwent symptomatic examination using the International Prostate Symptom Score (IPSS) and Quality of Life (QOL) index. In addition, water filling cystometry and pressure-flow study were performed before surgery to evaluate the existence of DO, the degree of BOO and the status of detrusor contraction. If involuntary detrusor contraction was ob-



Naoya Masumori

Of the 92 patients, 43 (46.7 %) were alive at the time of the survey in February 2008. Nine patients were excluded because of prostate cancer, neurological diseases and the impossibility of symptomatic examination. The IPSS and QOL index were determined at baseline, three months, three years, seven years and twelve years after surgery for 34 patients.

Results

Although the improved IPSS and QOL index at three months gradually deteriorated as time passed, those at twelve years were still perative urodynamic findings, the QOL index remained improved for twelve years. Two-thirds of patients with DUA but not BOO were satisfied with their urinary condition at twelve years.

Discussion

To our knowledge, the present study is the first report demonstrating the long-term outcome of TURP using the IPSS and QOL index compared to the preoperative urodynamic findings based on cystometry and pressure-flow study. Although deterioration of the IPSS in patients without BOO was faster than in tho-

IPSS	baseline	3 months ²⁾	3 years ²⁾	7 years ²⁾	12 years ²⁾	annual slope ³⁾	p-value 4)
All patients	16.7 (34) 1)	4.1*** (34)	5.6*** (30)	8.1*** (28)	9.9** (34)	0.48	
without BOO	13.5 (16)	4.9*** (16)	7.5** (14)	10.0 (13)	14.2 (16)	0.77	0.020
with BOO	19.5 (18)	3.5*** (18)	3.9*** (16)	6.5*** (15)	6.1*** (18)	0.22	0.029
without DUA	18.5 (22)	3.6*** (22)	4.7*** (18)	9.1** (18)	9.8** (22)	0.52	0.000
with DUA	13.3 (12)	5.2*** (12)	6.9** (12)	6.5** (10)	10.1 (12)	0.41	0.693
without DO	16.0 (20)	5.1*** (20)	6.6*** (18)	9.2* (17)	12.3 (20)	0.60	0 272
with DO	17.7 (14)	2.8*** (14)	4.1*** (12)	6.5** (11)	6.5** (14)	0.31	0.273

1) Mean (No. of patients), 2) vs. baseline: *p < 0.05, **p < 0.01, ***p < 0.001, 3) Difference between 3 months and 12 years divided by 12

Table 1: Changes in the IPSS after TURP compared with preoperative urodynamic findings

QOL index	baseline	3 months ²⁾	3 years ²⁾	7 years ²⁾	12 years ²⁾	annual slope ³⁾	p-value 4)
All patients	4.6 (34) 1)	1.5*** (34)	1.9*** (30)	2.2*** (28)	2.2*** (34)	0.063	
without BOO	4.3 (16)	1.8*** (16)	2.2*** (14)	2.5*** (13)	2.8** (16)	0.080	0.520
with BOO	4.9 (18)	1.2*** (18)	1.7*** (16)	1.9*** (15)	1.7*** (18)	0.048	0.529
without DUA	4.8 (22)	1.3*** (22)	2.0*** (18)	2.2*** (18)	2.2*** (22)	0.076	0.456
with DUA	4.3 (12)	1.8** (12)	1.8*** (12)	2.1*** (10)	2.2** (12)	0.037	0.456
without DO	4.7 (20)	1.6*** (20)	2.2***(18)	2.5*** (17)	2.6*** (20)	0.081	0.290
with DO	4.6 (14)	1.3*** (14)	1.6*** (12)	1.7*** (11)	1.7*** (14)	0.036	0.380
1) Mean (No. of patie	nts), 2) vs. baselir	ne: *p < 0.05, **p < 0	0.01, ***p < 0.001,	3) Difference betw	ween 3 months and	d 12 years divided b	y 12

Table 2: Changes in the QOL index after TURP compared with preoperative urodynamic findings

served during the filling phase, it was defined as DO. LinPURR scores of two to six and weak/very weak contractility on the Schäfer's nomogram were defined as BOO and DUA, respectively. significantly better than those at baseline (Table 1, 2). The IPSS in patients without BOO deteriorated faster than in those with it, whereas neither DUA nor DO influenced the IPSS slope. Regardless of the preose with it, the IPSS at 12 years was still comparable to that before TURP despite the passage of twelve years. In addition, the QOL index showed durable improvement up to twelve years. The preoperative status of detrusor contractility influenced neither the IPSS slope nor the QOL slope. It is hard to interpret why the IPSS in patients with DO showed sustained improvement for twelve years whereas in those without DO it did not, because we did not confirm whether preoperative DO disappeared after surgery. However, the QOL index showed durable reduction in both the groups with DO and without DO. Thus, TURP can provide an acceptable long-term outcome regardless of the preoperative urodynamic findings.

Conclusion

The symptomatic improvement provided by TURP lasts for over 10 years, although there is gradual deterioration with the passage of time. The QOL index remained improved for twelve years regardless of the preoperative urodynamic findings.

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Session 11 (Poster) - Gerontology & BPH, Thursday, 1st october, 16:00-17:30, Hall E

Reference

1. TANAKA Y, MASUMORI N, ITOH N, et al. Is the short-term outcome of transurethral resection of the prostate affected by preoperative degree of bladder outlet obstruction, status of detrusor contractility or detrusor overactivity? Int J Urol 13: 1398-1401, 2006

The first known measure of its kind

A new catheter-related quality of life instrument for long-term urinary catheter user

ROCHESTER – A catheter-related quality of life (C-IQoL) instrument was developed and tested in two studies to support research with long-term urinary catheter users who use indwelling urethral or suprapubic catheters permanently.

The initial instrument, which was modified after each study, was based on an International Continence Society (ICS) validated generic incontinence quality of life tool. ICS guidelines were used to develop content, including using descriptive and qualitative literature and subjective measures. Literature related to content included issues related to sexuality, embarrassment, and everyday catheter management/care. The initial C-IQoL consisted of 29 items scored on a 1-5-point scale, with agreement from 1 = extremely, 2 = quite a bit, 3 = moderately, 4 = a little, and 5 = not at all. skills to 11 long-term urinary catheter users over a six month period of time. The measure was used at six months. Cronbach's alpha for internal consistency reliability was .85. Based on feedback from the

were easier to interpret, i.e., a fivepoint Likert type scale of strongly agree, agree, neutral, disagree, and strongly disagree.

After these changes, the tool was tested in a repeated measures pro-

	INTAKE Mean	INTAKE Reliability	6 MONTH Mean	6 MONTH Reliability	Follow Up Mean	Follow Up Reliability
TOTAL Scale	3.27	0.90	3.31	0.93	3.70	0.86
Management subscale	3.01	0.86	3.10	0.91	2.67	0.89
Interpersonal subscale	3.34	0.83	3.27	0.88	2.89	0.83
Psychosocial subscale	3.68	0.81	3.77	0.81	3.70	0.86
Test-retest between 6 month & Follow Up						.897

Table 1: C-IQoL Reliabilities and means from Prospective Study on Long-term Catheter Use

The new measure performed adequately in a pilot study of an intervention to teach self-monitoring study participants, who were interviewed on the phone, the response items were simplified to terms that spective study of catheter-related complications in 43 people with longterm urinary catheters. Tests were

conducted for internal consistency reliability at intake, six months, and for test-retest reliability one week later (Table 1). Exploratory factor analysis was conducted using principal axis factoring with Promax rotation, comparing the factors at baseline and six months. Seven items did not show consistency in the pattern matrices over time; therefore, those items were removed. Then confirmatory factor analysis was done with 3 and 4 factor solutions, and all items loaded on the same three factors at baseline and six months. (See items listed below.) As a result of these analyses, the instrument was shortened to 22 items (from 29).

blockage.

grow older.

5 I am concerned about others

6 I am concerned about my cathe-

7 I have to watch what I drink.

urinary tract infection.

before it gets too full.

of my catheter.

Factor 2: Interpersonal

perly.

8 I am concerned about getting a

9 I am concerned about not being

10 I am concerned about being em-

11 I am concerned having to ins-

truct my care attendants about

how to care for the catheter pro-

barrassed or humiliated because

able to empty my drainage bag

ter causing more problems as I

smelling urine on me.

continued from page 14

Results

Reliabilities were satisfactory and they are reported in Table 1 for each of the factors and the entire instrument, as well as mean scores for the scales.

22 questionnaire items are listed by factors below:

Factor 1: Catheter management/problems (Management)

- 1 I am concerned about getting wet because of the catheter leaking.
- 2 I am concerned about where toilets are in new places.
- 3 I am concerned about whether the toilets are accessible and private for emptying the drainage bag.

- 4 I am concerned about catheter 12 I am concerned about doctors and nurses not knowing about autonomic dysreflexia.
 - 13 I am concerned about conflicts in care management with my doctors and/or nurses.
 - 14 I have a hard time because of catheter pain.
 - 15 I am concerned about how the catheter might affect my having sex.
 - 16 I am concerned about getting supplies for my catheter.
 - 17 My catheter limits my choice of

Factor 3: Psychosocial

clothing.

- 18 My catheter makes me feel like I'm not a healthy person.
- 19 I get less enjoyment out of life because of my catheter.
- 20 I feel frustrated because my ca-

- theter prevents me from doing Authors: what I want.
- 21 My catheter makes me feel helpless.
- 22 I don't feel free to leave my home for long periods of time.

Conclusion

This catheter-specific quality of life instrument is the first known measure of its kind, and psychometric testing for reliability and identifiable factors indicated that the tool performed adequately. The measure has been used by colleagues developing a similar quality of life tool in a larger sample of people with long-term urinary catheters, and it should be particularly useful for tests of construct validity.

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Session 6 (Poster) - Quality of Life & Epidemiology, Thursday 1st October, 13:30-15:30, Hall C

"It's all in your head"

The effect of sacral neuromodulation on brain responses in women with Fowler's Syndrome

PITTSBURGH – In the past, young women who developed an unexplained inability to void (and therefore went into urinary retention) were told that it was "hysterical" or "all in the head".

Professor Clare Fowler, one of the co-authors of this paper, has devoted much of her working life to identifying an organic basis for this problem, aiming to convince others that it is a "real" medical condition (Fowler's Syndrome), requiring proper treatment.

She and her colleagues have shown that women with the syndrome not only are unable to void, but also have impaired sensation of bladder filling. The problem is related to overactivity of the striated urethral sphincter, which exerts abnormally high pressures and produces a characteristically abnormal EMG signal, sounding like a whale song. The impairment of bladder sensation suggests that signals from the bladder that reach the brain may be abnormally weak. This idea is supported by the fact that electrical simulation of the sacral nerves (sacral neuromodulation, SNM) leads to improved voiding and restoration of sensation of desire to void, presumably because the stimulation sends stronger signals to the brain. In the last few years there has been an explosion of knowledge about how the various regions of the brain respond during bladder filling and voiding, and how and where sensations such as desire to void are registered. We therefore examined the brain responses to bladder filling in a group of six women aged 18 – 39 years with the syndrome, expecting that at the least we should find evidence of reduced bladder signals (afferents) and reduced sensation, as shown respectively by reduced exci-



Fig. 2: Diagram showing how afferent signals from urethra may inhibit afferents from bladder at sacral level, causing deactivation of brain responses in periaqueductal grey and higher centres.

to void is registered (the insula).

We examined brain responses to bladder filling both at baseline and immediately after SNM, using functional magnetic resonance imaging, which is able to show changes in neural activity in the different regions of the brain. Data were collected in four

changes in desire to void.

sessions: post-SNM with near-empty and full bladder, and at baseline with near-empty and full bladder. In each session, 280 wholebrain scans were acquired while repeatedly infusing and withdrawing 50 ml of saline in and out of the bladder. Subjects also reported

The results were surprising. At baseline (i.e. without SNM) and with a near-empty bladder, the responses were not just weaker than normal but reversed (see top left panel in Figure 1): they were deactivations instead of the activations predominant in normal individuals. This was true for example in the right insula, the seat of visceral sensation. We found also that there was significant correlation between the brain deactivations and the maximum urethral closure pressure measured separately in each patient, implying that the more severe the condition (higher resting urethral pressure), the stron-

rents.

ger were the abnormal deactivations.

Increasing the bladder volume or treatment with SNM reduced these deactivations and strengthened the positive (normal) responses, and also strengthened sensation (Figure 1). This was true for example in the

PAG, the terminus for ascending spinal affe-

These observations show that brain responses to bladder filling are highly abnormal in Fowler's Syndrome. A possible explanation is that the overactive urethra generates abnormally strong inhibitory signals that block bladder afferent activity at sacral level and cause deactivation of PAG and higher centres, with consequent loss of bladder sensation and ability to void (see Figure 2). Apparently a normal mechanism for suppression of incontinence, involving the striated urethral sphincter, becomes exaggerated and prevents voiding. SNM may act at sacral level, by blocking the inhibition by urethral afferents.

Whether the above explanation is correct or not, it is clear that meaning to the phrase "it's all in your head."

Authors:

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Session 22 (Podium) - Neurourology II, Saturday 3rd October, 11:00-12:00, Hall A

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tation of the afferent terminus in the midbrain (the periaqueductal grey, PAG) and reduced excitation of the visceral sensory cortex where desire there is an objectively measurable abnormality in the brain activity of Fowler's Syndrome patients. This both confirms the "real" nature of



Fig. 1: With bladder near-empty and without SNM treatment, most brain responses to bladder filling are deactivations (blue color, top left panel, showing responses rendered on 6 views of the brain). Increased bladder volume (top right), SNM treatment (bottom left), or both (bottom right) all lead to increasingly positive (normal) activations (red color).



Saturday 3rd October 2009, 07:00

New possible drug approach for OAB

Effects of CL316,243 and intravesical prostaglandin E₂ on the primary bladder afferent activity of the rat

ANTWERP/MASUMOTO – Previous studies have demonstrated that intravesical administration of PGE_2 can induce bladder overactivity accompanied with decreased micturition interval and volume, which were referred to reflect the afferent function, in the rat and also that systemic administration of a β_3 -AR agonist inhibited the PGE_2 -induced bladder overactivity.

Thus β_3 -ARs and EP1 receptors might interact in controlling afferent activity. In the present study, we focused on the afferent function of the β_3 -ARs and EP1 receptors, and investigated the effects of intravenous administration of a β_3 -AR agonist (CL316,243; CL) and intravesical instillation of PGE₂ alone or in combination directly on single fiber activities of the primary bladder afferent nerves in the rat.

Materials and Methods

Female Sprague-Dawley rats were used. Under urethane anesthesia, a stimulation electrode was placed around the pelvic nerve and sealed. A polyethylene catheter was inserted in the bladder through the dome. After laminectomy, both L6 dorsal roots were cut close to their entrance to the spinal cord. Afferent fibers originating from the bladder were identified by electrical stimulation of the pelvic nerve and bladder distention with saline. Conduction velocity (CV) was calculated from the latency of response to electrical stimulation and the conduction distance between stimulation and recording sites. Fibers were grouped based on CV. Those with a CV < 2.5 m/sec were considered to correspond with unmyelinated C-fibers and those with $CV \ge$ 2.5 m/sec to myelinated A δ -fibers. To facilitate permeability of the bladder urothelium for drugs, protamine sulfate solution (10 mg/ml, 0.3 ml) was instilled intravesically and kept in the bladder for 60 minutes just before the measurement. Single fiber afferent activity was recorded during constant filling cystometry with 0.08 ml/min saline at room temperature. Filling continued until an intravesical pressure of 30 cmH₂O was reached. At the beginning of the experiments, recording was repeated consecutively three times at 5 minute intervals to evaluate the reproducibility. The third recording served as the base-line value. Then, CL (10 μ g/kg) or its vehicle (saline) was administrated intravenously (i.v.). Three minutes later, PGE. (10-4 M) or saline was instilled intravesically and three further consecutive bladder fillings performed. To evaluate the time-dependency and reproducibility of the drug-effect, all the three cycles of recording were used for analysis.







Fig. 1: Typical bladder pressure (BP) and firing rate (FR) of the A δ -fiber activities during bladder filling with saline or Prostaglandin E_2 (PGE₂; 10-4 M) before (Base) and after (-1, -2, -3) intravenous CL316,243 (CL; 10 μ g/kg)- or vehicle-administration.

A: saline-instillation after CL-administration

B: saline-instillation after vehicle-administration

C: PGE2-instillation after vehicle-administration

After the CL-administration (A), the firing rate of the $A\delta$ -fiber activities during bladder filling decreased from Base. Such decrease was not found after the vehicle-administration (B). Intravesical PGE₂ itself did not affect the firing rate of the $A\delta$ -fiber activities (C).

Fig. 2: Typical bladder pressure (BP) and firing rate (FR) of C-fiber activities during bladder filling with saline or Prostaglandin E_2 (PGE₂; 10-4 M) before (Base) and after (-1, -2, -3) intravenous CL316,243 (CL; 10 µg/kg)or vehicle-administration.

A: saline-instillation after CL-administration.

B: PGE2-instillation after vehicle-administration.

C: PGE2-instillation after CL-administration.

Administration of CL itself did not affect the firing rate of the C-fiber activities during bladder filling (A). When instilled with PGE_2 , the firing rate increased (B). The stimulatory effect of PGE_2 on the C-fiber activities was more pronounced with repeated instillation (B). After pretreatment with CL, such increase in the firing rate with PGE_2 instillation was not observed (C).

Fig. 3: Responses of the A δ -fibers integrated during the whole filling phase based on pressure (A) and volume (B) with intravesical instillation of saline or Prostaglandin E_2 (PGE₂; 10-4 M) and intravenous CL316,243 (CL; 10 μ g/kg)- or vehicle-administration.

The values are expressed as a percentage of base-line activity (mean \pm S.E.M.).

After CL-administration, the A δ -fiber activities significantly decreased (*P < 0.05, **P < 0.01: significant difference from Base), such change was not found after the vehicle-administration. The decrease in the A δ -fiber activities observed in the CL-administration group were significant when compared with Control group, "saline-instillation after vehicle-administration" (+P < 0.05). The inhibitory effect of CL on the activity of A δ -fibers was more pronounced when analyzed based on volume-changes instead of pressure-changes. Intravesical PGE₂ did not affect the A δ -fiber activities.

Fig. 4: Responses of the C-fibers integrated during the whole filling phase based on pressure (A) and volume (B) with intravesical instillation of sa-



Unitary afferent activity was evaluated in relationship to intravesical pressure and volume. Afferent nerve activity is expressed as a percentage of base-line activity, integrated for the whole filling phase. line or Prostaglandin E_2 (PGE₂; 10-4 M) and intravenous CL316,243 (CL; 10 $\mu g/kg$)- or vehicle-administration.

The values are expressed as a percentage of base-line activity (mean \pm S.E.M.).

The C-fiber activities during bladder filling significantly increased after instillation of PGE_2 (*P < 0.05, **P < 0.01: significant difference from Base, +P<0.05: significant difference from Control group "saline-instillation after vehicle-administration"). The stimulatory effect of PGE2 on the C-fiber activities was more pronounced with repeated instillation. Pretreatment with CL significantly inhibited the increase in the C-fiber activities induced by PGE2-instillation (#P < 0.05: significant difference between "PGE₂-instillation after vehicle-administration").

In all 43 single-unit afferent fibers were isolated from 34 rats. Twenty units corresponded to criteria for myelinated Aδ-fibers (CV:

Results

 3.94 ± 0.55 m/sec), and twenty-three for unmyelinated C-fibers (CV: 1.36 \pm 0.08 m/sec).

After CL-administration, bladder compliance did not change significantly, whether the bladder was filled with saline- or PGE₂-instillation, although there was a slight tendency for an increase after saline- and a decrease after PGE₂-

continued from page 14

instillation (Table 1). After CL-administration, the afferent activity of $A\delta$ -fibers in response to salineinstillation decreased significantly; such change was not found after the vehicle-administration (Figs. 1

and 3). In contrast to the response of the A δ -fibers, the C-fiber activity in response to saline-instillation was not affected by CL-administration (Figs. 2 and 4). When the bladder was filled with PGE₂-solution, the activities of the A δ -fibers in response to filling were not significantly different Naoki Aizawa from those filled with sali-

ne (Figs. 1 and 3). On the other hand, the C-fiber activities during bladder filling significantly increased from the base-line value (filled with saline before the PGE₂-instillation) when instilled with PGE₂ (Figs. 2B

and 4). This increase observed in the PGE_a-instillation group was statistically significant when compared with that in the control group with saline-instillation (Fig. 4). The stimulatory effect on the C-fiber activities was more pronounced with repeated instillation (Figs. 2B and 4). Pretreatment with CL

significantly inhibited the increased response of C-fibers to intravesical instillation of PGE₂ (Figs. 2 and 4).

Conclusions

The β_2 -AR agonist CL decreases Aδ-fiber

activity elicited by stimulation of bladder distention. No such effect is seen on C-fibers. It is more likely that the β_2 -AR agonists can directly inhibit the A δ -fibers of the mechanosensitive primary bladder afferents because bladder

intravenously	intra- vesically	Base (before)	after-1	after-2	after-3	
vehicle (saline)	saline	0.0154±0.0022	0.0163±0.0023	0.0162±0.0022	0.0167±0.0023	(n=6)
CL316,243 (10 µg/kg)	saline	0.0182±0.0016	0.0193±0.0017	0.0197±0.0019	0.0195±0.0019	(n=8)
vehicle (saline)	PGE2 (10-4 M)	0.0153±0.0017	0.0143±0.0014	0.0136±0.0014	0.0136±0.0015	(n=14)
CL316,243 (10 µg/kg)	PGE2 (10-4 M)	0.0131±0.0012	0.0139±0.0017	0.0134±0.0017	0.0136±0.0019	(n=9)

The values are indicated as mean ± S.E.M. No significant differences were found before and after administration (two-way ANOVA followed by Tukey's test). Table 1: Bladder compliance (ml/cmH2O) calculated between start and end (intravesical pressure of 30 cmH2O) of the filling phase

compliance did not change. On the other hand, the CL also inhibited Cfiber activity elicited by intravesical PGE₂-instillation, not saline-instillation. These results suggest that CL as a β_2 -AR agonist can not directly inhibit the mechanosensitive Cfiber activities, but when chemosensitive C-fibers are stimulated by for example intravesically instilled PGE, the increased C-fiber activities can be inhibited by CL-admi-

nistration probably through $\beta_{\alpha}AR$ stimulation. To our knowledge, this is the first demonstration of the direct effects of a β_2 -AR agonist, as well as intravesical PGE₂, on single afferent fibers in the rat bladder, and indicates a possible additional action to the direct relaxing effect on detrusor, if these drugs are used in the treatment of OAB or other bladder sensory disorders.

periods consent forms were found

in every set of notes. Surprisingly,

being such an important aspect of

surgical care, only 28.3 % of pati-

ents fulfilled all the defined crite-

ria for fully informed consent in

2003.

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Session 25 (Poster) - Basic Pharmacology, Saturday 3rd October, 13:30-14:30, Hall C

The importance of proper consent

Procedure specific consent forms improve the process before elective surgical procedures

WRIGHTINGTON - Informed consent is the most basic pre-requisite for elective surgical procedures such as those for Stress Urinary Incontinence. In the UK, guidance on consent has been given by both the GMC and the Government (Dept. of Health).

ssentially the patient needs to be Linformed about, and understand, the treatment, its aims and chances of success, any alternative treatments and the potential side effects and complications.

During 2004 the North West Regional Urology Audit Group, as part of its audit on continence surgery, looked at the process of consent and its documentation in the case notes for patients undergoing continence surgery by an urologist within the group during the calendar vear 2003. This audit was repeated in 2008 to look at patients undergoing the same surgical procedures by members of the group during the twelve month period November 2006 - October 2007 (designated 2007 data). The data collection was retrospective and carried out by the same two audit co-ordinators on both occasions, giving a consistent approach to collection and interpretation of data. Operations included in the two audits were colposuspension (all of which were open), fascial sling (of any type) and a variety of synthetic sub-urethral slings (tape procedures). Patients undergoing peri-urethral bulking injections were excluded from this analysis as the consent is more straight forward and institutions varied as to whether or not consent forms were required for procedures under local anaesthetic.

consent form. As it was retrospective study, it was necessary to rely solely on what was documented and no assessment could be made about whether the patients remembered or understood what they had been told. The accuracy of what the patients were told was also not

During 2003, there were 145 procedures under the care of 25 urological surgeons at 15 centres in the region. During 2007, there were 202 procedures performed by 22 surgeons at 15 centres. The numbers of each type of procedure performed are shown in Figure 1.



Fig. 1: Numbers of procedure by type in two audit periods

assessed, simply whether or not a Other options discussion about each factor was



being documented in at least 95% of cases, with the sole exception of warning about rectocoele occur-

Firstly, the increased awareness of the need for accurate documentation following the poor performance during the first audit period may have produced some benefit. However, it is doubtful that this factor alone could have produced such a significant change in practice that was still evident two years after the original audit had been presented to the group.

Secondly, is the publication in 2005 of procedure specific consent forms by the British Association of Urological Surgeons. These forms are available for all common urological procedures and detail the potential complications and alternative treatments for each individual operation. They were not in use during the first audit period but had been available in 12 departments during the follow-up audit - either as the actual consent form or as a patient information resource and potential aide memoire to the surgeon. It is reasonable to conclude that the consent process was surprisingly poorly carried out in 2003 but dramatically improved by the availability of the procedure specific consent forms in 2007. This supports the recommendation that other groups of surgeons, in the UK and elsewhere, should seek access to the BAUS resource where appropriate, or endeavor to develop their own set of procedure specific consent forms.

Clinical notes were examined and data was collected from the hand written entries, letters to the patients or General Practitioner regarding consultations and the documented. Patients were deemed to have been informed about alternative treatments if there was at least one reference to an alternative procedure for treatment of SUI. Any documented discussion about the chance of a successful outcome, or mentioning the possibility of failing to improve, fulfilled the audit criteria for discussion about success rates.

The complications requiring discussion were development of frequency +/- urgency after surgery and the risk of needing to intermittently catheterise for all procedures. In addition for colposuspension was the risk of developing a rectocoele, and for synthetic tapes were the risks of infection or erosion of the tape.



Fig. 2: Propotion of patients properbly consented about each issue

The 2007 data confirms the trend seen in other series towards the increased use of synthetic sub urethral slings, particularly at the expense of colposuspension procedures. In both data collection

ence after colposuspension (see Figure 2). Two potential reasons to explain the improvement in the consent process for this group of patients can be proposed.

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Session 1 (Podium) - Surgery for Stress Incontinence, Thursday 1st October, 09:00-10:30, Hall A



Multidisciplinary test system: the bladder

Bladder regeneration in animal models might prove interesting for general tissue regeneration

PITTSBURGH - Regeneration of

the urinary bladder has been studied for over a century including studies by Daniel Liang in the 1960's, demonstrating that both humans and rats have the ability to regenerate the bladder following removal of a large part of the organ.

espite this knowledge, most preclinical studies have employed the use of scaffolds to guide regeneration of the bladder. In fact, the first autologous tissue-engineered neo-bladder has recently been successfully implanted in patients. This seminal study documents that the body is a sufficient incubator for successful bladder regeneration. Improvements in the utility, efficacy and clinical applicability of tissue engineering/regenerative medicine, including therapies for urological disease(s) will undoubtedly benefit from increased understanding of the normal regenerative process in vivo. As a first step in this direction, we have begun to more completely characterize bladder regeneration in vivo in a rodent model. The overall goal of this study is to elucidate the cellular, molecular and physiological characteristics of the regenerating bladder.

Twelve-week-old female F344 rats underwent trigone-sparing, subtotal cystectomy (STC; removal of ≈70% of the bladder), and the regenerative process that followed was monitored in several ways. For functional characterization, in vivo filling

cystometry studies were performed on conscious, freely-moving animals at 2, 4, and 8 wks post-STC. To monitor bladder growth/morphology high-resolution micro CT scans were performed at 0, 1, 2, 4, and 8 weeks post-STC, and linked to in vivo filling cystometry studies on David Burmeister

the same animal. After harvesting tissue, in vitro contractility of bladder detrusor muscle in response to cholinergic and electric field stimulation was characterized in vitro. Immunostaining was also performed in order to examine the differentiation status of the urothelium (Uroplakin3); demonstrate innervation of the bladder (PGP9.5); and to begin to identify cell populations involved in the regenerative process (CD117).

Consistent with previous studies, the rat bladder grows in volume following STC, approaching, but not exceeding, control values. This was shown not only with micro CT scans (see images right), but also with filling cystometry. Cystometric capacity in control animals was 0.96 \pm .05 ml which decreased to 0.46 \pm 0.03 ml at two weeks post-STC, then

gradually increased to 0.73 ± 0.16 ml at 4 weeks post-STC and was similar to control values at eight weeks (0.85 \pm 0.08 ml). Normal detrusor function

> was seen at all timepoints post-STC, with little or no non-voiding contractions, and the animals were continent. Maximum (micturition) pressure was also reduced following STC $(30.5 \pm 5.9 \text{ cm H}_20) 2$ weeks post-STC compared to controls (49.2 \pm 3.7 cm $H_{2}O$, but did show some functional recovery at 4 weeks $(38.1 \pm 4.9 \text{ cm H}_{0})$

and 8 weeks (37.3 ± 3.3 cm H₂O) after STC. Bladder circumference form the anterior view as calculated by

In vitro, the carbachol-induced maximal steady state contraction of isolated detrusor tissue strips from regenerating bladders 2-weeks post STC (30.91 \pm 4.49 g/g tissue) was greatly reduced compared to controls (148.0 \pm 10.23 g/g tissue). However, by eight weeks post-STC, some functional recovery was observed as the maximal response improved (54.03 + 5.36 g/g tissue). Electrical field stimulation followed the same pattern, although induced responses from tissue at all timepoints post-STC suggests the presence of nerves in regenerating bladders. This observation was supported by positive PGP9.5 immunostaining in the regenerating bladder wall at 4 weeks post-STC. A mature urothetive immunostaining to uroplakin 3. Immunohistochemistry staining was positive for c-kit (CD117) in the detrusor, denoting a possible role for progenitor cells in regeneration of the muscle layer.

Importantly, despite the observed differences, the regenerating bladders emptied normally and the animals were continent. The longterm anatomy/physiology of the regenerating bladder remains to be determined. Further investigations to determine the identity and source of specific cells involved in tissue formation are a priority. In addition, the key molecular events or growth factors associated with certain aspects of bladder regeneration such as reinnervation and angiogenesis will



Fig. 1: Longitudinal images from a bladder filled with contrast medium from the same rat. Images are pre-STC (A),1 week (B), 4 weeks (C) and 8 weeks (D) post-STC.

micro CT analysis also positively correlated with micturition pressure, r = .634, p < 0.05.

lium (i.e., terminally differentiated umbrella cells) was shown as early as 1-week after surgery via posiprovide further insight into this process. The combination of high resolution imaging with direct measures of bladder function in vivo and tissue function and histology in vitro will help establish the baseline characteristics of bladder regeneration as well as noninvasive markers for important physiological milestones associated with this process. With this information, it may be possible to harness the body's natural ability to regenerate the bladder, and extend these applications to the clinic.

These initial investigations establish the utility of an important preclinical animal model using the bladder as an appropriate multidisciplinary test system for studying and elucidating the characteristics of tissue regeneration in mammals. The power of this approach stems from the longitudinal multidisciplinary comparison of the regenerated bladder with the native bladder from the same animal. In addition to their potential direct impact on basic and clinical urological research, these findings should point toward more general features of tissue regeneration that would be helpful to advancing the field of regenerative medicine in multiple tissue and organ systems.



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Session 13 (Poster) - Physiology, Friday 2nd October, 11:00-12:30, Hall B