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## UROLOGICAL SURVEY

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## STONE DISEASE

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### **Nifedipine versus tamsulosin for the management of lower ureteral stones**

Propiglia F, Ghignone G, Fiori C, Fontana D, Scarpa RM

From the Division of Urology, University of Turin, Orbassano, Turin, Italy

*J Urol.* 2004; 172: 568-571

**Purpose:** We evaluate and compare the effectiveness of 2 different medical therapies during watchful waiting in patients with lower ureteral stones.

**Materials and Methods:** A total of 86 patients with stones less than 1 cm located in the lower ureter (juxtavesical or intramural tract) were enrolled in the study and were randomly divided into 3 groups. Group 1 (30) and 2 (28) patients received daily oral treatment of 30 mg deflazacort, (maximum 10 days). In addition group 1 patients received 30 mg nifedipine slow-release (maximum 28 days) and group 2 received 1 daily oral therapy of 0.4 mg tamsulosin (maximum 28 days), Group 3 patients (28) were used as controls. Statistical analyses were performed using Student's test, ANOVA test, chi-square test and Fisher's exact test.

**Results:** The average stone size for groups 1 to 3 was 4.7, 5.42 and 5.35 mm, respectively, which was not statistically significant. Expulsion was observed in 24 of 30 patients in group 1 (80%), 24 of 28 in group 2 (85%) and 12 of 28 in group 3 (43%). The difference in groups 1 and 2 with respect to group 3 was significant. Average expulsion time for groups 1 to 3 was 9.3, 7.7 and 12 days, respectively. A statistically significant difference was noted between groups 2 and 3. Mean sodium diclofenac dosage per patient in groups 1 to 3 was 19.5, 26, and 105 mg, respectively. A statistical significant difference was observed between groups 1 and 2 with respect to group 3.

**Conclusions:** Medical treatments with nifedipine and tamsulosin proved to be safe and effective as demonstrated by the increased stone expulsion rate and reduced need for analgesic therapy. Moreover medical therapy, particularly in regard to tamsulosin, reduced expulsion time.

### **Editorial Comment**

A number of trials have demonstrated the utility of pharmacologic therapy in promoting spontaneous ureteral stone passage and in reducing the time for and pain associated with stone expulsion. The efficacy of calcium channel blockers (nifedipine) in conjunction with corticosteroids has now been proven in several prospective, randomized clinical trials, and recently the combination of an alpha-1 receptor antagonist (tamsulosin) and a corticosteroid has likewise demonstrated benefit in the medical management of distal ureteral calculi. Propiglia and colleagues performed a head-to-head comparison of the 2 medical regimens (nifedipine/deflazacort versus tamsulosin/deflazacort) compared with a control, no-treatment arm and found that both treatment groups demonstrated a significantly higher rate of stone expulsion, a shorter time to spontaneous passage (only the tamsulosin arm was statistically significant compared with control) and a reduced need for analgesics.

Although adverse effects associated with the use of nifedipine and tamsulosin are low, all trials involving these drugs have reported a small number of patient drop-outs as a result of perceived side effects from the medication. Given the perhaps greater potential for problems due to nifedipine compared with tamsulosin, as well the proven benefit of the tamsulosin regimen in reducing time to stone passage, the combination of tamsulosin/corticosteroid may provide the best chance of spontaneous passage for distal ureteral stones. It remains to be seen if pharmacological therapy will prove to be as effective in promoting the spontaneous passage of stones located in the middle and proximal ureter as well as stones in the distal ureter. Furthermore, these studies have not separated the effect of the corticosteroid from that of the calcium channel blocker or alpha-1 blocker. Hopefully, future study will define the role of each agent in reducing symptoms and promoting

stone passage. However, for now, there is ample evidence supporting the use of these agents in appropriate patients with < 1 cm distal ureteral stones.

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**Metabolic risk factors and the impact of medical therapy on the management of nephrothiasis in obese patients**

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*J Urol.* 2004; 172: 159-163

**Purpose:** Previous studies have demonstrated that obesity can increase the risk of stone formation as well as recurrence rates of stone disease. Yet appropriate medical management can significantly decrease the risk of recurrent stone disease. Therefore, we analyzed our obese patient population, assessing the risk factors for stone formation and the impact of selective medical therapy on recurrent stone formation.

**Materials and Methods:** A retrospective chart review was performed to identify obese patients with stone disease from our Stone Center. Metabolic risk factors for stones were identified as well as patient response to medical therapy. A similar analysis was performed on a group of age and sex matched nonobese stone formers.

**Results:** Of 1,021 patients 140 (14%) were identified as obese (body mass index greater than 30). Of these patients complete metabolic evaluations were available in 83 with an average follow-up of 2.3 years. The most common presenting metabolic abnormalities among these obese patients included gouty diathesis (54%), hypocitraturia (54%) and hyperuricosuria (43%), which presented at levels that were significantly higher than those of the nonobese stone formers ( $p < 0.05$ ). Stone analysis was available in 32 obese patients with 63% having uric acid calculi. After initiating treatment with selective medical therapy obese and nonobese patients' demonstrated normalization of metabolic abnormalities, resulting in an average decrease in new stone formation from 1.75 to 0.15 new stones formed per patient per year in both groups.

**Conclusions:** Obesity, as a result of dietary indiscretion, probable purine gluttony and possible type II diabetes, appears to have a significant role in recurrent stone formation. Appropriate metabolic evaluation, institution of medical therapy and dietary recommendations to decrease animal protein intake can significantly improve the risk of recurrent stone formation in these often difficult to treat patients.

**Editorial Comment**

With an increase in the proportion of obese individuals, interest in medical evaluation and treatment of problems unique to or overrepresented in this patient population has expanded. Stone disease is no exception, and the unique challenges posed by the surgical treatment of morbidly obese individuals have encouraged efforts to reduce the risk of stone occurrence. Ekeruo and colleagues reviewed the outcomes of medical evaluation and treatment of 83 obese stone formers at an average follow-up of 2.3 years, and found that gouty diathesis, hypocitraturia and hyperuricosuria were the most common metabolic abnormalities identified, and that these abnormalities were more pronounced than those identified in a group of matched non-obese stone formers. Moreover, uric acid stone composition was overrepresented in this patient group (63%) compared with the non-

obese group in whom uric acid stones comprised only 11% of stones. Some of these findings are expected based solely on overindulgent eating patterns (elevated urinary calcium, uric acid and oxalate). However, the finding of low urine pH is particularly interesting given the recent report showing that insulin resistance (commonly seen in obese patients) is associated with a defect in ammoniogenesis, thereby leading to an acid urine and subsequent promotion of uric acid stones (1). Although a high acid ash diet (from overindulgence in animal protein) can itself cause a decrease in urinary pH, the findings seen above persisted even when patients were maintained on a controlled metabolic diet, suggesting that the effect is, at least in part, diet-independent.

Of note, the initiation of directed medical and dietary therapy aimed at correcting the underlying metabolic abnormalities resulted in normalization of urinary parameters and a reduction in the rate of stone formation. As such, metabolic evaluation and medical and dietary therapy should be encouraged in these patients, with a good expectation of reduced stone recurrence and consequently less frequent need for surgical intervention.

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## ENDOUROLOGY & LAPAROSCOPY

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### **Nifedipine versus tamsulosin for the management of lower ureteral stones**

Propiglia F, Ghignone G, Fiori C, Fontana D, Scarpa RM

From the Division of Urology, University of Turin, Orbassano, Turin, Italy

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Conclusions: Medical treatments with nifedipine and tamsulosin proved to be safe and effective as demonstrated by the increased stone expulsion rate and reduced need for analgesic therapy. Moreover medical therapy, particularly in regard to tamsulosin, reduced expulsion time.

### Editorial Comment

This group from Italy has contributed much to the active pharmacologic management of ureteral stones. They and others have demonstrated the effectiveness of nifedipine (calcium-channel blocker) or tamulosin (alpha-1 blocker) in combination with corticosteroids and non-steroidal anti-inflammatory agents to facilitate stone passage from the ureter. Spontaneous ureteral stones and ureteral fragments after extracorporeal shock wave lithotripsy both have been shown to pass more frequently, sooner, and with less pain compared to controls. Unfortunately, all of the randomized studies have included corticosteroids and non-steroidal anti-inflammatory agents in the treatment arms, and the distinct effects of the calcium-channel blocker or alpha-1 blocker alone cannot be ascertained. Nonetheless, at our institution we have used the combination of calcium-channel blockers and non-steroidal anti-inflammatory agents for the treatment of ureteral colic. We have been unwilling to subject stone patients, with potential upper urinary tract obstruction and risk for infection, to the risks of corticosteroids. Anecdotally we have seen favorable results, but we cannot make any statement as to the comparative effectiveness to a treatment also including corticosteroids. This new study, however, leads us to believe that the alpha-1 blocker tamulosin may have even greater effectiveness than nifedipine. Although the incidence of adverse effects was low in this study (only one patient in each of the treatment groups had to suspend therapy owing to adverse effects), one would expect tamulosin to have fewer adverse effects in general. The use of tamulosin and non-steroidal anti-inflammatory agents (plus corticosteroids if the studied treatment is to be applied exactly) should be considered the current best pharmacologic management of ureteral colic.

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### **15-Year experience with the management of extrinsic ureteral obstruction with indwelling ureteral stents**

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*J Urol. 2004; 172: 592-5*

Purpose: We assessed the success of retrograde placement of indwelling ureteral stents in the management of ureteral obstruction due to extrinsic compression.

Materials and Methods: Between July 1987 and December 2002 adequate followup was available for 101 patients who underwent primary retrograde ureteral stenting for extrinsic ureteral obstruction. Mean age at presentation was 61.4 years (range 33 to 90). Chart review was performed on all patients for primary diagnosis, symptomatology, degree of hydronephrosis, creatinine levels (baseline, treatment and post treatment), location of compression, size and number of stents used, progression to percutaneous nephrostomy tube (PNT), stent failure, days to stent failure, post-stent therapy and status at last followup.

Results: Mean length of followup was 11 months (range 1 to 127). In 101 patients 138 ureteral units (UU) were stented. Total stent failure occurred in 41 (40.6%) patients and 58 (42.0%) UU. A total of 40 (29.0%) UU required PNTs at a mean of 40.3 days (range 0 to 330) with 18 PNTs placed in less than 1 week.

Cases of stent failure that did not undergo PNT placement included 18 (13.0%) UU at a mean of 52.4 days (range 3 to 128). A total of 90 (89.1%) patients had metastatic cancer at stenting with 32.2% dead at 5.8 months (range 1 to 32). Univariate and multivariate analyses identified cancer diagnosis, baseline creatinine greater than 1.3 mg/dl and post-stent systemic treatment as predictors of stent failure. Proximal location of compression and treatment creatinine greater than 3.11 mg/dl were marginal predictors of failure on univariate analysis, while proximal location of obstruction was also marginally significant on multivariate analysis. No predictors were identified for early stent failure (less than 1 week).

Conclusions: At almost 1 year followup stent failure due to extrinsic compression occurred in nearly half of treated patients. Analysis of data revealed a diagnosis of cancer, baseline mild renal insufficiency and metastatic disease requiring chemotherapy or radiation as predictors of stent failure. Managing extrinsic compression by retrograde stenting continues to be a practical but guarded decision and should be tailored to each patient.

### Editorial Comment

The article reviews a common clinical situation, that being placement of a ureteral stent for extrinsic ureteral obstruction. Almost half of the patients treated with ureteral stents failed within the first year, which is remarkably similar to prior reports. In the later years of this current series the success rate improved to greater than 60%. This might be due to different stent materials, but unfortunately the chart review was such that the authors could not reliably assess this factor. It makes sense that a stiffer and less compressible stent would fare better in this situation. Although one small series suggested that a stiffer stent maintained patency longer (1), this has yet to be confirmed in other series. An internal stent has attractiveness over a percutaneous nephrostomy tube for long-term management, but this approximately 50% failure rate must be acknowledged when counseling patients and when performing follow-up.

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## IMAGING

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### **Baseline staging of newly diagnosed prostate cancer: a summary of the literature**

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*J Urol.* 2004; 171 (6 Pt 1): 2122-7

Purpose: Staging for prostate cancer often includes bone scanning and computerized tomography (CT). We systematically reviewed the published evidence for these tests.

**Materials and Methods:** We searched MedLine for articles on these investigations in newly diagnosed cases of prostate cancer. Data were pooled based on prostate specific antigen (PSA), grade and tumor stage.

**Results:** Among 23 studies examining the role of bone scan metastases were detected in 2.3%, 5.3% and 16.2% of patients with PSA levels less than 10, 10.1 to 19.9 and 20 to 49.9 ng/ml, respectively. Scanning detected metastases in 6.4% of men with organ confined cancer and 49.5% with locally advanced disease. Detection rates were 5.6% and 29.9% for Gleason scores 7 or less and 8 or greater, respectively. Among 25 studies CT documented lymphadenopathy in 0 and 1.1% of patients with PSA less than 20 and 20 ng/ml or greater, respectively. CT detection rate was 0.7% and 19.6% in patients with localized and locally advanced disease, respectively. Detection rates in patients with Gleason scores 7 or less and 8 or greater were 1.2% and 12.5%, respectively. These risks were typically much greater on pathological evaluation.

**Conclusions:** Patients with low risk prostate cancer are unlikely to have metastatic disease documented by bone scan or CT. Therefore, these investigations should not be standard practice. However, patients with PSA 20 ng/ml or greater, locally advanced disease, or Gleason score 8 or greater are at higher risk for bone metastases and should be considered for bone scan. CT may be useful in patients with locally advanced disease or Gleason score 8 or greater but appears not to be of benefit in patients with increased PSA alone.

### **Editorial Comment**

This is a very useful summary of the literature regarding the value of performing CT and bone scan in patients with newly diagnosed prostate cancer. Although these data is not new, this study clearly emphasizes that these tests should be done only in patients with high risk of presenting nodal or bone metastasis (PSA > 15 or Gleason score above 7 or clinical stage T3-4). In this group of patient, bone scan should be the first test to be done. If negative, CT of the abdomen and pelvis should be the next step. Since lymph node size does not correlate with the presence of metastasis, any abnormal lymph node demonstrated by CT should be further biopsied (CT-guided lymph node biopsy). Previous study has shown that in asymptomatic patients with newly diagnosed prostate cancer and serum PSA levels of less than 20 ng/ml, the likelihood of positive findings on abdominal/pelvic CT is extremely low (< 1%). In the USA, elimination of staging abdominal/pelvic CT in these patients would reduce medical expenditures for prostate cancer management by \$20-50 million per year (1). In our opinion, it would be more beneficial to perform an endorectal MR imaging in the group of patients with moderate or high risk of harboring extraprostatic disease. This test is the best one available for adequate local staging of the disease. Endorectal MR imaging of the prostate has remarkable strength in the prediction of extra-prostatic extension of the disease and plays an important role in the evaluation of prostate cancer particularly when evaluated by an urologist (2).

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**Patient radiation dose at CT urography and conventional urography**

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*Radiology 2004; 232: 126-32*

**Purpose:** To measure and compare patient radiation dose from computed tomographic (CT) urography and conventional urography and to compare these doses with dose estimates determined from phantom measurements.

**Materials and Methods:** Patient skin doses were determined by placing a thermoluminescent dosimeter (TLD) strip (six TLD chips) on the abdomen of eight patients examined with CT urography and 11 patients examined with conventional urography. CT urography group consisted of two women and six men (mean age, 55.5 years), and conventional urography group consisted of six women and five men (mean age, 58.9 years). CT urography protocol included three volumetric acquisitions of the abdomen and pelvis. Conventional urography protocol consisted of acquisition of several images involving full nephrotomography and oblique projections. Mean and SD of measured patient doses were compared with corresponding calculated doses and with dose measured on a Lucite pelvic-torso phantom. Correlation coefficient (R(2)) was calculated to compare measured and calculated skin doses for conventional urography examination, and two-tailed P value significance test was used to evaluate variation in effective dose with patient size. Radiation risk was calculated from effective dose estimates.

**Results:** Mean patient skin doses for CT urography measured with TLD strips and calculated from phantom data (CT dose index) were 56.3 mGy +/- 11.5 and 54.6 mGy +/- 4.1, respectively. Mean patient skin doses for conventional urography measured with TLD strips and calculated as entrance skin dose were 151 mGy +/- 90 and 145 mGy +/- 76, respectively. Correlation coefficient between measured and calculated skin doses for conventional urography examinations was 0.95. Mean effective dose estimates for CT urography and conventional urography were 14.8 mSv +/- 90.0 and 9.7 mSv +/- 3.0, respectively. Mean effective doses estimated for the pelvic-torso phantom were 15.9 mSv (CT urography) and 7.8 mSv (conventional urography).

**Conclusion:** Standard protocol for CT urography led to higher mean effective dose, approximately 1.5 times the radiation risk for conventional urography. Patient dose estimates should be taken into consideration when imaging protocols are established for CT urography.

**Editorial Comment**

CT urography is an evolving concept and developing technique, which combine the ultimate diagnostic capabilities of intravenous urography and CT. In many institutions, intravenous urography has already been replaced by CT urography to evaluate patients with hematuria and other genitourinary conditions. This paper emphasizes the most important drawback of this technique, which is related to the radiation exposure. In our institution the miliamper seconds (mAs) settings are chosen depending upon clinical indication and patients' age and body habitus. Recent studies have shown that low-dose (reduced mAs) unenhanced CT is appropriate for the diagnosis of ureteral stones. Similarly efforts have been made in order to perform a low-dose protocol for CT urography. The standard protocol for multislice CT urography usually include 4 phases of imaging [noncontrast, arterial phase (25-30 seconds after intravenous injection of contrast); nephrographic phase (100 seconds) and excretory phase (180 seconds)]. In order to obtain a significant reduction in patient effective radiation dose without deterioration of imaging quality one should optimize the number of phases to be done and also do not include the kidneys and the pelvis in every phase. This can be done by adequate adjustment of the technical parameters to the patient's weight and clinical situation. To obtain good results with a low-dose

CT urography protocol is possible. Since CT urography is still an evolving technique we believe that further improvement of an optimized protocol will be developed very soon.

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## UROGENITAL TRAUMA

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### **Traumatic rupture of the urinary bladder: is the suprapubic tube necessary?**

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*J Trauma. 2003; 54: 431-6*

**Background:** Although surgical principles are well accepted for the treatment of an intraperitoneal or extraperitoneal rupture of the urinary bladder, the type and number of drainage catheters needed to obtain a satisfactory outcome with minimal patient morbidity have yet to be determined.

**Methods:** This was a retrospective review of data on injured patients with the diagnosis of an intraperitoneal or extraperitoneal rupture of the urinary bladder from penetrating or blunt trauma.

**Results:** Of the 51 patients identified, 28 were treated with suprapubic and transurethral catheters, whereas 23 received a transurethral catheter only. Complications and catheter duration times were similar regardless of type of bladder injury or drainage catheter used ( $p > 0.5$ ).

**Conclusion:** These data suggest that there are similar outcomes and complication rates for patients treated with suprapubic and transurethral catheters versus transurethral catheter only. Transurethral catheters alone seem effective in draining all types of bladder injuries.

### **Editorial Comment**

For many years, by habit, many of us have been placing suprapubic tubes (SPT) at the time of open bladder repair. However, this is only one of many papers that advocate using only a urethral catheter alone in these patients (1-3). It appears that using a urethral Foley catheter alone allows for low complications with minimal morbidity. The rate of urinary tract infection, in this study at least, is identical between both groups. In no cases in this small group of 51 patients did a patient seem to “require” the SPT (either as a “safety valve” or to facilitate irrigation).

Although I agree that most bladder injuries may be treated with urethral catheterization alone, there are some theoretical benefits to using a SPT. Patients with SPTs get their urethral catheters removed 11 days earlier in this series (with continued drainage via SPT), which may be more comfortable for the patient. Also, the suprapubic catheter allows for a theoretic “safety valve” if the urethral catheter becomes clogged or inadvertently dislodged, although this was not necessary in this series.

There are probably some uncommon cases where a suprapubic tube would be prudent. In cases of severe ongoing hematuria which is observed in the operating room, or in cases of truly devastating bladder injuries (such as close range shotgun wounds to the bladder), an SPT might help to maximize bladder drainage, especially in the unreparable or unreliably repaired bladder. Otherwise, the data is clear: after bladder repair, consider using just a urethral catheter. We tend to use a 2-way catheter, as we feel that continuous bladder

irrigation is improper in a recently repaired bladder, but the authors of this study place a 3 way Foley and do use continuous bladder irrigation when necessary.

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#### **Straddle injuries to the bulbar urethra: management and outcomes in 78 patients**

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*J Urol.* 2004; 171 (2 Pt 1): 722-5

**Purpose:** We describe our experience with blunt straddle injuries to the anterior urethra and identify factors that may affect patient outcome.

**Materials and Methods:** We reviewed the San Francisco General Hospital Urologic Trauma data base to identify men with blunt straddle injury. We analyzed presentation and initial management, location and length of urethral stricture, surgical options, and long-term outcome after reconstruction.

**Results:** Of 78 patients, 40% presented to the emergency department acutely and 60% presented 6 months to 10 years after injury complaining of obstructive symptoms, of whom 30% reported at least 1 episode of urinary retention. Initial acute management was suprapubic cystostomy in 81% of cases and primary realignment in 19%. Urethral strictures were predominantly located in the proximal bulb. Mean stricture length was significantly longer in men with delayed presentation (2.7 vs 1.8 cm,  $p < 0.05$ ). No relationship was found between stricture length and the mechanism of injury or initial management technique. However, patients who had undergone primary realignment required complex flap or graft urethroplasty at a greater rate compared with men who had undergone suprapubic diversion ( $p = 0.054$ ). Transperineal urethroplasty was required in 92% of patients with the majority undergoing end-to-end anastomosis. The success rate was 95% at a mean followup of 25 months (range 10 to 180). Recurrent stricture occurred in 4 men with prior urethral manipulation and it was managed successfully by direct vision internal urethrotomy alone.

**Conclusions:** After blunt straddle injury to the perineum the primary morbidity is anterior urethral stricture, for which suprapubic cystostomy is appropriate initial management. The majority of patients require surgery but with careful preoperative planning and adequate resection of fibrotic tissue the long-term success rate can approach 95%. If it arises, recurrent stricture responds well to direct vision internal urethrotomy alone.

### Editorial Comment

Acute, blunt posterior urethral injuries, I believe, have ample data in the literature to support early endoscopic realignment over a catheter instead of suprapubic tube placement. I was surprised to see that in this series, acute realignment of significant acute blunt anterior urethral injuries was certain no better and potentially worse than suprapubic urinary diversion.

Seventy-eight patients are reported here, of which roughly half present acutely and half present long after the injury (all of these late cases had urethral stricture). Nine percent of those treated with urinary diversion required urethroplasty and 17% of those treated with primary catheter realignment needed surgery ( $p =$  not significant). More importantly, the length of the stricture seemed to be much longer on those managed with a urethral catheter ( $p < 0.5$ ). The reason for this is unclear, and explanations involving “damage to the corpora spongiosum” are usually invoked in the literature. No matter what the reason, the data appears reasonably robust to suggest that acute catheter realignment of these injuries is not a good idea.

Of note, this article, which deals with blunt injury, should not be confused with previously printed works concerning penetrating anterior urethral trauma. This, too, is controversial with some advocating immediate repair and others advocating suprapubic diversion alone.

Although it will be psychologically difficult for me to avoid early urethral realignment of anterior strictures over a catheter (as I so strongly believe that it helps greatly in posterior urethral stricture) this and other series seem to indicate that suprapubic diversion may be the better option.

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## **PATHOLOGY**

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### **Fat invasion in ten-core prostate needle biopsies: incidence, biopsy and clinical findings**

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*Mod Pathol. 2004; 17 (suppl. 1): 186A*

**Background:** Presence of prostate cancer in the periprostatic adipose tissue signifies an advanced disease if seen on radical prostatectomy (stage pT3a). The significance of fat invasion on needle-core biopsies has not been well studied. The aim of the study is to investigate the incidence of the fat involvement and the associated clinical and biopsy findings on ten-core needle biopsy.

**Design:** From 07/00 to 12/01, 1,017 patients demonstrated prostate cancer on ten-core needle biopsy in our centralized Urological Pathology for the Calgary Health Region. The clinical and pathology data for all patients have been collected in our prostate cancer database. Fat involvement on one or more biopsy cores has been reported in 23 patients. Only one patient had undergone a radical prostatectomy in our institution until 09/03. All biopsies reported as positive for fat involvement and the prostatectomy specimen were reviewed.

**Results:** The incidence of fat involvement on needle biopsy was 2.2%. Most common site of fat involvement was the prostatic base (83%) and in 9/23 (39%) patients' fat involvement was present in more than one site. The patients mean age was 70.1 years (range 57-83). Digital rectal examination and ultrasound findings were abnormal in 14/24 (58%) and 12/24 (50%) patients, respectively. Mean serum PSA was 52.3 ng/ml (median 15.55) and mean PSA density was 2 .1 (median 0.45). Prostatic carcinoma was bilateral in 19/23

(83%) of the patients. Perineural involvement was identified in all biopsies with fat invasion; one biopsy showed also muscle involvement. The number of cores positive for prostate cancer ranged from 4 to 10 (mean 8). Mean biopsy Gleason score was 8 (range 7-10) and in 12/24 (50%) of the patients Gleason score was 8. Focal extraprostatic extension was confirmed in the patient who underwent radical prostatectomy.

Conclusions: Invasion of the fat by prostate cancer is uncommonly seen in ten-core prostatic biopsies. It is associated with adverse clinical and biopsy findings, including extensive and multiple core involvement, high Gleason biopsy score, and perineural invasion. It is most commonly seen in the biopsy cores from the prostatic base. Fat involvement should be always reported when identified on prostatic needle biopsies. The fact that during the follow-up period radical prostatectomy was performed only in one patient with fat involvement on biopsy, suggests that these patients, in addition to the adverse biopsy findings, presented with clinically advanced disease.

### Editorial Comment

Invasion of fat is almost always a manifestation of extraprostatic spread by cancer. However, a published observation has indicated that rarely, significant expanses of fat may exist within the prostate, where its invasion by carcinoma would be misleading and might be considered evidence of extraprostatic spread (1).

To address this finding we dissected 150 prostates from consecutive autopsies of men over 40 (mean and median age, 61 years) who died of diseases other than carcinoma of the prostate (2). Fat was found amid preceding the most peripheral acini of the gland in only 1 of 150 (0.66%) prostates examined. This fat, comprising a group of 6 adipose cells was seen in only 1 of 45 sections of this prostate, corresponding to 1 of the total of 5,712 sections (0.01%) examined. This section with fat was located in the anterolateral part of the gland.

The study by Yilmaz and Trpkov supports our findings. There are 3 criteria for extraprostatic extension, depending on the site and composition of the extraprostatic tissue: 1) - cancer in adipose tissue, 2) - cancer in perineural spaces of the neurovascular bundles, and 3) - cancer in anterior muscle (3). Our study demonstrated that intraprostatic fat is extremely rare. Invasion of fat in a needle biopsy specimen of the posterolateral region of the prostate appears to always be a manifestation of extraprostatic spread by cancer.

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### **Sarcomatoid renal cell carcinoma: an examination of underlying histologic subtype and an analysis of associations with patient outcome**

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*Am J Surg Pathol.* 2004; 28: 435-41

A sarcomatoid component can occur in all histologic subtypes of renal cell carcinoma (RCC) and indicates an aggressive tumor. We studied 2381 patients treated with radical nephrectomy for RCC between 1970 and 2000. A urologic pathologist reviewed the microscopic slides from all tumor specimens for the presence of a sarcomatoid component, defined as a RCC with any malignant spindle cell component. All tumors with a sarcomatoid component were classified as nuclear grade 4. A total of 120 (5.0%) patients had RCC with a sarcomatoid component, including 94 who died of RCC at a mean of 1.4 years following nephrectomy (median 8 months; range 44 days to 10 years). Cancer-specific survival rates at 2 and 5 years following nephrectomy were 33.3% and 14.5%, respectively. The presence of distant metastases at the radical nephrectomy and histologic tumor necrosis were significantly associated with death from RCC among patients with sarcomatoid RCC. Patients with clear cell (conventional) RCC and chromophobe RCC were more likely to have tumors with a sarcomatoid component (5.2% and 8.7%, respectively) compared with patients with papillary RCC (1.9%). The presence of a sarcomatoid component was significantly associated with death from RCC for all three subtypes ( $P < 0.001$ ). Even among patients with grade 4 clear cell RCC, the presence of a sarcomatoid component was significantly associated with outcome, both univariately (risk ratio 1.59;  $P = 0.010$ ) and after adjusting for TNM stage, tumor size, and histologic tumor necrosis (risk ratio 1.46;  $P = 0.037$ ).

### Editorial Comment

The Heidelberg classification of renal cell tumors is based on genetic alterations and classifies malignant parenchymal neoplasms as: 1) - common or conventional renal cell carcinoma which includes tumors with clear and/or eosinophilic cytoplasm; 2) - papillary renal cell carcinoma; 3) - chromophobe renal cell carcinoma; 4) - collecting duct carcinoma which includes the variant medullary carcinoma associated to sickle cell trait; and, 5) - renal cell carcinoma, unclassified (1). From group 5 was separated a new entity named “low-grade mucinous tubular and spindle cell carcinoma” possibly originated from the loop of Henle (2).

It is recognized that sarcomatoid change has been found to arise in all of these types of renal cell carcinoma in this classification. Sarcomatoid features thus do not constitute a type per se, but rather are an indication of progression in renal cell carcinoma.

In the study by Cheville JC et al., patients with chromophobe renal cell carcinoma had a higher frequency of sarcomatoid transformation (8.7%) comparatively to conventional (clear cell) carcinoma (5.2%) and papillary carcinoma (1.9%). This high frequency was also found by Akhtar M et al. (3) in Saudi Arabia where chromophobe renal cell carcinoma has the highest prevalence.

Sarcomatoid change should always be reported by the pathologist. The presence of a sarcomatoid change has an important impact on prognosis. In the study by Cheville et al. the presence of a sarcomatoid component was significantly associated with death both univariately and after adjusting for TNM stage, tumor size, and histologic tumor necrosis.

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## INVESTIGATIVE UROLOGY

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### Comparison of gene expression profiles between Peyronie's disease and Dupuytren's contracture

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*Urology* 2004; 64: 399-404

**Objectives:** To compare the gene expression alterations in human Peyronie's disease (PD) and Dupuytren's disease (DD) to determine whether they share a common pathophysiology. Multiple mRNA expression profiles of human PD have previously shown that genes that regulate fibroblast replication, myofibroblast differentiation, collagen metabolism, tissue repair, and ossification are involved. DD, a palmar fascia fibrosis, may be associated with PD.

**Methods:** Total RNA samples from PD plaques, normal tunica albuginea, Dupuytren's nodules, and normal palmar fascia (nine samples per group) were subjected to differential gene expression profile analysis (Clontech Atlas DNA microarray) comparing PD with tunica albuginea and DD with normal palmar fascia. Changes of more than 2.0 in PD and DD compared with tunica albuginea and normal palmar fascia, respectively, were recorded. Reverse transcriptase-polymerase chain reactions were performed for some genes whose expression was altered in PD.

**Results:** Some of the gene families upregulated in both PD and DD were (a) collagen degradation: matrix metalloproteinase (MMP), with MMP2 and MMP9, and thymosins (MMP activators), with TM $\beta$ 10 and TM $\beta$ 4; (b) ossification: osteoblast-specific factors (OSFs) OSF-1 and OSF-2 (DD only); and (c) myofibroblast differentiation: RhoGDP dissociation inhibitor 1. The genes upregulated in PD only were decorin (an inhibitor of transforming growth factor-beta1 and a part of fibroblast replication/collagen synthesis) and early growth response protein. Reverse transcriptase-polymerase chain reaction confirmed these changes.

**Conclusions:** These data demonstrate that the pattern of alterations in the expression of certain gene families in PD and DD is similar, suggesting that they share a common pathophysiology and may be amenable to the same therapeutic regimens.

### Editorial Comment

The authors present one more wonderful contribution to the knowledge of Peyronie's disease.

One of the most accepted etiologies for Peyronie's disease is that it is caused by trauma to the erect penis, resulting in extravasation of fibrin and other blood proteins into the tunica albuginea that, together with other unknown factors, elicit an inflammatory reaction followed by the production of pro-fibrotic agents, such as transforming growth factor-beta1 and reactive oxygen species. Peyronie's disease may be associated with Dupuytren's disease, which occurs in the palmar fascia in 21% of the cases. Dupuytren's disease is characterized by similar fibrotic alterations, although its relationship to trauma is less established.

Analyzing gene expression, this study provides targets of potential pharmacologic modulation of the levels of genes associated with antifibrotic mechanisms. The authors speculate that stimulation of myofibroblast apoptosis and blockade of its differentiation with Rho inhibitors or cortactin may be beneficial, because accumulation of these cells in an abnormal healing process subsequent to trauma may relate to the fibrosis seen in Peyronie's disease and Dupuytren's disease.

Previous studies by the same group (1) demonstrated that treatment with L-arginine and phosphodiesterase inhibitors, both stimulating apoptosis and remodeling by nitric oxide/cyclic guanosine monophosphate or cyclic guanosine monophosphate alone, respectively, has been shown to prevent the fibrotic plaque in the TGF- $\beta$  animal model of Peyronie's disease.

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### **Effects of peppermint teas on plasma testosterone, follicle-stimulating hormone, and luteinizing hormone levels and testicular tissue in rats**

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*Urology 2004; 64: 394-8*

**Objectives:** To justify the effects of *Mentha piperita labiatae* and *Mentha spicata labiatae* herbal teas on plasma total testosterone, luteinizing hormone, and follicle-stimulating hormone levels and testicular histologic features. We performed this study because of major complaints in our area from men about the adverse effects of these herbs on male reproductive function.

**Methods:** The experimental study included 48 male Wistar albino rats (body weight 200 to 250 g). The rats were randomized into four groups of 12 rats each. The control group was given commercial drinking water, and the experimental groups were given 20 g/L *M. piperita* tea, 20 g/L *M. spicata* tea, or 40 g/L *M. spicata* tea.

**Results:** The follicle-stimulating hormone and luteinizing hormone levels had increased and total testosterone levels had decreased in the experimental groups compared with the control group; the differences were statistically significant. Also, the Johnsen testicular biopsy scores were significantly different statistically between the experimental groups and the control group. Although the mean seminiferous tubular diameter of the experimental groups was relatively greater than in the control group, the difference was not statistically significant. The only effects of *M. piperita* on testicular tissue was segmental maturation arrest in the seminiferous tubules; however, the effects of *M. spicata* extended from maturation arrest to diffuse germ cell aplasia in relation to the dose.

**Conclusions:** Despite the beneficial effects of *M. piperita* and *M. spicata* in digestion, we should also be aware of the toxic effects when the herbs are not used in the recommended fashion or at the recommended dose.

## **Editorial Comment**

This is the first report concerning the effects of peppermint tea on plasma total testosterone, LH, and FSH levels and testicular histologic features.

Peppermint tea is generally considered a safe drink for regular consumption. The authors demonstrate that both *M. piperita* and *M. spicata* tea intake decreased plasma testosterone and increased plasma LH and FSH levels in rats. Histologic studies revealed extensive degenerative changes in the germinal epithelium and spermatogenesis arrest when compared to controls.

Changes in the pituitary-testicular axis may be responsible for the testicular maturation arrest. The statistically significant decrease in both spermatogenesis and plasma total testosterone levels in the experimen-

tal groups was associated with an increase in the plasma FSH and LH levels. These observations prompted the authors to consider the pituitary-testicular axis. The plasma total testosterone levels had decreased and plasma FSH and LH levels increased, as expected. Therefore, the mechanism of spermatogenic abnormalities was more likely a result of the direct effect on germinal epithelium, and the hormonal deficit appeared to be a result of Leydig cell dysfunction. The pituitary gland or hypothalamus may also be affected, and the maturation arrest could have been the result of hypothalamic-pituitary-testicular axis deficiency. However, this hypothesis should be elucidated by additional studies focused on the hypophysial or hypothalamic tissues.

Consumption of *M. piperita* and *M. spicata* teas affected spermatogenetic activity at the 20 g/L and 40 g/L dose, respectively, in rats. The authors remember us that despite *M. piperita* and *M. spicata* beneficial effects in digestion, people should be aware of their toxic adverse effects when not used in the recommended fashion or at the recommended dose.

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## RECONSTRUCTIVE UROLOGY

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### **Current and future strategies for preventing and managing erectile dysfunction following radical prostatectomy**

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*Eur Urol. 2004; 45: 123-133*

**Introduction and Objectives:** As radical prostatectomy remains a commonly used procedure in the treatment of clinically localized prostate cancer, we critically analyzed current and future strategies for preventing and managing postoperative erectile dysfunction.

**Methods:** Systematic literature review using Medline and CancerLit from January 1997 to June 2003. Abstracts published in the journals *European Urology*, *The Journal of Urology* and the *International Journal of Impotence Research* as official proceedings of internationally known scientific societies held in the same time period were also assessed.

**Results:** Patient selection and surgical technique are the major determinants of postoperative erectile function. Apoptosis of corporeal smooth muscle cells plays a role in the development of cavernous veno-occlusive dysfunction following radical prostatectomy. Pharmacological prophylaxis and treatment of postoperative erectile dysfunction is effective and safe. The concepts of cavernous nerve reconstruction and neuroprotection have been associated to promising results.

**Conclusions:** In the hands of experienced surgeons, properly selected patients undergoing a nerve sparing radical prostatectomy should achieve unassisted or medically assisted erections postoperatively.

### **Editorial Comment**

This paper written by a team of young experts on the treatment of sexual dysfunction nicely describes how erectile function can currently be treated after oncological pelvic surgery. It is a valuable reference for both the pelvic surgeons performing potency preserving techniques and those who deal with these patients postop-

eratively. Nerve preservation is currently the only clinically truly proven method of preserving potency after radical prostatectomy or cystoprostatectomy. Although there are data that have shown the results of autologous nerve interposition if autonomic periprostatic nerves cannot be preserved, the true value and applicability needs to be reproduced in larger patient cohorts. Another interesting future aspect may be the use of neurogenesis inducing drugs or pharmatherapeutically protective substances such as immunophilin ligands, which are currently under clinical investigation.

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### **Neuroanatomy of the human female lower urogenital tract**

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*J Urol. 2004; 172: 191-5*

**Purpose:** The neuroanatomy of the female lower urogenital tract remains controversial. We defined the topographical anatomy and differential immunohistochemical characteristics of the dorsal nerve of the clitoris, the cavernous nerve and the nerves innervating the female urethral sphincter complex.

**Materials and Methods:** A total of 16 normal female human pelvic specimens at 14 to 34 weeks of gestation were studied by immunohistochemical techniques. Serial sections were stained with antibodies raised against the neuronal markers S-100 and neuronal nitric oxide synthase (nNOS), vesicular acetylcholine transporter, calcitonin gene-related peptide and substance P. The serial sections were computer reconstructed into 3-dimensional images.

**Results:** Under the pubic arch at the hilum of the clitoral bodies, the branches of the cavernous nerves joined the clitoral dorsal nerve to transform its immunoreactivity to nNOS positive. The cavernous nerves originated from the vaginal nervous plexus occupying the 2 and 10 o'clock positions on the anterolateral vagina and they traveled at the 5 and 7 o'clock positions along the urethra. The urethral sphincter complex was innervated by nNOS immunoreactive and nonimmunoreactive nerve fibers arising from the vaginal nervous plexus and pudendal nerve, respectively.

**Conclusions:** The dorsal nerve of the clitoris receives nNOS positive branches from the cavernous nerve as a possible redundant mechanism for clitoral erectile function. The urethral sphincter complex has dual innervation, which pierces into the urethral sphincter complex at different locations. The study of the neuroanatomy of the female lower urogenital tract is germane to the strategic design of female reconstructive surgery.

### **Editorial Comment**

This is the second paper on the neuroanatomy of the human clitoris of this group. They examined female human fetal pelvic specimens with regards to neural immunoreactivity. In an elegant study, they were able to demonstrate findings, which are important for some of the more recently available reconstructive techniques in women undergoing pelvic floor or pelvic surgery.

nNOS immunoreactive nerve fibers were demonstrated in the distal clitoris but not in the proximal clitoris. It might be speculated that NO not only plays an important role in female sexual physiology but also

that these specific nerves derive from the cavernous within the clitoral bodies and therefore are supplied by the pelvic autonomic nerves.

The location of these autonomic pelvic nerves were seen at the level of the urethra at the 5 and 7 o'clock joining more cranially the more nervous complex located at the anterior lateral sides of the vagina at the 2 and 10 o'clock positions. There was also a nNOS non-immunoreactive but otherwise autonomic nerve entering the muscular layer of the urethral sphincter complex at the mid urethra. There were no other autonomic nerves seen in the mid urethra.

The location of a dense network of autonomic nerves at the level of the vagina supplied by the inferior hypogastric plexus occupying the 2 and 10 o'clock positions at the rectum mainly at the lateral and anterior vaginal wall which were thinning out on the anterior wall towards the urethra. From there, fibers traveled either along the pathways described above towards the clitoris or towards the proximal a mid urethral sphincter.

We learn from these studies for complex surgical procedures at the level of the pelvic floor and urethra to maintain micturition, continence and sexuality in female patients the preservation of autonomic nerves is mandatory and must put there pathways within the whole pelvis into consideration. Further studies will have to follow to demonstrate the functional value and possible changes in adulthood but definitely these data warned consideration during surgery.

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## UROLOGICAL ONCOLOGY

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### **A single immediate postoperative instillation of chemotherapy decreases the risk of recurrence in patients with stage Ta T1 bladder cancer: a meta-analysis of published results of randomized clinical trials**

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J Urol. 2004; 171: 2186-90

**Purpose:** We determined if 1 immediate instillation of chemotherapy after transurethral resection (TUR) decreases the risk of recurrence in patients with stage Ta T1 single and multiple bladder cancer overall and separately.

**Materials and Methods:** A meta-analysis was performed of the published results of randomized clinical trials comparing TUR alone to TUR plus 1 immediate instillation of chemotherapy.

**Results:** Our study included 7 randomized trials with recurrence information on 1476 patients. Based on a median followup of 3.4 years and a maximum of 14.5 years, 267 of 728 patients (36.7%) receiving 1 postoperative instillation of epirubicin, mitomycin C, thiotepa or (2'R)-4'-O-tetrahydropyranyl-doxorubicin (pirarubicin) had recurrence compared to 362 of 748 patients (48.4%) with TUR alone, a decrease of 39% in the odds of recurrence with chemotherapy (OR 0.61,  $p < 0.0001$ ). Patients with a single tumor (OR 0.61) and those with multiple tumors (OR 0.44) benefited. However, after 1 instillation 65.2% of patients with multiple tumors had recurrence compared to 35.8% of patients with single tumors, showing that 1 instillation alone is insufficient treatment for patients with multiple tumors.

Conclusions: One immediate intravesical instillation of chemotherapy significantly decreases the risk of recurrence after TUR in patients with stage Ta T1 single and multiple bladder cancer. It is the treatment of choice in patients with a single, low risk papillary tumor and is recommended as the initial treatment after TUR in patients with higher risk tumors.

### Editorial Comment

This paper should be read by every urologist dealing with superficial bladder cancer. Briefly, the facts are clear—single-shot instillation is a highly effective treatment with low cost. It should be given after every TUR. High-risk tumors deserve further therapy, to my opinion with BCG.

Intravesical cytotoxic drug instillations have their clear role in urology now: as single shot therapy.

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## FEMALE UROLOGY

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### Urinary urgency and frequency, and chronic urethral and/or pelvic pain in females. Can doxycycline help?

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*J Urol.* 2004; 172: 232-5

Purpose: Persistent urinary urgency and frequency, and chronic urethral and/or pelvic pain in women are often a diagnostic and therapeutic challenge. This can be frustrating for patients and physicians. The search for an infectious agent often proves futile and after multiple ineffective treatment regimens patients may be classified as having interstitial cystitis or referred to a psychiatrist as the last option. We evaluated whether treatment with doxycycline of the patient and her sexual partner would be beneficial.

Materials and Methods: Women presenting with a history of urinary urgency and frequency, and chronic urethral and/or pelvic pain often associated with dyspareunia and/or a history of recurrent urinary tract infection were evaluated. Initial examinations included urethral and cervical/vaginal swabs, serum analysis, urine examination and culture, and bladder barbitage. A total of 103 women with a median age of 46 years (range 21 to 84) and with a median symptoms history of 60 months (range 3 to 480) were included. All patients had trigonal leukoplakia at cystoscopy, in 15% an infectious organism was identified and 30% had leukocyturia. All were treated with doxycyclines, and a vaginal antimicrobial and/or antimycotic agent following the same regimen, including treatment of the sexual partner.

Results: After treatment with doxycycline 71% of the women were symptom-free or had a subjective decrease in symptoms.

Conclusions: Treatment with doxycycline is effective in more than two-thirds of patients complaining of persistent frequency and urgency, chronic urethral and/or pelvic pain, and dyspareunia as well as a history of recurrent urinary tract infections. In women with negative urinary cultures but a history of urgency/frequency probative treatment with doxycycline is justified and endoscopic findings may support the hypothesis of chronic infection. This should be done especially before contemplating psychiatric treatment or diagnosing the patient

with interstitial cystitis. We attribute this high success rate to simultaneous treatment of the sexual partner, who may be an asymptomatic carrier, although this remains to be proved.

### Editorial Comment

The authors review the efficacy of doxycycline therapy for one month on female patients with urinary urgency, frequency, chronic urethral and/or pelvic pain. Of note is that only 15% of the patients had an identified infectious organism. All patients have trigonal leukoplakia at cystoscopy. At the time of treatment with doxycycline the patient also underwent therapy with a vaginal antimicrobial and/or antimycotic agent. In addition, all sexual partners underwent synchronous therapy.

The use of antibiotics in the absence of a true positive culture is a therapy that many of us have tried, in both males and female. Who can say that he has never treated a man with prostatitis with long-term antibiotics in the absence of a positive culture and then experienced a positive clinical result. The subselection of patients to receive therapy with leukoplakia is interesting. Leukoplakia has been described and discussed previously in the literature (1). In addition, it was noted that the patients had synchronous therapy with a vaginal antimicrobial or antimycotic agent and had the sexual partners treated as well. It would be interesting to subdivide the success rates between those patients who had a sexual partner that was treated and those patients who did not have a sexual partner thus obviating the need for therapy for same. Potential difference in success rate would have perhaps shed light on the ping-pong reinoculation effect with a sexual partner versus a difficult primary problem of a non-infectious nature. In addition, that patients had a synchronous therapy with a vaginal antimycotic and/or antimicrobial agent does confuse the issue to a degree. Perhaps vaginal pathology was as much to blame for the troublesome symptoms as was a primary bladder difficulty. The efficacy of doxycycline may be multifactorial including that it is the only medication in its class that is renally excreted thus potentially achieving excellent bladder urine levels. If increased serum antibiotic levels do lend themselves to an increased therapeutic effect, then direction instillation of antimicrobial solutions in the bladder should not be discounted or forgotten in this challenging patient population (2).

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### **Does Valsalva leak point pressure predict outcome after the distal urethral polypropylene sling?**

#### **Role of urodynamics in the sling era**

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*J Urol*. 2004; 172: 210-4

**Purpose:** Recently sling procedures have been shown to be effective in the treatment of all types of incontinence. In this study we evaluated the role of preoperative Valsalva leak point pressure (VLPP) in predicting the outcome of sling surgery.

**Materials and Methods:** We prospectively evaluated 174 consecutive patients who underwent a distal polypropylene sling procedure for the treatment of stress urinary incontinence (SUI). Using SEAPI scores patients were divided by VLPP into group 1-60 patients who did not leak on urodynamics, group 2-27 patients with VLPP greater than 80 cm H<sub>2</sub>O, group 3-71 patients with VLPP 30 to 80 cm H<sub>2</sub>O and group 4-16 patients with VLPP less than 30 cm H<sub>2</sub>O. Surgical outcomes were determined by symptom, bother and quality of life questionnaires filled out by patients. The physicians were blinded to patient response.

**Results:** Mean followup was 14.7 months (range 12 to 30) and mean patient age was 62 years (range 32 to 88). The groups were well matched before surgery with respect to age, number of previous surgeries, and severity of SUI symptoms and urge incontinence. The percentage of patients who were cured or improved was similar among groups. After surgery there was no statistical difference among patient mean self-reported symptoms of or bother from SUI or urge incontinence.

**Conclusions:** The distal urethral polypropylene sling provides similar symptom improvement in all patients regardless of preoperative VLPP. VLPP is helpful in the diagnosis of SUI but appears to be of minimal benefit in predicting the outcome of the distal urethral polypropylene sling procedure.

### **Editorial Comment**

The authors review the Valsalva leak point pressures obtained preoperatively before the placement of a distal urethral polypropylene sling and then correlate those values with the outcome of sling surgery. This paper is well written and is of great value. It was noted that the valsalva leak point pressure was helpful in evaluating stress urinary incontinence but could not accurately predict which patients would be a surgical success or not. This further highlights the utility of the minimally invasive sling procedure as a therapeutic option for all degrees of stress urinary incontinence. The authors found that patients with lower valsalva leak point pressures were likely to have significantly more severe stress urinary incontinence symptoms. This finding has been noted before (1). The value and role of urodynamic testing in stress urinary incontinence has been a long time subject of discussion in the field of urology (2). This academic contribution continues that intellectual discourse.

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## PEDIATRIC UROLOGY

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### **Abnormal dimercapto-succinic acid scans predict an increased risk of breakthrough infection in children with vesicoureteral reflux**

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*J Urol.* 2004; 172: 1075-7

**Purpose:** The management of high grade vesicoureteral reflux remains controversial, with breakthrough infections being an indication for surgical repair. We sought to determine if technetium dimercapto-succinic acid (DMSA) scan could help predict which children are at risk for breakthrough urinary tract infection.

**Materials and Methods:** A retrospective review was performed on children presenting with a febrile urinary tract infection and prenatal hydronephrosis who were found to have vesicoureteral reflux and underwent a DMSA scan. Reflux was tabulated according to the highest grade. DMSA results were graded as 0-normal, no parenchymal or size defects, grade 1-focal parenchymal defects or less than a quarter of a renal unit involved, or grade 2-severe defects to include at least half of a renal unit, bilateral defects or unilateral atrophy.

**Results:** A total of 120 consecutive patients were evaluated. An abnormal DMSA scan was documented in 57 (33 females and 24 males), and 35 with grade 1 and 22 with grade 2 defects. Of the patients 53 females and 10 males had a normal scan. Of the 57 children with an abnormal DMSA scan 6% presented with grades 1 and 2 vesicoureteral reflux, 24% with grade 3, 38% with grade 4 and 26% with grade 5. Of the children with grades 3 to 5 reflux 60% had a subsequent breakthrough infection. Of the 63 children with a normal DMSA scan 11% presented with grade 1 reflux, 28% with grade 2, 48% with grade 3, 11% with grade 4 and 2% with grade 5. Of these children 5 had a subsequent breakthrough infection.

**Conclusions:** An abnormality on DMSA scan in the presence of grade 3 to 5 reflux correlates with a greater chance of having a breakthrough infection (60%). We conclude that children with grade 3 to 5 vesicoureteral reflux and an abnormal DMSA scan are at increased risk for breakthrough urinary tract infection.

### **Editorial Comment**

It has been clearly demonstrated that DMSA scanning is a highly sensitive modality for detecting renal scarring. In particular, it has many advantages over renal ultrasound for this purpose. On the other hand, it is expensive and in terms of cost-effectiveness, the utility of DMSA scanning for determining renal injury in children with reflux has been questioned. In particular, it is important to determine whether the results of DMSA scanning alter management or outcome.

This study looks at differences in outcome of children with reflux based on the results of DMSA scanning. Of 120 children evaluated, 57 had abnormal scans, including 33 girls and 24 boys. In contrast, of the 63 normal scans, only 10 were boys. Furthermore, in follow-up, 60% of those with an abnormal DMSA scan had a breakthrough UTI whereas only 8% of those with a normal DMSA had a breakthrough infection.

The implications of these data are significant. First, as anticipated, boys with reflux have more renal injury, perhaps related to more abnormal neonatal voiding patterns with high intravesical pressures that are passed to the kidney. Second, those who already demonstrated a tendency to renal injury (because of either more abnormal voiding or a host resistance problem that results in a greater rate or more severe UTIs) are more likely to get further UTIs. Not only is this important in the pathophysiology of reflux and reflux nephropathy,

but it suggests that more aggressive management of reflux in this population may be warranted. This in turn suggests value in obtaining a DMSA scan in children with grades 3-5 reflux.

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### **Vaginal construction using sigmoid colon in children and young adults**

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**Objective:** To evaluate the age at which patients who required vaginal replacement (an uncommon procedure in children) were diagnosed, and the cause of their anomaly, and to relate these variables to the surgical outcome.

**Patients and Methods:** Patients who had vaginal replacement at the author's institution between 1990 and 2002 were reviewed retrospectively. Depending on the age at reconstructive surgery, patients were divided into pre- and post-pubertal groups. **Results:** A neovagina was constructed in 23 patients during the study period; sigmoid colon was used in 20 but not in two patients with cloacal exstrophy and in one with Mayer-Rokitansky-Kuster-Hauser syndrome (MRKHS). These cases were excluded from the analysis of outcomes and complications. Group 1 comprised patients diagnosed and treated before puberty and group 2 those diagnosed and/or treated afterward. In group 1 the presenting diagnoses included androgen insensitivity syndrome (AIS) in six patients, MRKHS in two, cloacal exstrophy in two, vaginal tumour in one, Mullerian duct renal aplasia cervicothoracic somite dysplasia, vertebral abnormalities, anal atresia, cardiac anomalies, tracheo-oesophageal fistula, and/or oesophageal atresia, renal abnormalities and limb defects syndromes in one each. In group 2 the presenting diagnoses included MRKHS in seven, AIS in two, and congenital adrenal hyperplasia in one. Complications included superficial wound infection (two patients), recurrent introital stenosis, and blind loop mucocele, complete stenosis of perineal neovaginal opening (one each) and dyspareunia in three. Neither age nor pelvic habitus (android vs gynaecoid) influenced the outcome, and the cosmetic results were excellent in all the patients.

**Conclusion:** Isolated sigmoid neovaginal construction appears to be applicable to many diagnoses and in patients at any age. Although an android pelvis can present technical challenges, in this experience it was not associated with a greater complication rate. The long-term satisfaction with the sigmoid neovagina for intercourse, especially in those constructed before puberty, still requires long-term evaluation.

### **Editorial Comment**

Vaginal reconstruction is an uncommon procedure, but carries special significance when done. It is, of course, most common in patients with some form of intersex and involves the genitalia, both of which raise the anxiety level of parents considerably. Moreover, the type of reconstruction varies considerably by specialty, with plastic surgeons and gynecologists generally recommending skin graft/dilation procedures and pediatric urologists recommending bowel vaginoplasty. Furthermore, the timing of the reconstruction remains highly controversial.

This is an interesting review that helps the reader in several ways. First, I believe that it provides the reader with a realistic estimate of the potential complications of bowel vaginoplasty. Three patients out of 20

had introital stenosis (of course these were quite fixable) and all three who are sexually active suffered from dyspareunia. Fortunately this was not severe enough to prevent sexual activity, but nonetheless, this would be important to mention in preoperative counseling. Interestingly, in the authors hands, bowel vaginoplasty was no more risky in children who were pre-pubertal (mean age 4) than in those who were post-pubertal. This is likely because these patients did not require dilation postoperatively. When using techniques that require dilation postoperatively, the procedure should surely be postponed until after puberty.

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