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## UROLOGICAL SURVEY

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**STONE DISEASE**

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**Forced Versus Minimal Intravenous Hydration in the Management of Acute Renal Colic: A Randomized Trial**

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J Endourol. 2006; 20: 713-6

**Background and Purpose:** The management of acute renal colic is a problem commonly encountered by both urologists and emergency medicine physicians. The classic approach to managing uncomplicated acute renal colic involves hydration, along with imaging and pain control. Previous studies have suggested that hydration has a significant impact on patient comfort, as well as spontaneous stone passage. This study evaluated the effects of maintenance vs forced hydration and its effect on the pain experienced from renal colic.

**Patients and Methods:** Forty male and 18 female patients with a mean age of 41 years suspected to have acute renal colic were identified in the emergency department. After screening and informed consent, the patients were enrolled in the study, and 43 patients were eventually available for analysis. Patients received intravenous (IV) analgesia, imaging with a noncontrast CT scan of abdomen and pelvis, and assignment to either forced IV hydration with 2 L of normal saline over 2 hours (N = 20) or minimal IV hydration at 20 mL of normal saline per hour (N = 23). A visual analog pain scale was completed hourly for a total of 4 hours. Demographic information, laboratory and imaging results, narcotic use in morphine equivalents (ME), and pain scores were recorded and compared. Spontaneous stone passage rates were also calculated by careful patient follow-up. Results were considered statistically significant at  $p < 0.05$ .

**Results:** Stone size was equivalent in the two treatment groups ( $p > 0.05$ ). There was no difference in the narcotic requirement in ME ( $p = 0.644$ ) between the two groups. Similarly, there was no difference in hourly pain score or stone-passage rates between the groups ( $p > 0.05$ ).

**Conclusions:** Treatment of uncomplicated renal colic has traditionally included vigorous intravenous hydration, as well as medications for the control of pain and nausea. Our data suggest that maintenance intravenous fluids are as efficacious as forced hydration with regard to patient pain perception and narcotic use. Moreover, it appears the state of hydration has little impact on stone passage.

**Editorial Comment**

This study demonstrates that in the emergency room (ER) setting, forced hydration for acute renal colic does not impact pain or stone passage. However, it is important to note that this study evaluates hydration only in the acute ER setting. It is common practice for patients to be instructed to force oral hydration after discharge from the emergency room. Compliance with this recommendation and its impact on subsequent stone passage was not evaluated in this study, and may be worthwhile of further investigation. While the study relies on chart review and self-reporting to document stone passage, other studies have suggested that self-reporting of stone passage may be inaccurate in a significant proportion of patients. The authors do not report the duration of follow-up or time to stone passage, though the 30% spontaneous stone passage rate is lower than one might expect in relation to the mean stone size. Location of ureteral calculi was not reported, and could be a confounding variable in the equation. In addition, the utility of forced hydration may depend on the fluid status of the patient and the time from onset of pain to presentation to the ER. As renal hemodynamics adapt to obstruction within the first 24 hours, the impact of hydration may diminish with delayed presentation. It may be useful to evaluate

response to hydration based on the presence of volume depletion (BUN/CR ratio) and the time to presentation (< or > 24 hours from onset of pain).

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### **One Week of Ciprofloxacin Before Percutaneous Nephrolithotomy Significantly Reduces Upper Tract Infection and Urosepsis: A Prospective Controlled Study**

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BJU Int. 2006; 98: 1075-9

**Objective:** To evaluate whether 1 week of ciprofloxacin before percutaneous nephrolithotomy (PCNL) in patients with stones of > or = 20 mm or pelvicalyceal dilatation, reduces urosepsis, as we previously reported that such patients have four times the risk of urosepsis after PCNL.

**Patients and Methods:** Patients undergoing PCNL, and who fulfilled strict selection criteria, were recruited prospectively into a study which was conducted in two phases. The study methods were similar to those previously described; patients with dilated pelvicalyceal systems and/or stones of > or = 20 mm from phase 1 (previously published) acted as controls. In the subsequent phase, the same selection criteria applied and only those with stones of > or = 20 mm and/or dilated pelvicalyceal systems were given ciprofloxacin 250 mg twice daily for 1 week before PCNL and comprised the treatment arm. Midstream urine samples, renal pelvic urine and fragmented stones were collected to assess culture and sensitivity. Systemic inflammatory response syndrome (SIRS) was used to define urosepsis after PCNL. The urologists monitoring the patients after PCNL and conducting the analysis were all unaware of the characteristics of the stones or intravenous urography findings before PCNL. In all, 115 patients (54 in phase 1 and 61 in phase 2) were recruited, of whom 46 in phase 1 and 52 in phase 2 had stones of > or = 20 mm and/or a dilated pelvicalyceal system, and became the control and treatment arms, respectively.

**Results:** The patient demographics were similar in both arms. There was three times less risk of upper tract infection (relative risk 3.4, 95% confidence interval 1.0-11.8, P = 0.04) and SIRS (2.9, 1.3-6.3, P = 0.004) in the patients receiving ciprofloxacin (treatment arm).

**Conclusions:** The administration of oral ciprofloxacin for 1 week before PCNL in patients with stones of > or = 20 mm or dilated pelvicalyceal systems significantly reduced the risk of urosepsis.

#### **Editorial Comment**

The authors selected patients with significant hydronephrosis or stone burdens greater than 2 cm as candidates for this study, based on an initial study, which suggested that these patients were at greater risk for having an infected upper tract at the time of PCNL (1). However, this study also concluded that there was no correlation between SIRS and stone burden or degree of hydronephrosis.

This is a non-blinded non-randomized study comparing results to a historical cohort. Accepting these limitations in study design, the results are still dramatic with regards to the 3-fold decrease in upper tract infection and SIRS. I am still not convinced regarding the clinical relevance of SIRS as defined by the criteria presented. For example, pain may increase the HR and RR, which would satisfy the criteria for SIRS. The stress of surgery can cause transient leukocytosis. Elevations in temperature and respiratory rates may be related to

atelectasis. Preoperative antibiotics would not be anticipated to impact any of these events. The authors do not state what measures were taken to exclude other common causes of fever, tachycardia, and tachypnea during post-PCNL recuperation, such as atelectasis, hypovolemia, and pain. The Consensus panel that developed the definition of SIRS states that it is “overly sensitive and non-specific”, and caution that major surgical procedures as well as cardiogenic events may result in the clinical picture similar to SIRS(2). The consensus panel also cautions that sepsis should be defined as the presence of SIRS and infection.

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## ENDOUROLOGY & LAPAROSCOPY

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### **Laparoscopic Dismembered Pyeloplasty in Children Younger Than 2 Years**

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*J Urol.* 2007; 177: 335-8

**Purpose:** Since the first laparoscopic pyeloplasty was described in a child in 1995, there have been several reports of pyeloplasty in older children. However, to date there have been few reports of laparoscopic pyeloplasty in infants and toddlers. The aim of this study was to evaluate the results of laparoscopic pyeloplasty in children younger than 2 years.

**Materials and Methods:** All laparoscopic Anderson-Hynes pyeloplasties performed in children younger than 2 years were retrospectively reviewed. The diagnosis of ureteropelvic junction obstruction was confirmed on renal sonography and diuretic renogram. Laparoscopic pyeloplasties were performed via a transperitoneal route as originally described, with key modifications. All children were investigated with postoperative diuretic renogram and renal ultrasonography.

**Results:** A total of 38 children with ureteropelvic junction obstruction underwent laparoscopic Anderson-Hynes Pyeloplasty between January 2001 and December 2005. Of these patients 11 (7 males and 4 females) were younger than 2 years at surgery (median 1.4, range 2 to 22 months) and 1 had bilateral ureteropelvic junction obstruction, for a total of 12 primary repairs. However, 2 patients (17%) required redo laparoscopic pyeloplasty, for a total of 14 laparoscopic dismembered pyeloplasties in this age group. Operative time ranged from 70 to

140 minutes (mean 100) and median hospital stay was 2 days. Followup studies showed normal drainage in all patients except 1, who after redo pyeloplasty exhibited significantly improved but still prolonged drainage.

Conclusions: This study suggests that laparoscopic pyeloplasty can now be performed in young children with good results.

### **Editorial Comment**

Laparoscopic Pyeloplasty still remains controversial in the pediatric population. The new era of reconstructive surgery with better laparoscopic knowledge and instrumentation, i.e.; fine needlescopic (minilaparoscopic) instruments, facilitated the ease of executing a precise and delicate reconstructive surgery, allowing surgeons to perform the anastomosis without handling or traumatizing the ureter or pelvic mucosa.

In a retrospective study, the authors evaluated their experience of 14 laparoscopic dismembered pyeloplasties performed in patients less than 2 years-old. The data demonstrated feasibility of this surgical technique with a good outcome measured objectively by nuclear renal lasix scan but with no subjective evaluation (pain free postoperatively).

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### **Laparoscopic Ice Slurry Coolant for Renal Hypothermia**

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J Urol. 2007; 177: 382-5

**Purpose:** We assessed the safety and efficacy of microparticulate ice slurry for laparoscopic hypothermia during renal ischemia in a single kidney porcine model.

**Materials and Methods:** A total of 18 farm pigs were randomized to 3 groups of 6 each. All groups underwent initial right laparoscopic nephrectomy, followed by 1 of 3 procedures on the left kidney. Group 1 underwent 90 minutes hilar clamping under warm ischemia, group 2 underwent 90 minutes hilar clamping under cold ischemia using laparoscopically delivered microparticulate ice slurry and control group 3 underwent hilar dissection, no clamping and no microparticulate ice slurry. Body and renal cortical temperatures were measured. Serum creatinine and the glomerular filtration rate were assessed preoperatively, and on postoperative days 1,3,8 and 15.

**Results:** Average time to achieve a renal temperature of 20°C or less was 9.7 minutes and it remained constant during the 90 minutes cold ischemia time. Mean serum creatinine was significantly higher in the warm ischemia group than in the cold ischemia and control groups on postoperative days 1 and 3. Additionally, mean serum creatinine in the cold ischemia and control groups was similar at all time points. The mean glomerular filtration rate was significantly lower in the warm ischemia group than in the cold ischemia and control groups on postoperative days 1,3 and 8. The mean glomerular filtration rate in the cold ischemia group was lower than in the control group on postoperative day 1, while it was similar on postoperative days 3,8 and 15.

Conclusions: In the porcine model laparoscopic renal hypothermia achieved with microparticulate ice slurry was safe and efficient. It significantly decreased renal dysfunction secondary to an ischemic insult with no adverse effects or complications associated with microparticulate ice slurry use.

### Editorial Comment

Prevention of renal ischemia-reperfusion injury remains a challenge, particularly in laparoscopic partial nephrectomy. Gill et al. first reported the use of ice slush laparoscopically to achieve cold ischemia in laparoscopic partial nephrectomy, but the delivery system was somewhat cumbersome. Conversely, this animal study used microparticulate ice slurry (MPS) for laparoscopic hypothermia during renal ischemia in a single kidney porcine model. MPS contains smooth globular ice particles (< 100  $\mu$ m in diameter) suspended in saline carrier medium. MPS may be pumped through a 4 mm catheter without plugging, in contrast to the standard ice slush which is composed of dendritic ice crystals that do not flow through narrow tubes, making it not applicable for laparoscopic surgery but it is used for regional hypothermia during open procedures. Survival studies comparing 3 different groups (Group 1 - 90 minutes warm ischemia, group 2 - 90 minutes cold ischemia using laparoscopically delivered MPS, and control group 3 - hilar dissection, no clamping and no microparticulate ice slurry), demonstrated significant difference in renal function in group 1 when compared to other groups. The authors concluded that MPS was safe and efficient to achieve renal hypothermia and to decrease renal dysfunction due to ischemia-reperfusion injury.

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## IMAGING

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### **MRI-Guided Biopsy of the Prostate Increases Diagnostic Performance in Men with Elevated or Increasing PSA Levels After Previous Negative TRUS Biopsies**

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Eur Urol. 2006; 50: 738-48

Objectives: Repeatedly negative prostate biopsies in individuals with elevated prostate specific antigen (PSA) levels can be frustrating for both the patient and the urologist. This study was performed to investigate if magnetic resonance imaging (MRI)-guided transrectal biopsy increases diagnostic performance in individuals with elevated or increasing PSA levels after previous negative conventional transrectal ultrasound (TRUS)-guided biopsies.

Methods: 27 consecutive men with a PSA > 4 ng/ml and/or suspicious finding on digital rectal examination, suspicious MRI findings, and at least one prior negative prostate biopsy were included. Median age was 66 years (mean, 64.5 +/- 6.8); median PSA was 10.2 ng/ml (mean, 11.3 +/- 5.5). MRI-guided biopsy was performed

with a closed unit at 1.5 Tesla, an MRI-compatible biopsy device, a needle guide, and a titanium double-shoot biopsy gun.

Results: Median prostate volume was 37.4 cm<sup>3</sup> (mean, 48.4±31.5); median volume of tumor suspicious areas on T2w MR images was 0.83 cm<sup>3</sup> (mean, 0.99±0.78). The mean number of obtained cores per patient was 5.22±1.45 (median, 5; range, 2-8). Prostate cancer was detected in 55.5% (15 of 27) of the men. MRI-guided biopsy could be performed without complications in all cases.

Conclusion: According to our knowledge, this is the largest cohort of consecutive men to be examined by MRI-guided transrectal biopsy of the prostate in this setting. The method is safe, can be useful to select suspicious areas in the prostate, and has the potential to improve cancer detection rate in men with previous negative TRUS-biopsies.

### **Editorial Comment**

New biopsy strategies with increased numbers of systematically placed biopsy cores have been developed to decrease the false-negative rate associated with conventional sextant prostate biopsy; however, many men still find themselves in this clinical dilemma, and the best way to care for these patients remains uncertain. Conventional and 3D-spectroscopic endorectal magnetic resonance imaging (3D-MRSI) techniques have shown promise in the improved detection of cancer within the prostate. One important drawback of using 3D-MRSI-guided biopsy is the process of overlaying the abnormal voxel seen of spectroscopic images on transrectal ultrasound scans. In other words to project a suspicious area for cancer seen on an endorectal magnetic resonance spectroscopic imaging into the scans obtained with transrectal ultrasound in order to adequate sample the suspicious areas. The authors present in this manuscript an interesting technique of MRI-guided biopsies. They used a non-metallic, fully automatic core-needle, double shot biopsy gun and a portable biopsy devise previously described. The major limitations of this study are related to the criterion used to consider suspicious lesion on conventional endorectal MR imaging of the prostate and the need for 2 consecutive MRI examinations. As we know prostate cancer of the peripheral zone appear as hypointense areas but this finding is not specific since other benign abnormalities such as inflammation, fibrosis and focal prostatic atrophy may have similar appearance. 3D-MRSI is superior to conventional MR imaging as a guide for repeat biopsy due its capacity of detect abnormal metabolic activities, thus allowing the differentiation between benign and malignant lesions. Detection of cancer in prostate with normal appearance on conventional MRI examination is also possible with 3D-MRSI. Perhaps in the near future, the ideal approach for these patients would be the use of this technique associated with 3D-MRSI of the prostate and during a single procedure.

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### **Dynamic Contrast Enhanced, Pelvic Phased Array Magnetic Resonance Imaging of Localized Prostate Cancer for Predicting Tumor Volume: Correlation with Radical Prostatectomy Findings**

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J Urol. 2006; 176: 2432-7

**Purpose:** We assessed the value of pelvic phased array dynamic contrast enhanced magnetic resonance imaging for predicting the intraprostatic location and volume of clinically localized prostate cancers.

**Materials and Methods:** Suspicious areas on prospective pre-biopsy magnetic resonance imaging in 24 patients were assigned a magnetic resonance imaging malignancy score and located with respect to anatomical features, gland side, and transition and peripheral zone boundaries. The largest surface area and volume were measured. These magnetic resonance imaging findings were compared with radical prostatectomy specimen histopathology findings.

**Results:** Histopathology maps detected 56 separate cancer foci. The largest tumor focus was located in the peripheral zone in 14 patients and in the transition zone in 10. T1-weighted dynamic contrast enhanced magnetic resonance imaging identified 30 of the 39 tumor foci greater than 0.2 cc and 27 of the 30 greater than 0.5 cc. T2-weighted sequences were suspicious in 22 of 30 foci greater than 0.2 cc that were identified by T1-weighted dynamic contrast enhanced magnetic resonance imaging sequences. Sensitivity, specificity, and positive and negative predictive values for cancer detection by magnetic resonance imaging were 77%, 91%, 86% and 85% for foci greater than 0.2 cc, and 90%, 88%, 77% and 95% for foci greater than 0.5 cc, respectively. Median focus volume was 1.37 cc (range 0.338 to 6.32) for foci greater than 0.2 cc detected by magnetic resonance imaging in the peripheral zone and 0.503 cc (range 0.337 to 1.345) for those not detected by magnetic resonance imaging ( $p < 0.05$ ). Corresponding median values for transition zone foci were 2.54 (range 0.75 to 16.87) and 0.435 (range 0.26 to 0.58).

**Conclusions:** Pre-biopsy pelvic phased array dynamic contrast enhanced magnetic resonance imaging is an accurate technique for detecting and quantifying intracapsular transition or peripheral zone tumor foci greater than 0.2 cc. It has promising implications for cancer detection, prognosis and treatment.

### **Editorial Comment**

The authors present a very interesting study for the detection and prediction of prostate tumor volume using 1.5 Tesla MRI - dynamic contrast enhanced protocol with a single pelvic phased array coil. As we know, estimation of tumor volume is improved by endorectal 3D-magnetic resonance spectroscopic imaging (3D-MRSI) and endorectal dynamic contrast enhanced technique, but errors are not infrequent. Although the authors' project is based on a controversial issue (we do not agree that the pelvic phased array coil provides similar image quality in comparison with endorectal coil), their results are impressive. Endorectal MR imaging and 3D- MRSI are useful for detecting the majority of peripheral zone tumors larger than 0.5 cc (1.0 cm). So far dynamic contrast enhanced endorectal-MRI also has the capability of detecting tumor foci greater than 0.5 cc, with 85.3% sensitivity and 92.6% positive predictive value. The authors results was very impressive since they had 77% sensitivity, 91% specificity, and 86% positive and 85% negative predictive values for detecting tumor foci greater than 0.2 cc (7 mm). Another important contribution of this technique was also the possibility of detecting transition zone tumors. Further studies with larger population are necessary to confirm the value of this new imaging approach.

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## UROGENITAL TRAUMA

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### **Specific Fracture Configurations Predict Sexual and Excretory Dysfunction in Men and Women 1 Year after Pelvic Fracture**

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J Urol. 2006; 176: 1540-5

**Purpose:** We determined the prevalence and predictors of sexual and excretory dysfunction in patients 1 year after pelvic fracture.

**Materials and Methods:** The multicenter Pennsylvania Trauma Outcomes Study enrolled 1,238 patients and contacted them 1 year after injury. Sexual limitations and excretory dysfunction (bladder/bowel incontinence) were defined based on responses from the Functional Capacity Index. Health related quality of life was determined using SF-36. The relationship between specific fracture patterns and dysfunction along with the effect of dysfunction on quality of life in patients with pelvic fracture were evaluated by multivariate analysis.

**Results:** Of 1,160 eligible patients 292 (26%) had pelvic fractures. Sexual dysfunction was reported in 21% vs 14% of those with vs without pelvic fractures and bowel or bladder incontinence was reported in 8% vs 4%. On multivariate analysis men with sacroiliac fractures were at higher risk for sexual (RR 4.0, 95% CI 2.3 to 6.8) and excretory (RR 4.3, 95% CI 1.4 to 13.5) dysfunction. In women symphyseal diastasis was associated with sexual (RR 4.8, 95% CI 2.0 to 11.2) and excretory (RR 12.5, 95% CI 1.9 to 80.2) dysfunction. Of patients with pelvic fractures men with sexual dysfunction and women with excretory dysfunction had significantly worse quality of life than those without dysfunction.

**Conclusions:** One year after trauma men with sacroiliac fractures and women with symphyseal diastasis were at increased risk for sexual and excretory dysfunction independent of overt pelvic organ injury. In patients with pelvic fracture male sexual dysfunction and female excretory dysfunction were associated with decreased quality of life. Our data highlight the need for further study of dysfunction following pelvic trauma and interventions to decrease the risk of long-term disability.

### **Editorial Comment**

Erectile dysfunction after pelvic fracture is interplay of injury to the penile arterial inflow, venous outflow or nerve innervation. Clearly injuries to the pubic rami that result in bony distraction, may also displace and injury the crus of the penis. Such patients may suffer from venous leak or arterial insufficiency, or both. The arterial and nervous supply to the penis is partially protected by the fascial walls of Alcock's canal, but is vulnerable to injury if the adjacent ischial bone is fractured. Erectile dysfunction (ED) after pelvic fracture has typically been associated with concomitant urethral disruption injury. Historically, with urethral injury ED rates are up to 75%. Surprisingly, Wright et al. determined that SI fractures have the highest rates of ED. Intuitively, one would assume pubic rami and open book fractures to have high rates of male ED. Clearly, quality of life as to urinary excretory control and erectile dysfunction after pelvic fractures are issues that the urologist should be familiar with. For it is the urologic consequences of pelvic fracture that are often prolonged, morbid and difficult to manage, long after the orthopedic injuries have healed.

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## **Experience with Wound VAC and Delayed Primary Closure of Contaminated Soft Tissue Injuries in Iraq**

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J Trauma. 2006; 61: 1207-11

**Background:** Wartime missile injuries are frequently high-energy wounds that devitalize and contaminate tissue, with high risk for infection and wound complications. Debridement, irrigation, and closure by secondary intention are fundamental principles for the management of these injuries. However, closure by secondary intention was impractical in Iraqi patients. Therefore, wounds were closed definitively before discharge in all Iraqi patients treated for such injuries at our hospital. A novel wound management protocol was developed to facilitate this practice, and patient outcomes were tracked. This article describes that protocol and discusses the outcomes in a series of 88 wounds managed with it.

**Methods:** High-energy injuries were treated with rapid aggressive debridement and pulsatile lavage, then covered with negative pressure (vacuum-assisted closure [VAC]) dressings. Patients underwent serial operative irrigation and debridement until wounds appeared clean to gross inspection, at which time they were closed primarily. Patient treatment and outcome data were recorded in a prospectively updated database.

**Results:** Treatment and outcomes data from September 2004 through May 2005 were analyzed retrospectively. There were 88 high-energy soft tissue wounds identified in 77 patients. Surprisingly, for this cohort of patients the wound infection rate was 0% and the overall wound complication rate was 0%.

**Conclusion:** This series of 88 cases is the first report of the use of a negative pressure dressing (wound VAC) as part of the definitive management of high-energy soft tissue wounds in a deployed wartime environment. Our experience with these patients suggests that conventional wound management doctrine may be improved with the wound VAC, resulting in earlier more reliable primary closure of wartime injuries.

### **Editorial Comment**

The vacuum assisted closure system is an effective, simple, and under-utilized method to help repair and close wounds. In the Iraq War, many of the injuries have devastating soft tissue defects that are ideal for negative pressure wound therapy. Numerous urologic injuries have also been seen during the Iraq conflict. Such complex urologic wounds on the penis, perineum, and scrotum are also ideal for such therapy after initial debridement.. The first report of negative pressure wound therapy (NPWT) was by Fleischmann et al., *Unfallchirg.* 1993; 96: 488-92. It has been FDA approved since 1995. To perform NPWT, place a sterile foam dressing into wound defect, followed by a non-collapsible fenestrated tubing exits foam parallel to skin, connected to vacuum pump. The open wound is then converted into controlled closed wound (adhesive transparent film dressing placed on top of foam). Machine settings are typically 125 mmHg of negative pressure continuously or cyclically (5 min on, 2 min off). Dressing changes are made every 48 hours or 3 x/ week.

NPWT helps wounds to close and heal by the following mechanisms: removal of excessive interstitial edema, decompresses small vessels and restores local blood flow; removes chronic wound fluids rich in matrix metalloproteases (inhibit wound healing); mechanical deformation of cells, with foam collapse, traction forces perturb the cytoskeleton and stimulate fibroblast, endothelial cell and vascular smooth muscle cell proliferation. Contraindications to NPWT are: malignancy in the wound, tissue necrosis (large amounts) with scar (debride before starting VAC), untreated osteomyelitis, insufficient vascularity to sustain any wound healing, untreated malnutrition.

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**PATHOLOGY****Adenoid Cystic/Basal Cell Carcinoma of the Prostate Strongly Expresses HER-2/neu**

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*J Clin Pathol. 2006; 59: 1327-30*

Adenoid cystic/basal cell carcinoma (ACBCC) is a rare neoplasm in the prostate. Definitive treatment is warranted, as among 19 patients previously reported by us, 5 had extraprostatic extension and 4 were metastatic. The HER-2/neu (c-erbB-2) gene has been reportedly overexpressed in adenoid cystic carcinomas in other organs, but its status in prostatic ACBCC was uncertain. Immunohistochemical staining and in situ hybridisation were carried out in 13 patients with ACBCC (11 from transurethral resection, 2 prostatectomy). One patient had metastasis to the lung. Citrate buffer and steam heat were used for antigen retrieval. Ten acinar adenocarcinomas of varying grades were also immunostained as controls. Protein and mRNA expression were 2+ to 3+ (of 3+) in all patients with ACBCC, compared to a breast cancer control with strong reactivity, whereas protein expression was noted in only one acinar carcinoma and mRNA expression was absent in all acinar carcinomas. Benign acini expressed HER-2/neu only in the basal layer. The finding of strong, consistent HER-2/neu expression in ACBCC suggests that treatment with Herceptin (trastuzumab) may be effective in patients with this rare tumour.

**Editorial Comment**

This is a rare tumor composed of prostatic basal cells. Due to few cases reported, it was considered that the tumor had indolent biologic potential and some authors called the lesion “adenoid cystic-like tumor of the prostate gland” (1). In 2003, Iczkowski et al. (2) published the largest series calling attention to the potential aggressiveness of this tumor requiring ablative therapy. From a total of 19 patients, 5 showed extraprostatic extension on radical prostatectomy and 4 (21%) metastases: liver (2 patients), lung (2 patients), bowel (1 patient), and corpus cavernosum (1 patient). It is worth mention that the PSA was normal in most of the patients. Only 5 patients had elevated serum PSA of 4.5 to 9.2 ng/mL. This is an important finding with implication in the biochemical monitoring post-prostatectomy.

Based on the fact that HER-2/neu (c-erb-2) gene has been reportedly overexpressed in adenoid cystic carcinomas in other organs, Iczkowski and Montironi studied the expression of this gene in prostate tissue of 13 patients previously reported. Based on the finding that adenoid cystic/basal cell carcinoma of the prostate strongly expresses HER-2/neu we hope that treatment with Herceptin (trastuzumab) may be effective in patients with this rare and aggressive tumor.

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## **Detection of Life-Threatening Prostate Cancer with Prostate-Specific Antigen Velocity during a Window of Curability**

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J Natl Cancer Inst. 2006; 98: 1521-7

**Background:** Prostate-specific antigen (PSA) level is typically used as a dichotomous test for prostate cancer, resulting in over diagnosis for a substantial number of men. The rate at which serum PSA levels change (PSA velocity) may be an important indicator of the presence of life-threatening disease.

**Methods:** PSA velocity was determined in 980 men (856 without prostate cancer, 104 with prostate cancer who were alive or died of another cause, and 20 who died of prostate cancer) who were participants in the Baltimore Longitudinal Study of Aging for up to 39 years. The relative risks (RRs) of prostate cancer death and prostate cancer-specific survival stratified by PSA velocity were evaluated in the three groups of men by Cox regression and Kaplan-Meier analyses. Statistical tests were two-sided.

**Results:** PSA velocity measured 10-15 years before diagnosis (when most men had PSA levels below 4.0 ng/mL) was associated with cancer-specific survival 25 years later; survival was 92% (95% confidence interval [CI] = 84% to 96%) among men with PSA velocity of 0.35 ng/mL per year or less and 54% (95% CI = 15% to 82%) among men with PSA velocity above 0.35 ng/mL per year ( $P < 0.001$ ). Furthermore, men with PSA velocity above 0.35 ng/mL per year had a higher relative risk of prostate cancer death than men with PSA velocity of 0.35 ng/mL per year or less (RR = 4.7, 95% CI = 1.3 to 16.5;  $P = 0.02$ ); the rates per 100,000 person-years were 1240 for men with a PSA velocity above 0.35 ng/mL per year and 140 for men with a PSA velocity of 0.35 ng/mL per year or less.

**Conclusions:** PSA velocity may help identify men with life-threatening prostate cancer during a period when their PSA levels are associated with the presence of curable disease.

### **Editorial Comment**

PSA velocity may help monitor patients in a period of “watchful waiting”. Due to rising frequency of prostate cancer detected in clinical stage T1c a higher number of cases have criteria for “insignificant” cancer and patients may elect “watchful waiting”. The term “insignificant” is not proper because it may imply that the tumor is latent (dormant or indolent). Unfortunately there is no marker for the biologic behavior of prostatic adenocarcinoma. The best term is “minimal volume carcinoma” and some predictive criteria include absence of Gleason grade 4 or 5, a maximum of 2 cores showing tumor and no more than 50% of the area of the core involved. Clinical stage must be T1c and PSA density less than 0.15 ng/mL (1). During the period of “watchful waiting” besides PSA velocity, free/total PSA should also be monitored and, very important, an annual needle prostatic biopsy. The reason for the biopsy is to detect an eventual change in extension and/or Gleason grading.

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## INVESTIGATIVE UROLOGY

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### **Detrusor Quantitative Morphometry in Obstructed Males and Controls**

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J Urol. 176: 2722-8

**Purpose:** We studied the usefulness of computer assisted morphometry for measuring detrusor muscle cell diameter and the connective tissue-to-smooth muscle ratio in patients with bladder outlet obstruction, acute urinary retention and a nonobstructed control group.

**Materials and Methods:** A prospective study was done in patients with bladder outlet obstruction undergoing transurethral prostate resection. Patients were divided into 33 with obstruction and 14 in acute urinary retention. A total of 15 males without obstruction undergoing transurethral prostate resection for bladder tumor formed the control group. Detrusor specimens were obtained during transurethral prostate resection. Detrusor muscle cell diameter was measured using light microscopy and a semiautomatic image analysis system. The connective tissue-to-smooth muscle ratio was automatically determined with computer assisted image analysis. Symptoms and urodynamic assessment were performed preoperatively and 6 months postoperatively.

**Results:** A total of 62 patients were included. The obstruction and acute urinary retention groups had a statistically higher detrusor muscle cell diameter and more fibrosis than the control group. Patients in acute urinary retention had more intrafascicular fibrosis (higher connective tissue-to-smooth muscle ratio at 40x magnification) than patients with obstruction. There were no differences in detrusor muscle cell diameter or interfascicular fibrosis (connective tissue-to-smooth muscle ratio at 10x magnification) between the obstruction and acute urinary retention groups. Detrusor muscle cell diameter correlated with symptom duration and functional recovery after transurethral prostate resection. Detrusor fibrosis correlated with preoperative detrusor pressure at maximum flow and postoperative compliance. Patients in acute urinary retention had fewer symptoms and higher residual volume. Other urodynamic parameters and their improvement after surgery were similar in the acute urinary retention and obstruction groups.

**Conclusions:** Morphometric differences in detrusor muscle cell diameter and the connective tissue-to-smooth muscle ratio were observed between controls and patients with obstruction. There is an increase in detrusor muscle cell diameter and fibrosis in bladder outlet obstruction and more intense intrafascicular collagen deposition in patients in acute urinary retention.

### **Editorial Comment**

Previous studies suggested that bladder outlet obstruction could produce histological changes in detrusor muscle and extracellular matrix; nevertheless, the results have been contradictory, with some authors reporting increase in smooth muscle and collagen decrease, while others reported collagen increase.

The authors studied 33 patients with bladder outlet obstruction (BOO) due to benign prostatic hyper trophy (BPH) and 14 patients in acute urinary retention (AUR). A total of 15 males without obstruction undergoing transurethral prostate resection for bladder tumor composed the control group. The present paper reported that the detrusor muscle cell diameter correlated with symptoms. It was found a positive correlation between the increase in cellular diameter and symptoms duration. The authors also studied the urodynamic parameters and found that there was no correlation in the obstructed and acute urinary retention groups with the detrusor muscle cell diameter. The authors found hypertrophy and an increase in fibrosis in patients with BOO. In patients with obstruction, there were slightly morphometric differences between those with an episode of AUR, that is higher intrafascicular fibrosis. There were no urodynamic differences preoperatively and postoperatively.

In a recent study (1), we analyzed the detrusor extracellular matrix in samples taken from bladders of 10 patients who underwent transvesical prostatectomy for treatment of BPH. Control material was composed of 10 vesical specimens, removed during autopsies performed in cadavers of accident victims, with ages between 18 and 35 years (mean = 26 years). We found that the components of connective tissue (collagen and elastic system fibers) are increased in the detrusor muscle of patients with infravesical obstruction, when compared to controls.

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#### **Dynamic Contrast Enhanced Magnetic Resonance Imaging as a Biological Marker to Noninvasively Assess the effect of Finasteride on Prostatic Suburethral Microcirculation**

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*J Urol.* 2006; 176: 2299-304

**Purpose:** We assessed dynamic contrast enhanced magnetic resonance imaging as a biological marker of in vivo changes in microcirculation in the prostatic suburethral region.

**Materials and Methods:** A total of 12 male beagle dogs with spontaneous benign prostatic hyperplasia were randomly allocated to 1 control group and 1 finasteride (Merck and Co., Whitehouse Station, New Jersey) treated group. Two baseline dynamic contrast enhanced magnetic resonance imaging examinations and 3 followups were performed to assess prostate microcirculation. Treatment duration was 3 months. The pharmacokinetic parameters evaluated in prostatic suburethral areas were the maximum enhancement ratio in AU, time to maximum signal enhancement in minutes, amplitude in AU and the exchange rate constant in minutes<sup>(-1)</sup>.

**Results:** After completion of the therapeutic regimen time to maximum signal enhancement was significantly longer in the finasteride group than in controls ( $p < 0.01$ ). Amplitude and the exchange rate constant decreased 39% and 34%, respectively, in the finasteride group at the end of treatment, which significantly differed from results in the control group ( $p < 0.05$ ).

**Conclusions:** Dynamic contrast enhanced magnetic resonance imaging is capable of noninvasively assessing the prostatic microcirculation changes induced by finasteride. Pharmacokinetic parameters show considerable promise to be biomarkers for the development of benign prostatic hyperplasia drugs such as 5 $\alpha$ -reductase inhibitors by the in vivo monitoring of microvascular changes. A relevant clinical application could be the pretreatment assessment of finasteride effectiveness to decrease perioperative bleeding at transurethral prostate resection and in treatment for hematuria.

#### **Editorial Comment**

During the last years we learned that finasteride could decrease prostatic bleeding, both in benign prostatic hyperplasia (BPH) and in transurethral resection of the prostate (TURP), and we have been using finasteride in

the clinical setting for these proposes. Nevertheless, the mechanism of finasteride action in stopping bleeding is still unknown.

The authors of the present paper used male beagle dogs to assess dynamic contrast enhanced magnetic resonance imaging as a biological marker of in vivo changes in microcirculation in the prostatic suburethral region. They found that subjects in the finasteride group had decreased microcirculation, as expressed by lower and slower contrast enhancement, and as quantified by increased Tmax, and decreased A and kep in the prostatic suburethral area. They concluded that finasteride would decrease the prostatic microcirculation and therefore diminish prostatic bleeding in BPH and TURP.

In a recent experimental paper, Canda et al. (1) evaluated the effects of finasteride on the vascular surface density (VSD), number of microvessels (NVES) and vascular endothelial growth factor (VEGF) expression of the rat prostate. After studying 19 adult rats, the authors found that the mean prostatic weights were decreased significantly in rats given finasteride ( $p=0.0001$ ). On the other hand, finasteride does not seem to decrease VSD, NVES and VEGF expression at the level of the rat prostate. The effect of reduction of bleeding in BPH is more likely to be due to its effect on shrinking glandular hyperplasia, which might enhance vessel wall stability, rather than decreasing overall vascularity (1).

From these two papers, we can infer that the exact mechanism of action of finasteride on the prostatic vessels is still open to research and discussion.

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## RECONSTRUCTIVE UROLOGY

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### **Gender Specific Chronological and Morphometric Ssessment of Fetal Bladder Wall Development**

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*J Urol.* 2006; 176: 2674-8

**Purpose:** To enhance our understanding of sonographically visible alterations in bladder wall thickness, we delineated phenotypic changes occurring in developing smooth muscle cells of the fetal and postnatal bladder with respect to gender specific differences.

**Materials and Methods:** Bladders of 30 male and 18 female fetuses and 4 stillborn infants were immunostained with an alpha-smooth muscle actin antibody. Morphological and morphometric assessment was performed with the assistance of an image analysis system.

**Results:** Alpha-smooth muscle actin expression in fetal bladder wall was detectable at 9 weeks of gestation. Bladder wall thickness and mean profile area of smooth muscle bundles increased significantly with advancing gestation, mediated by linear growth patterns. Fetal bladder wall development occurred uniformly, unrelated to gender.

Conclusions: Although the lower urinary tract emerges in a gender specific way, our results suggest that in normal fetal growth detrusor muscle formation proceeds independent of genital sex.

### **Editorial Comment**

The current paper deals with histologic and morphometric assessment of 18 female and 30 male bladder specimens of human fetuses at 9 to 35 weeks of gestation. The findings underline the theory of those favoring a gender independent development of the lower urinary tract. At various times during fetal development no differences between male and female specimens of the muscular structure and configuration of the bladder was seen contrary to previous reports (1). Furthermore, the growth of the muscular bladder wall was linear with gestational age.

This is a very elegant study with nice fetal specimens and reveals several interesting aspects. Apart from the main conclusions outlined above it was also interesting to see that the bladder seems to develop relatively late compared to the gut. At 9 weeks, only immature smooth muscle cells were observed in the bladder whereas the bowel already demonstrated clearly visible inner and outer muscular layers. In addition, smooth muscle cells developed first in the ventral portion of the bladder close to the dome. One may speculate that this has something to do with the umbilical vessels.

Only through the development of the bladder the muscle bundles start to change their shape, direction and intermingling. Unfortunately we do not get any clue from this study when and how neural development starts.

With studies like that we get important information for further tissue engineering of the urinary bladder. We suppose that at the time of in vitro cultivation intermingling and growth may not be our major goal but that we somehow have to have functional and growth stimulations at the time of implantation, which will bring our cultivated smooth muscle cells to a structure, which resembles the native bladder.

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### **Miniature Intravesical Urethral Lengthening Procedure for Treatment of Pediatric Neurogenic Urinary Incontinence**

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*J Urol.* 2006; 176: 2663-6

Purpose: Resistance to flow in a fluid conduit is proportional to tube length divided by the radius to the fourth power (Poiseuille's law). We report the results of a miniature intravesical urethral lengthening procedure where outlet resistance is increased by minimizing the diameter of the intravesical urethral tube.

Materials and Methods: Nine pediatric patients with preoperative intractable incontinence underwent the miniature intravesical urethral lengthening procedure along with continent catheterizable stoma (9 patients)

and bladder augmentation (8). The intravesical portion of the urethral lengthening was 3 cm (traditionally 6 cm), and the urethra was tubularized around an 8Fr feeding tube (traditionally a 16Fr catheter). After the tubularized caudal portion was tunneled under the trigone the cephalad part of the urethra was placed as an onlay to the posterior bladder wall without ureteral reimplantation.

Results: At a mean followup of 31 months (range 10 to 47) 8 patients reported dry intervals of 3 hours or more, with minor leak per urethra only if they were overdue on the catheterization schedule. Mean postoperative abdominal leak point pressure was 71 cm H<sub>2</sub>O (range 28 to 116). Upper tracts were well preserved in all patients. One patient required bladder neck closure for intractable incontinence.

Conclusions: The miniature intravesical urethral lengthening procedure requires minimal bladder tissue and is easy to perform. It appears to be an effective alternative in bladder neck reconstructive techniques, avoiding the need for ureteral reimplantation due to its small size, while functioning as a pop-off valve when the bladder is overly full. This procedure should be avoided in patients who lack a trigonal bar.

### Editorial Comment

The reconstructive surgeon strives to benefit the patient with improved surgical approaches. Urinary incontinence, especially in patients with a neurogenic bladder, presents a significant surgical challenge and requires high level of experience (1). The technique of Kropp further developed by Pippi-Salle demonstrated the step-by-step perfection of the more advanced approach with the presented MIULP technique. This technique refreshed specific aspects of current approaches and further developed thoughts that are reflected in the described modified technique. However, the surgeon's responsibility is continued with the surgeon's legacy and sense of duty through long-term patient follow-up.

On the one hand, the tunneling of the lengthened urethra reduces the chance of fistula development; however, on the other hand the smaller urethral diameter might cause difficulties during catheterization. In our experience, the majority of patients prefer to use a catheterizable stoma. With the improved concept of regular sterile intermittent catheterization, there is a significant reduction in urinary infections and stone occurrence today, which reduces the chance of an endoscopic surgical approach.

The increased leak point pressure meets the patient's request to be dry and the "pop-off" valve makes allowance to limit the bladder pressure. With the introduction of Botulinum toxin, bladder augmentation can be often avoided or at least delayed securing the low-pressure storage (2).

This urethral lengthening technique might be a legitimate technique for the experienced surgeon to improve patient's long-term outcome.

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## UROLOGICAL ONCOLOGY

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### **Pathological Outcomes and Biochemical Progression in Men with T1c Prostate Cancer Undergoing Radical Prostatectomy with Prostate Specific Antigen 2.6 to 4.0 vs 4.1 to 6.0 ng/ml**

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J Urol. 2006; 176: 554-8

**Purpose:** Recent studies have suggested that the cut point for recommending prostate biopsy among men with a normal digital rectal examination should be greater than 2.5 ng/ml as opposed to the more traditional greater than 4.0 ng/ml. We compared outcomes between men with clinical stage T1c disease undergoing radical prostatectomy who had a low vs slightly increased prostate specific antigen.

**Materials and Methods:** The study population consisted of 2,896 men treated with radical prostatectomy between 1985 and 2004 at a tertiary care referral center with clinical stage T1c disease and a pre-biopsy prostate specific antigen between 2.6 and 6.0 ng/ml. Using multivariate analysis we evaluated the association between pre-biopsy prostate specific antigen 2.6 to 4.0 ng/ml (784) vs 4.1 to 6.0 ng/ml (2,112), and pathological outcomes and biochemical progression.

**Results:** After adjusting for multiple clinical and pathological characteristics, lower preoperative serum prostate specific antigen values were associated with decreased odds of Gleason score 7 or greater in the surgical specimen ( $p = 0.004$ ), positive surgical margins ( $p = 0.02$ ) and extraprostatic extension ( $p = 0.001$ ). There was no significant association between these preoperative prostate specific antigen groups and odds of seminal vesicle invasion ( $p = 0.47$ ) or lymph node metastasis ( $p = 0.90$ ). Among the 1,534 men with followup information available there was a trend for increased risk of biochemical progression associated with a higher preoperative prostate specific antigen, although this trend did not reach statistical significance (relative risk 1.48, 95% CI 0.69-3.19,  $p = 0.31$ ).

**Conclusions:** In the current study of men with clinical stage T1c treated with radical prostatectomy a lower preoperative prostate specific antigen was associated with significantly more favorable pathological findings. Whether this degree of improved outcomes justifies the limitations associated with decreasing the prostate specific antigen cut point (e.g. increased biopsies performed and diagnosis of insignificant cancers) remains to be determined.

#### **Editorial Comment**

The authors focus on a rather large series of patients with a low serum PSA and biopsy-confirmed prostate cancer undergoing radical prostatectomy. Indeed, 784 patients with a PSA between 2.6 and 4.0 ng/mL were compared to patients with a PSA between 4.1 and 6.0 ng/mL. I wonder how suspicion of prostate cancer was generated in the first group, e.g. by abnormal digital examination?

Nevertheless, the results are interesting and give support to the notion that prostate cancer is an aggressive disease, even with low PSA. Positive surgical margins and capsular penetration were found in 6% and 14%, respectively, in the first group and in 9% and 21% in the higher PSA group. Recurrence-free survival was inferior after 10 years in the elevated PSA group.

What does that mean for the practicing urologist? To my opinion: detect and treat prostate cancer as early as possible.

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### **Long-Term Followup of a Randomized Study of Locally Advanced Prostate Cancer Treated with Combined Orchiectomy and External Radiotherapy versus Radiotherapy Alone**

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J Urol. 2006; 176: 544-7

**Purpose:** In a randomized study we compared the combination of orchiectomy and radiotherapy to radiotherapy alone as treatment for locally advanced prostate cancer. Patients who were treated only with radiotherapy initially underwent castration therapy at clinical progression, providing the opportunity to compare immediate vs deferred endocrine intervention.

**Materials And Methods:** In this prospective study 91 patients with locally advanced prostate cancer were randomized to receive external beam radiotherapy (46) or combined orchiectomy and radiotherapy (45) after surgical lymph node staging. Survival rates were calculated.

**Results:** During 14 to 19 years of followup 87% of the patients in the radiotherapy group and 76% in the combined orchiectomy and radiotherapy group died (log rank  $p = 0.03$ ). Prostate cancer mortality was 57% and 36%, respectively (log rank  $p = 0.02$ ). The difference in favor of combined treatment was mainly caused by lymph node positive tumors. For node negative tumors there was no significant difference in the survival rates.

**Conclusions:** Immediate androgen deprivation should be considered instead of deferred endocrine treatment started at clinical progression for prostate cancer with spread to regional lymph nodes. While awaiting evidence from randomized trials, one should consider full dose radiotherapy for local control of locally advanced prostate cancer even when it is lymph node positive.

#### **Editorial Comment**

This paper gives the long-term results of a simple but well-done trial: immediate or deferred hormone ablative treatment in patients undergoing external beam radiation therapy (ERBT) after surgical lymph node staging.

The answer is clear-cut: immediate hormone ablative therapy is better than deferred therapy with regard to survival. This difference was most predominant in lymph node positive patients. In conclusion, these data and other papers strongly support the use adjuvant endocrine treatment in radiotherapy against prostate cancer.

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## **NEUROUROLOGY & FEMALE UROLOGY**

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### **Transurethral Radiofrequency Energy Collagen Micro-Remodeling For the Treatment of Female Stress Urinary Incontinence**

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Neurourol Urodyn. 2006; 25: 331-6

**Aims:** This prospective, randomized, controlled clinical trial was performed to demonstrate the 12 months safety and efficacy of transurethral radiofrequency energy (RF) collagen micro-remodeling in women with stress urinary incontinence (SUI).

**Materials and Methods:** Women with SUI, bladder outlet hypermobility, and leak point pressure (LPP)  $\geq$  60 cmH<sub>2</sub>O were randomized to RF micro-remodeling or “sham treatment.” Adverse events (AEs) were recorded. Incidence of  $\geq$  10 point incontinence quality of life (I-QOL) score improvement, a magnitude of improvement with a demonstrated responsiveness to patient satisfaction with treatment and to  $\geq$  25% reduction in both incontinence episode frequency and stress pad weight, served as a subjective outcome measurement. Change in mean LPP served as an objective outcome measurement.

**Results:** 110 women underwent RF micro-remodeling and 63 underwent virtually identical “sham treatment” (with the exception of RF delivery). The 12 months RF micro-remodeling safety profile was statistically no different than that of sham treatment (a brief bladder catheterization). Seventy-four percent of women with moderate to severe baseline SUI experienced  $\geq$  10 point I-QOL score improvement at 12 months ( $P = 0.04$ ). Women who underwent RF micro-remodeling demonstrated LPP elevation at 12 months, while sham treated women demonstrated LPP reduction ( $P = 0.02$ ).

**Conclusions:** Non-surgical, transurethral RF micro-remodeling is a safe treatment for women with SUI. In women with moderate to severe SUI, this novel therapy resulted in statistically significant improvement in quality of life of a magnitude associated with patient satisfaction with the treatment. Women who underwent RF micro-remodeling demonstrated a statistically significant elevation in mean LPP at 12 months.

### **Editorial Comment**

In a well-constructed scientific study, the authors describe and analyze a technique to address female stress urinary incontinence utilizing radiofrequency energy to denature collagen in multiple microscopic sites causing a change in the compliance of the tissue. This anatomic change will theoretically reduce the inappropriate opening of the bladder neck and proximal urethra with stress maneuvers much in the manner of the sub urethral support of a sling. The technique utilizes less energy than that used by radiofrequency tissue ablation for renal masses and/or gynecological conditions. During the study, the authors used the Incontinence Quality of Life questionnaire (I-QOL) to grade the patient’s incontinence (as opposed to pad weight test) as well as urodynamics including leak point pressure determination. These metrics did make it a little challenging to note if any of the patients were absolutely dry post procedure. Nevertheless, treated patients were able to exhibit a statistically significant increase in leak point pressure at the 12-month follow-up period as opposed to those patients who underwent a sham treatment thus indicating a measure of efficacy (1). This study does speak volumes to the effect of placebo therapy for at the 12-month period almost 50% of both treated and sham groups had a  $\geq$  10 point I-QOL score improvement. The authors do clearly highlight the safety and tolerability of this procedure and denote that radiofrequency micro remodeling clearly responds to the incontinent patients who will settle for improvement as opposed to cure in a trade-off for having a minimally invasive procedure. Similar patient desires with regards to injectable therapy have been noted in this journal (2).

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### **Vaginal Discharge and Bleeding in Girls Younger than 6 Years**

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J Urol. 2006; 176: 2632-5

**Purpose:** Persistent unexplained vaginal discharge or bleeding in the pediatric population may be the only manifestation of a serious underlying medical or social problem. Therefore, these symptoms require careful and complete evaluation to identify the primary pathology accurately. We retrospectively reviewed charts of patients who presented for evaluation of persistent vaginal discharge or bleeding to determine if noninvasive imaging was a sensitive means of screening for gynecological pathology.

**Materials and Methods:** The records of 24 girls younger than 6 years who presented with vaginal discharge or bleeding were reviewed retrospectively. All patients were evaluated with noninvasive imaging, a pelvic examination while under anesthesia, vaginoscopy and cystoscopy.

**Results:** Noninvasive imaging was useful in identifying 5 of 7 vaginal foreign bodies. However, noninvasive imaging identified only 2 of 6 malignancies. These malignancies consisted of rhabdomyosarcoma (3 patients) and endodermal sinus tumor (3). Two girls also had benign vaginal mullerian papillomas that were not identified by noninvasive imaging. Noninvasive imaging did not aid in the diagnosis of sexual abuse.

**Conclusions:** Based on these data, we recommend that all girls younger than 6 years who present with persistent vaginal discharge or bleeding be evaluated with pelvic examination while under anesthesia, to be followed by vaginoscopy and cystoscopy if no readily identifiable pathology is found by simple genital examination alone, regardless of the results of noninvasive imaging studies.

#### **Editorial Comment**

The authors reviewed the efficacy of non-invasive imaging (including abdominal x-ray, ultrasound, CT scan and MR of the pelvis) in the population of females younger than 6 years old who presented to their clinic with vaginal discharge and bleeding as opposed to a physical examination with potential endoscopy under anesthesia; in addition, notation was made of the diagnoses found after evaluation. The patients had for the most part already been treated with antibiotic therapy prior to presentation to the authors. The study found that approximately half of the patients with vaginal discharge had a vaginal vault foreign body while one-third of the patients had no identifiable cause of the discharge. Of the patients with vaginal bleeding, almost half had a vaginal malignancy while approximately 15% had a foreign body within the vagina. The authors thus highlight the difference of potential diagnosis of vaginal discharge versus vaginal bleeding in this young population. Based on their findings, the presentation of vaginal bleeding in a female younger than 6 years old should engender an evaluation without hesitation under anesthesia since there is a high likelihood of the presence of malignancy.

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## PEDIATRIC UROLOGY

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### **Lack of Usefulness of Positioned Instillation of Contrast Cystogram after Injection of Dextranomer/Hyaluronic Acid**

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J Urol. 2006; 176: 2654-6

**Purpose:** Positioned instillation of contrast cystograms have been touted as possibly being more sensitive than standard cystograms for evaluation of vesicoureteral reflux. We performed positioned instillation of contrast cystograms intraoperatively, immediately after the injection of dextranomer/hyaluronic acid to treat vesicoureteral reflux, to determine whether they might be predictive of operative success and obviate the need for the standard postoperative voiding cystourethrogram, which is usually performed at 3 months.

**Materials and Methods:** Patients with vesicoureteral reflux and no confounding conditions were treated with dextranomer/hyaluronic acid and subsequent positioned instillation of contrast cystogram while under the same anesthesia between November 2003 and March 2005. The results of this intraoperative cystogram were compared to the results of the postoperative voiding cystourethrogram performed 3 to 4 months later.

**Results:** A total of 61 patients met the inclusion criteria and underwent positioned instillation of contrast cystogram after dextranomer/hyaluronic acid injection. Only 53 patients (86 ureters) completed the necessary postoperative evaluation. Positioned instillation of contrast cystogram added 4 minutes to the procedure and required about 4 seconds of fluoroscopy per ureter evaluated. The overall success rate for correcting reflux was 84% (72 of 86 ureters cured). None of the 14 ureters with persistent postoperative reflux was identified by intraoperative cystogram, and 3 patients were misidentified as having reflux despite cure confirmed postoperatively. Intraoperative positioned instillation of contrast cystogram was predictive of treatment failure 0% of the time (sensitivity 0%). There were no complications.

**Conclusions:** Positioned instillation of contrast cystogram performed immediately after injection of dextranomer/hyaluronic acid was not useful in predicting which patients would have persistent reflux postoperatively. Patients are best served with the extant protocol of conventional cystography 3 to 4 months postoperatively.

### **Editorial Comment**

This study is an ingenious attempt to improve the efficacy of endoscopic Dx/HA injection for the treatment of vesicoureteral reflux. The authors proposed that by doing a "PICC" study intraoperatively they could identify those patients who were going to fail endoscopic treatment (and in theory they could re-treat them at the same setting). Furthermore, if they could predict those who would ultimately fail with certainty, they could avoid an uncomfortable postoperative cystogram. Unfortunately, their idea did not prove effective.

Despite verbal reports to the contrary, correction of reflux in patients with endoscopic Dx/HA is effective in only 70-80% of patients on the first attempt. In this paper, as in many, the results were reported in terms of % ureters corrected. In this case it was 72 of 86 (84%). But of course patients and parents are much more concerned with the individual patient being cured of their reflux. In this study, reading between the lines, 14 of 53 patients had persistent reflux (in other words, 74% of patients were cured at 3 months). I believe this is typical of the results of most centers.

The idea of finding reflux on an intraoperative test that could result in immediate correction of the problem is great. Similarly, a study that would allow avoidance of a postoperative VCUG would be great. However, the composition of Dx/HA is such that the HA is absorbed over time. Hence, the size of the implant is very likely to get smaller with time. This makes it likely that patients that do not demonstrate reflux at the

time of the procedure, may well demonstrate reflux later, as the implant shrinks. What was interesting in this case was the fact that 3 patients had reflux demonstrated with PICC studies, but these same 3 did not show reflux at the later study. In this case, PICC appeared to be overly sensitive. Of course all types of cystograms miss about 20% of patients with reflux. Perhaps more important, the clinical course of these patients is not known, hence we really do not know whether the PICC study was clinically relevant or not or most important, whether the patients successfully treated with Dx/HA did better than those who failed. Much more work needs to be done in this area.

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### **Preoperative Anxiety, Postoperative Pain, and Behavioral Recovery in Young Children Undergoing Surgery**

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Pediatrics. 2006; 118: 651-8

**Objective:** Findings from published studies suggest that the postoperative recovery process is more painful, slower, and more complicated in adult patients who had high levels of preoperative anxiety. To date, no similar investigation has ever been conducted in young children.

**Methods:** We recruited 241 children aged 5 to 12 years scheduled to undergo elective outpatient tonsillectomy and adenoidectomy. Before surgery, we assessed child and parental situational anxiety and temperament. After surgery, all subjects were admitted to a research unit in which postoperative pain and analgesic consumption were assessed every 3 hours. After 24 hours in the hospital, children were discharged and followed up at home for the next 14 days. Pain management at home was standardized.

**Results:** Parental assessment of pain in their child showed that anxious children experienced significantly more pain both during the hospital stay and over the first 3 days at home. During home recovery, anxious children also consumed, on average, significantly more codeine and acetaminophen compared with the children who were not anxious. Anxious children also had a higher incidence of emergence delirium compared with the children who were not anxious (9.7% vs 1.5%) and had a higher incidence of postoperative anxiety and sleep problems.

**Conclusions:** Preoperative anxiety in young children undergoing surgery is associated with a more painful postoperative recovery and a higher incidence of sleep and other problems.

### **Editorial Comment**

The authors studied the relationship between preoperative anxiety and recovery in a large series of children undergoing tonsillectomy and adenoidectomy. They show clearly that higher levels of preoperative anxiety are associated with increased postoperative morbidity, including more pain, use of more pain medication and less sleep. The differences between the more anxious and less anxious group resolved in about 3 days.

This study is unique in that it is the only study of its kind in children. Its message is important to those of us doing surgery on children. Based on these results, it suggests the hypothesis that reducing preoperative

anxiety will lead to better outcomes in the immediate postoperative period. Hence, better preoperative preparation may yield better outcomes.

Although this result is something most pediatric urologists would support intuitively, there are some issues with the study. First, all patients had a preoperative visit to the hospital. This is not usually done for minor surgical procedures. Would this have lessened or heightened the anxiety? More important, the study design prohibited the use of preoperative sedation or parents entering the operating room with the child (except in extreme cases). Though good for the study design, this is not typical in the real world. Nearly all our patients get preoperative sedation. Would the high anxiety patients have done better if they had the benefit of preoperative sedation with an amnesic? One would guess so. Further, for purposes of the study, all patients were admitted for 24 hours postoperatively. This is not typical of the procedure that was done and might also have increased the anxiety in those patients with high anxiety to start with.

Overall, the study is fascinating and tends to agree with common perception. However, more work needs to be done to evaluate whether education and/or pharmacological interventions, which are commonly accepted as standard of care, are truly successful in improving the postoperative course of children undergoing surgery and/or whether selected populations of those most anxious would benefit even more than others.

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