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UROLOGICAL SURVEY

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STONE DISEASE

Renal Stone Epidemiology in Rochester, Minnesota: An Update

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Kidney Int. 2006; 69: 760-4

Studies in Western countries have suggested an increasing incidence of nephrolithiasis (NL) in the latter part of the 20th century. Therefore, we updated NL epidemiology data for the Rochester population over the years 1970-2000. All Rochester residents with any diagnostic code that could be linked to NL in the years of 1970, 1980, 1990, and 2000 were identified, and the records reviewed to determine if they met the criteria for a symptomatic kidney stone as defined in a previous Rochester, MN study. Age-adjusted incidence (+/-s.e.) of new onset symptomatic stone disease for men was 155.1 (+/-28.5) and 105.0 (+/-16.8) per 100,000 per year in 1970 and 2000, respectively. For women, the corresponding rates were 43.2 (+/-14.0) and 68.4 (+/-12.3) per 100,000 per year, respectively. On average, rates for women increased by about 1.9% per year (P=0.064), whereas rates for men declined by 1.7% per year (P=0.019). The overall man to woman ratio decreased from 3.1 to 1.3 during the 30 years (P=0.006). Incident stone rates were highest for men aged 60-69 years, whereas for women, they plateaued after age 30. Therefore, since 1970 overall NL incidence rates in Rochester have remained relatively flat. However, NL rates for men have declined, whereas rates for women appear to be increasing. The reasons remain to be determined.

Editorial Comment

Though most recent studies suggest an increase in the incidence of nephrolithiasis, attributed to dietary and lifestyle changes, this interesting study suggests the contrary. An increase in incidence in females is balanced by a decrease in incidence in males, leading to a flat incidence rate when compared to 30 years ago.

The authors note that affluence and dietary factors associated with higher socioeconomic status have been implicated as risk factors for stone disease. It would be important therefore to evaluate any changes in the socioeconomic status of their study group; for example has the average income, unemployment rate, average education etc. remained stable during this time period? The intriguing question remains what has changed in men from 1980 onwards that has dramatically decreased the incidence of stone disease? What has changed in women from 1970 onwards that has resulted in a dramatic increase in stone disease? Is it dietary, hormonal, environmental, iatrogenic (increased use of oral contraceptives, calcium supplements, or other agents)? The authors reported only the incidence of symptomatic stones, though they did extract all stones including those detected incidentally by high-resolution imaging technologies. It would be interesting for the investigators to report these numbers also, so as to predict the increased volume of patients being referred for prophylactic surgical and medical therapy.

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Type 2 Diabetes Increases the Risk for Uric Acid Stones

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An increased prevalence of nephrolithiasis has been reported in patients with diabetes. Because insulin resistance, characteristic of the metabolic syndrome and type 2 diabetes, results in lower urine pH through impaired kidney ammoniagenesis and because a low urine pH is the main factor of uric acid (UA) stone formation, it was hypothesized that type 2 diabetes should favor the formation of UA stones. Therefore, the distribution of the main stone components was analyzed in a series of 2464 calculi from 272 (11%) patients with type 2 diabetes and 2192 without type 2 diabetes. The proportion of UA stones was 35.7% in patients with type 2 diabetes and 11.3% in patients without type 2 diabetes ($P < 0.0001$). Reciprocally, the proportion of patients with type 2 diabetes was significantly higher among UA than among calcium stone formers (27.8 versus 6.9%; $P < 0.0001$). Stepwise regression analysis identified type 2 diabetes as the strongest factor that was independently associated with the risk for UA stones (odds ratio 6.9; 95% confidence interval 5.5 to 8.8). The proper influence of type 2 diabetes was the most apparent in women and in patients in the lowest age and body mass index classes. In conclusion, in view of the strong association between type 2 diabetes and UA stone formation, it is proposed that UA nephrolithiasis may be added to the conditions that potentially are associated with insulin resistance. Accordingly, it is suggested that patients with UA stones, especially if overweight, should be screened for the presence of type 2 diabetes or components of the metabolic syndrome.

Editorial Comment

As obesity, the metabolic syndrome and type 2 diabetes increase in prevalence in the Western world, newly recognized associated morbidities continue to increase the impact on patients and healthcare. This article demonstrates a strong link between uric acid urolithiasis and type 2 diabetes. The hypothesis rests in the lower urine pH noted in type 2 diabetes predisposing to uric acid stone formation. The authors combined calcium oxalate and calcium phosphate stones into one group: “calcium-stones”, though calcium oxalate stones are predisposed to formation in more acidic urine while calcium phosphate stones are predisposed to formation in more alkaline urine. A repeat analysis separating these two stone compositions may be of benefit. In the small group of patients (25) with type 2 diabetes who underwent urinary evaluations, the urine pH was comparable to patients without diabetes who formed uric acid stones, raising questions regarding the validity of the hypothesis proposed. Though the pathophysiology may not be clear, the 7-fold risk of a uric acid stone composition in type 2 diabetes suggests a strong link, and supports the recommendation that uric acid stone formers be screened for the metabolic syndrome.

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ENDOUROLOGY & LAPAROSCOPY

Retrospective Comparison of Retroperitoneal Laparoscopic Versus Open Dismembered Pyeloplasty for Ureteropelvic Junction Obstruction

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Purpose: We evaluated the clinical value of retroperitoneal laparoscopic dismembered pyeloplasty for ureteropelvic junction obstruction compared with open surgery.
Materials and methods: The clinical data of 56 patients who underwent retroperitoneal laparoscopic dismembered pyeloplasty were retrospectively compared with those of 40 patients who underwent open dismembered pyeloplasty through a retroperitoneal flank approach. The Student t test, Pearson chi-square test and Mann-Whitney rank sum test were applied for statistical analysis as appropriate.
Results: Patient demographic data were similar between the 2 groups. In the laparoscopic group operative time (80 vs 120 minutes), estimated blood loss (10 vs 150 ml), recovery of intestinal function (1 vs 2 days), analgesic requirements (diclofenac sodium suppository) (75 vs 150 mg), incision length (3.5 vs 21 cm) and postoperative hospital stay (7 vs 9 days) were better than in the open group ($p < 0.001$ for all). No intraoperative complications occurred in either group. The incidence of postoperative complications (2 of 56, 3.6% vs 3 of 40, 7.5%, $p = 0.729$) and success rates (55 of 56, 98.2% vs 39 of 40, 97.5%, $p = 0.058$) were equivalent in the 2 groups.
Conclusions: Retroperitoneal laparoscopic dismembered pyeloplasty is a minimally invasive, safe and effective therapy for ureteropelvic junction obstruction with low morbidity, shorter convalescence and excellent outcomes, and can be accomplished reasonably quickly in experienced hands.

Editorial Comment

The new era of reconstructive surgery demonstrates the evolvement of minimally invasive approaches to the Ureteropelvic junction (UPJ) repair. In a retrospective study, the authors compared the retroperitoneal laparoscopic dismembered pyeloplasty technique to the open pyeloplasty approach with comparable results and complication rates. Significant difference between both techniques included blood loss and incision length. Moreover, Dr. Winfield discussed in his editorial comment "Management of Adult Ureteropelvic Junction Obstruction - Is it Time for a New Gold Standard?" (J. Urol, 176, September 2006, 866-867) the diversity of different surgical techniques available to repair the UPJ obstruction but caution to report post-operative success should be critically evaluated:1) objectively (nuclear renal lasix scan) and 2)subjectively (pain free post-op).

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Laparoscopic Cytoreductive Nephrectomy: The M. D. Anderson Cancer Center Experience

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Objectives: Cytoreductive nephrectomy (CN) is an integral component in treating patients with metastatic renal cell carcinoma. Critics of CN argue that perioperative morbidity or postoperative disease progression may preclude patients from receiving systemic therapy. Laparoscopic cytoreductive nephrectomy (LCN) may allow for reduced morbidity and may increase the likelihood of patients receiving systemic therapy.
Methods: From April 2001 to March 2005, 38 patients underwent LCN at our institution. We evaluated perioperative parameters such as demographics, blood loss, operative time, complications, follow-up time, interval to systemic therapy, and survival. A contemporary open cytoreductive surgery group was evaluated for comparison.
Results: The median patient age was 62 years (range 41 to 82). Most patients had a performance status of 1 or less. The median operative time was 188 minutes, and the median blood loss was 175 mL. All specimens were removed intact. The median tumor size was 8 cm (range 3.5 to 14). The median hospitalization was 3 days. Two major (5.7%) and four minor (11.4%) complications occurred, but no perioperative mortality. Postoperatively, 97.4% of patients were eligible for, or received, systemic therapy at a median of 41 days. The overall median survival was 18.1 months. In contrast to open CN, LCN resulted in decreased blood loss and hospital stay, with no differences in complications, operative time, or interval to systemic therapy.
Conclusions: LCN is a safe and effective surgical approach for select patients with metastatic renal cell carcinoma. Our results have indicated that with proper patient selection, LCN is feasible, morbidity is minimized, and systemic therapy is delivered in a timely fashion.

Editorial Comment
The new possibilities of targeted adjuvant therapy for renal cell cancer encouraged the practice of cytoreductive nephrectomy. One of the pivotal issues against this approach is the possible delay of institution of systemic therapy. With the advent of less invasive surgery, i.e.; laparoscopic cytoreductive nephrectomy, initiation of systemic therapy can be started sooner increasing the possibility of better survival.

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IMAGING

Fat Poor Renal Angiomyolipoma: Patient, Computerized Tomography and Histological Findings

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Purpose: We reviewed our experience with fat poor cases of angiomyolipoma.
Materials and methods: The records of patients with angiomyolipoma, as determined by pathological study, from 1998 to 2004 were reviewed by recording patient demographics and outcomes. Fat poor cases were defined as the failure of imaging to demonstrate fat in a lesion. Computerized tomography and histological characteristics were assessed.
Results: Histologically confirmed angiomyolipoma was found in 15 patients. Multiple lesions were found in 3 of 15 cases (20%). Of these 15 patients who underwent surgery 11 (73%) had unsuspected angiomyolipoma

due to absent fat on computerized tomography and they underwent intervention for presumed renal cell carcinoma. Mean age +/- SD in this group was 54 +/- 15 years and 8 of 11 patients (73%) were female, of whom 4 (50%) had uterine fibroids. These lesions were found incidentally in 7 of 11 cases (64%). Operative complications developed in 2 of 11 patients (18%). Average maximal diameter on pathological evaluation was 3.2 +/- 1.3 cm (range 1.5 to 6). Nonenhanced computerized tomography was available in 7 of 11 cases, of which 3 of 7 (42%) showed hyperdense lesions and 4 of 7 (57%) showed isodense lesions. The percent of fat identified per high power field was less than 25% in 12 of 13 fat poor angiomyolipoma lesions (92%) compared to 2 of 4 classic lesions (50%) known to be angiomyolipoma before surgery ($p = 0.04$).
Conclusions: We suggest that a general definition of fat poor angiomyolipoma should be the failure of imaging to reveal fat within a lesion, thus, making it unsuspected at surgery. A pathological definition should be less than 25% fat per high power field, which to our knowledge is a formerly undefined quantity. Not all cases are hyperdense on nonenhanced computerized tomography. These lesions cannot be reliably identified by imaging and they should be managed like all enhancing renal masses.

Editorial Comment
CT is the method of choice for identification of angiomyolipomas (AMLs), even those with small amounts of fat. However, 5-14% of these tumors do not present detectable fat by CT examination .Classically the finding of a homogeneously hyperdense renal mass on pre-contrast scans with homogeneously and prolonged enhancement on contrast-enhanced scans, has been considered suspicious for AML without radiological evidence of fat.
The authors present an original contribution to this subject by showing that fat poor AMLs tended to have less than 25% fat per high power field when compared with AMLs with radiological evidence of fat. We agree with the authors regarding the unreliable criteria for specific imaging diagnosis of AMLs without radiological evidence of fat. When there is no detectable fat within a single or multiple renal mass by CT, two main differential diagnoses should be considered: renal cell carcinoma and oncocytoma. Thus, CT or US-guided percutaneous biopsy of the renal mass should be performed in order to establish the correct diagnosis before surgery.

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Combined MRI and MR Spectroscopy of the Prostate before Radical Prostatectomy

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Objective: The purpose of this study was to evaluate a routine protocol for combined MR and spectroscopic imaging of the prostate for staging accuracy.
Subjects and methods: Fifty patients with biopsy-proven prostate carcinoma were examined with our sequence protocol, which consisted of T2-weighted fast spin-echo sequences and a pelvic T1-weighted spin-echo sequence. For spectroscopy, we used a 3D chemical shift imaging (CSI) spin-echo sequence. Image interpretation was performed by two radiologists. The total number of tumor voxels and tumor voxels per slice were counted to estimate the tumor volume in every patient. The potential of MR spectroscopy to differentiate between T2 and T3 tumors, based on the estimated tumor volumes, was compared with the staging performance of MRI.

Results: The MR measurement time was 19.01 minutes, and the total procedure time averaged 35 minutes. Seventy-six percent of the spectroscopic examinations were successful. Statistically significant differences in the number of tumor voxels per slice and tumor volumes were found between T2 and T3 tumors. The descriptive parameters of MRI and MR spectroscopy did not differ significantly; sensitivity and specificity were 75% and 87%, respectively, for MRI and 88% and 70%, respectively, for MR spectroscopy. The combination of both methods resulted in only a slight improvement in staging performance and was not statistically significant.
Conclusion: Combined MRI and MR spectroscopy of the prostate has no diagnostic advantage in staging performance over MRI alone. The mean tumor volumes, estimated by MR spectroscopy, differ statistically significantly between T2 and T3 tumors.

Editorial Comment

Nowadays, the ideal way to adequately stage prostate cancer is by the combination of conventional MRI techniques and 3D-MR spectroscopic imaging (MRSI).In other words, 3D-MRSI of the prostate must be done together with conventional MRI.MRSI can be useful for the diagnosis and detection of extra-prostatic disease and seminal vesicle invasion based on the capability of estimation of tumor volume and tumor location. The presence of more than 4 contiguous voxels with cancer indicates higher probability of extra-prostatic extension of the disease. The authors of this manuscript concluded that the differences of the staging performance between MRI and MRSI were not statistically significant and thus they do not recommend the routine use of their combined sequence protocol for staging purposes of patients with histologically proven prostate carcinoma. By using their spectroscopic technique, they also had relatively unexpected high rates of false positive (13%) and false negative (25%).

We must consider these data with caution since several important aspects of the technique used by the authors should be discussed since the authors used different parameters from those currently used by other investigators. First 3D-MR spectroscopic imaging is acquired by water and lipid-suppressed double-spin-echo point-resolved spectroscopy sequence, which is optimized for quantitative detection of both choline and citrate. Data sets are acquired as 16 x 8 x 8 phase-encoded spectral arrays (1024 voxels; nominal spatial resolution, 0.34 cm^3; 1000/130; acquisition time, 17 minutes. The authors used a 3D-MRSI technique where by choosing k-space-weighted acquisition, the scanning time was shorter, 10 minutes 45 seconds, for a 12 x 12 x 8 scan with a TR of 1,300 milliseconds and four averages. With the application of a Hamming filter, the voxel size was increased from a nominal 6.7 x 6.7 x 10 mm to an effective size of 10 x 10 x 15 mm corresponding to an effective volume of 1.5 cm^3. The nominal voxel size obtained by the authors was 0.45 cm^3 significantly larger than 0.34 currently used .When we increase the nominal voxel size we might expect undesirable partial volume and loss of spatial resolution. This can be considered one important drawback of their technique and perhaps could explain their higher rates of false-negatives results. Another important point to discuss is that the authors did not mention whether they replaced or not the air within the endorectal coil by liquid perfluorocarbon. Liquid perfluorocarbon is very useful to reduce the high magnetic field susceptibility at the air-tissue interface and improve the quality of MR spectroscopic imaging data (by reducing the line width). Among 50 patients evaluated in this study, the authors had only 38 patients (76%), with MR spectroscopic imaging sufficient for analysis. One might speculate that by using perfluorocarbon within the endorectal coil instead of air their results would be significantly better.

Another point that we must consider is that the authors uses a higher value of the ratio choline + creatine / citrate to consider tumor voxel. They consider, tumor voxel when the ratio of (choline + creatine) / citrate was equal to or higher than 1.1. Although there is no consensus about spectral interpretation, the classification system described by Kurhanewicz et al (1) has been used in the more recent studies on this subject. In that system, voxels are considered suspicious for cancer if the ratio of choline and creatine to citrate is at least 2 standard deviations (SDs) higher than the average ratio for the normal peripheral zone. Voxels are

considered very suspicious for cancer if the ratio of choline and creatine to citrate is higher than 3 SDs above the average ratio (equal or higher than 0.86). By using a considerably higher ratio to consider tumor voxel one could expect larger number of false negative.
In our opinion, the association of conventional MRI and 3D-MRSI is very important for the outcome of a patient with prostate cancer.

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UROGENITAL TRAUMA

Predicting Major Hemorrhage in Patients with Pelvic Fracture

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Background: Pelvic fractures can be an important source of major hemorrhage in victims of blunt trauma. However, no rapid and reliable noninvasive method exists for predicting which subjects will have major hemorrhage. The objective of this study is to use information available upon presentation to the trauma center to develop a clinical prediction rule to identify subjects with pelvic fracture who are at high risk of major hemorrhage.
Methods: A retrospective cohort study was performed on all subjects with pelvic fracture from blunt force mechanism at a single level one trauma center during a 4.3 year period. Chart review identified findings from initial pelvic radiographs and from emergency department care including mechanism of injury, and hemodynamic status. Major hemorrhage was defined by angiographic findings, transfusion requirement and pelvic hemorrhage volume. Logistic regression was used to formulate a clinical prediction rule to stratify subjects based on probability of major hemorrhage.
Results: Complete data were available on 627 of 783 eligible subjects. Predictors of major hemorrhage included emergency department hematocrit 30 or less, pulse rate of 130 or greater, displaced obturator ring fracture and pubic symphyseal wide diastasis. Combinations of predictors defined groups with probability of major hemorrhage from 1.6% to 66%.
Conclusions: Probability of major pelvic fracture related hemorrhage can be estimated from initial pelvic radiograph, pulse, and hematocrit.

Editorial Comment

When dealing with pelvic fractures and a hypotensive patient (in shock) it is essential to first determine where the bleeding is coming from, whether from the chest, abdomen or pelvis. Initial methods to determine this are by physical exam, plain films of the pelvis and chest, and FAST scan. When the bleeding source is the pelvis,

bleeding is either from a venous and/or arterial source. Pelvic fractures that increase the volume of the true pelvis can result in massive blood loss. Open book pelvic fractures are examples of potential great blood loss since a small increase in pelvis radius results in a volume increase of radius cubed. Methods to control venous bleeding then are to reduce the pelvic fracture and return the true pelvis to its original size. Such methods to reduce and stabilize pelvic fracture include pelvic binder, C clamp device, pelvic external fixation device, and internally rotating the lower legs and tying them together. For arterial bleeding, embolization of the pelvic vessels via angiography is typically needed.

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Abdominal Computed Tomographic Scan for Patients with Gunshot Wounds to the Abdomen Selected For Nonoperative Management

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J Trauma. 2005; 59: 1155-60; discussion 1160-1

Background: Computed tomographic (CT) scanning is increasingly used in patients with abdominal gunshot wounds (AGSWs) selected for nonoperative management (NOM). Triple-contrast CT scanning (i.e., intravenous, oral, and rectal) has produced encouraging initial results. The exact role and usefulness of CT scanning with intravenous contrast only is unknown.
Methods: Hemodynamically stable AGSW patients without generalized abdominal tenderness were offered a trial of NOM, underwent single-contrast (intravenous) CT scanning, and were prospectively followed from July 1, 2002, to May 31, 2004. The sensitivity and specificity of CT scanning to detect organ injuries requiring repair were calculated against the clinical results of NOM. The effect of CT scanning in management was recorded.
Results: One hundred patients with nontangential AGSWs were included. Twenty-six required laparotomy, which was nontherapeutic in five (19%). These five patients underwent operation on the basis of misleading CT findings (n = 3) or development of clinical symptoms (n = 2). Two CT scans were false-negative, and these patients were operated on at 121 and 307 minutes after arrival for hollow visceral injuries and recovered without postoperative complications. Three CT scans were false-positive and resulted in nontherapeutic laparotomies without postoperative complications. The sensitivity and specificity of CT scanning was 90.5% and 96%, respectively. CT findings resulted in a change of management in 40 patients. In nine, the decision to operate was changed to a decision to manage nonoperatively; whereas in eight, the opposite occurred. In addition, in 17, the decision to observe was changed to a decision to discharge; whereas in 1, the opposite occurred. Finally, five patients had additional tests after the findings of CT scanning.
Conclusion: Abdominal CT scanning is a safe and useful method of selecting AGSW patients for NOM. Further exploration is needed to define the precise benefits of routine CT scanning over clinical examination with selective CT scanning.

Editorial Comment

It is well accepted that most blunt trauma to solid organs can be managed effectively by a nonoperative approach. In the past, it was dogma that all penetrating injuries to the abdomen or retroperitoneum required surgical exploration. However, there is mounting evidence that in the properly selected patient, there has been a paradigm shift to an increasing nonoperative or expectant management of penetrating abdominal injuries (where the patient has no peritoneal signs and is hemodynamically stable). Overall, kidney injuries that end up needing surgical exploration is often determined by the mechanism of injury, namely, blunt trauma 2 to 4 %, stab wounds roughly 50%, and gunshot wound roughly 75%. The reason penetrating injuries more commonly require exploration is that the injuries are typically of higher Grade 3 to 5, which more commonly require exploration. Logically, grade for grade, kidney injuries should be teated the same, regardless of the mechanism. Thus, in highly select cases where the kidney is an isolated injury, expectant management can be considered. The proviso being that delayed bleeding may be more common, and secondary procedures such as selective embolization or ureteral stent placement needed in a delayed fashion.

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PATHOLOGY

A Working Group Classification of Focal Prostate Atrophy Lesions

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Focal atrophy is extremely common in prostate specimens. Although there are distinct histologic variants, the terminology is currently nonstandardized and no formal classification has been tested for interobserver reliability. This lack of standardization hampers the ability to study the biologic and clinical significance of these lesions. After informal and formal meetings by a number of the authors, focal atrophy lesions were categorized into 4 distinct subtypes as follows: (i) simple atrophy, (ii) simple atrophy with cyst formation, (iii) postatrophic hyperplasia, and (iv) partial atrophy. In phase 1 of the study, pathologists with varying levels of experience in prostate pathology were invited to view via the Internet a set of "training" images with associated descriptions of lesions considered typical of each subtype. In phase 2 of the study, each participant provided diagnoses on a series of 140 distinct "test" images that were viewed over the Internet. These test images consisted of the 4 subtypes of atrophy and images of normal epithelium, high grade prostatic intraepithelial neoplasia, and carcinoma. The diagnoses for each image from each pathologist were compared with a set of "standard" diagnoses and the kappa statistic was computed. Thirty-four pathologists completed both phases of the study. The interobserver reliability (median kappa) for classification of lesions as normal, cancer, prostatic intraepithelial neoplasia, or focal atrophy was 0.97. The median kappa for the classification of atrophy lesions into the 4

subtypes was 0.80. The median percent agreement with the standard diagnosis for the atrophy subtypes were: simple 60.6%, simple with cyst formation 100%; postatrophic hyperplasia 87.5%; partial atrophy 93.9%. The lower percentage for simple atrophy reflected a propensity to diagnose some of these as simple atrophy with cyst formation. Seven pathologists completed the phase 2 analysis a second time, and their intraobserver reproducibility was excellent. Three of 4 pathologists with low agreement with the standard diagnosis for simple atrophy improved their scores after repeating the analysis after re-examination of the "training set" of images. In conclusion, these criteria for variants of focal prostate atrophy may facilitate studies to examine the relation between various patterns of prostate atrophy and prostate cancer.

Editorial Comment

Seven pathologists with interest and expertise in genitourinary pathology took part in a sponsored meeting to present a morphological classification for prostatic atrophy: simple atrophy, postatrophic hyperplasia, simple atrophy with cyst formation and partial atrophy. Other morphological classifications for prostatic atrophy also exist (1,2). The histologic subtypes of prostatic atrophy do not represent distinct entities but a morphologic continuum of acinar atrophy (3). Subtyping atrophy is useful only to allow recognition of the lesion and to distinguish it from mimics. The study surveyed checked the inter-reproducibility among 34 pathologists from 25 different institutions from 10 different countries of the morphological classification proposed by 7 pathologists.

Prostatic atrophy is one of the most frequent benign mimickers of prostatic adenocarcinoma (4). Atrophy is commonly associated with chronic prostatitis which may have an active component characterized by presence of neutrophils. The lesion can also be the result of treatment with radiation and antiandrogens. Although many examples of atrophy are still considered idiopathic in nature, in cases of age related atrophy there is strong evidence that it may be a manifestation of chronic ischemia due to local arteriosclerosis (1).

Some reports suggest that focal atrophy may be causally linked to prostate cancer and to other pre-neoplastic lesions (5). However, other studies do not support this hypothesis (1,2). Another exciting link of atrophy is related to serum PSA levels. We have just finished in our Institution a study showing that, regardless of cause, there is a significant positive association between extent of atrophy and serum total or free PSA elevation in patients with biopsies showing no cancer, high-grade prostatic intraepithelial neoplasia (HGPIN) or areas suspicious for cancer (ASAP). The findings suggest that damaged epithelial cells in atrophic acini may be source of serum PSA elevation.

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Widespread High-Grade Prostatic Intraepithelial Neoplasia on Prostatic Needle Biopsy: A Significant Likelihood of Subsequently Diagnosed Adenocarcinoma

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In comparison with earlier studies, recent reports have demonstrated a lower incidence of prostate carcinoma after an initial diagnosis of high-grade prostatic intraepithelial neoplasia (HGPIN). The latter has led to a general tendency to reconsider the absolute need for a rebiopsy in this setting. The current retrospective study assesses the subsequent likelihood of identifying prostatic adenocarcinoma (PCa) in 41 patients with an initial diagnosis of "widespread" HGPIN defined as HGPIN present in 4 or more biopsy cores. All patients underwent at least 1 follow-up (F/U) sampling procedure in a period of 1 to 41 months. PCa was found in 16/41 patients (39%), all except 1 identified on the first F/U biopsy with the remaining patients diagnosed on a transurethral resection after a negative first F/U biopsy. All but 1 prostatic carcinoma diagnoses were obtained within 2 years from initial biopsy with 10 rendered within the first year. On average, prostate cancer was identified at 10.4 months (range: 1 to 36). One-fourth of all identified prostatic carcinomas were of Gleason score 7 or more. In 4 additional patients (9.7%), F/U biopsy revealed HGPIN with adjacent atypical small glands suspicious but not diagnostic of carcinoma (PINATYP). Of 41 patients, 10 (24.3%) continued to show HGPIN with the remaining 11/41 patients (26.8%) showing benign prostatic tissue. Patients >or=70 years of age at the time of initial biopsy had a statistically significant higher rate of PCa or HGPIN/PINATYP diagnosis on repeat biopsy compared with younger patients (P=0.02), with 55% of older men being diagnosed with cancer as compared with 33% in younger men. Patients with fewer cores sampled on initial biopsy were more likely to be diagnosed with carcinoma as opposed to HGPIN/PINATYP on F/U (P=0.015). Other factors such as the number of F/U procedures, serum prostate-specific antigen level before initial HGPIN biopsy, number of cores per F/U biopsy, and F/U interval length did not affect the likelihood of finding carcinoma. In summary, our study reveals a 39% risk of finding PCa on repeat biopsies obtained after an initial diagnosis of widespread HGPIN. Our findings support the need for a repeat biopsy in this subset of patients.

Editorial Comment

There are many evidences for the association of high-grade prostatic intraepithelial neoplasia (HGPIN) and prostatic carcinoma (1): the cytologic features are similar, both are located most frequently in the peripheral zone, both have more than 3 times the proliferative activity of benign glands, highest grade of PIN has loss of basal cell layer that is similar to carcinoma, increased frequency, extent and severity of PIN in the presence of carcinoma, age incidence peak precedes carcinoma, and similar immunophetype.

Atypical glandular proliferation, dysplastic lesion, atypical lesion, intraductal dysplasia among others were designations used to refer to this lesion. In 1989 (2), in a workshop sponsored by the American Cancer Society in Bethesda, a unified comenclature was adopted: prostatic intraepithelial neoplasia (PIN). Considering that grade 1 (low-grade) PIN has a very poor reproducibility among pathologists and a very low (if any) association to carcinoma, it is proposed to report only grade 2 or 3 PIN (high-grade PIN)

Recent reports have shown that due to an increased needle biopsy core sampling, which detects many associated cancers on initial biopsy, there is a decreased incidence of cancer following a diagnosis of HGPIN. Due to this facts, it is now recommended that men do not need routine repeat needle biopsy within the first year following the diagnosis of HGPIN (3). The study surveyed showed that there is an exception to this recommendation in case HGPIN is extensive (present in 4 or more cores). In this case there is a 39% risk of finding prostate cancer on repeat biopsies.

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INVESTIGATIVE UROLOGY

Concentration of Elastic System Fibers in the Corpus Cavernosum, Corpus Spongiosum, and Tunica Albuginea in the Rabbit Penis

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The corpus cavernosum (CC) extracellular matrix is essential for normal penile erection and is implicated in erectile dysfunction. Although investigations of these issues have used the rabbit CC, organization of its components is not well known to date. We characterized and quantified the volumetric density (Vv) of the elastic system fibers in the corpus spongiosum (CS), CC and tunica albuginea (TA) of the rabbit penis. Adult New Zealand rabbits (n = 10) were used. The penile mid-shaft fragments were fixed with 4% phosphate-buffered formalin solution and/or Bouin's liquid for 24-48 h, and processed using standard histological techniques. The sections were stained with Weigert's Fucsin-Resorcin with previous oxidation. The elastic system fibers Vv (%) was determined in 25 random fields of each fragment, using the M-42 test grid. The histochemical methods detected elastic system fibers in CS, CC and TA of all animals. The Vv of elastic fibers average was 25.03+/-2.0% for CC, 32.23+/-1.41% for CS and 22.38+/-3.61% for TA. Results for CC and CS were not significantly different. The great amount of elastic fibers distribution beneath the endothelium suggests that these fibers may have an important role in the erection process in rabbits. The present data should therefore provide important information for devising experiments and interpreting results when using the rabbit penis as a model for penile dysfunctions, especially when making comparisons with humans.

Editorial Comment

The general understanding of the morphological changes and physiology of penile erection has been obtained considering different animal models such as rats, domestic animals, primates and rabbits. Therefore, normative data on the erectile tissue of these animals are important when studying diverse physiological situations and experimental pathological conditions, and comparing the findings obtained with findings in humans.

The purpose of this study was to better understanding the rabbit penis using morphometrical analysis of the elastic fibers in the corpus spongiosum (CS), corpus cavernosum (CC) and tunica albuginea (TA).

A previous study demonstrated that the volumetric density (Vv) of elastic system fibers in the rat CC was 9%, and therefore, it was concluded that the cellular and matricial components of the rat CC differ markedly from those of humans in content and organization (1). Consequently, inferences and correlations based on physiological

and pathological findings derived from experiments that use the rat as an erection model may be misleading if these differences are not considered.

In mammals, the classification of different penis types is based on erectile or connective tissue. In animals with vascular penis (rabbit or man), erection is a consequence of increase in size and hardening of the organ. In animals with a fibroelastic penis, the erection is essentially a result of length increasing, with the penis emerging from the prepuce due to sigmoid flexure straightening (2).

Interesting, the present study showed that the elastic system fibers were abundant in the CS of the rabbit, demonstrating a greater Vv in contrast to the CC and TA. It was demonstrated that the New Zealand rabbit penis is a vascular organ with prominent elastic fibers in the CS (Vv = 32.3%) and CC (Vv = 25.1%), as well as in the TA (Vv = 22.4%). It was observed a larger amount of elastic fibers in the rabbit penis than in human penis components. As the rabbit has been used as the better animal model for studying erectile function, this information is of utmost importance and should be taken into account when comparing the experimental findings with those of humans.

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Expression of COX-2 in Normal and Pyelonephritic Kidney, Renal Intraepithelial Neoplasia, and Renal Cell Carcinoma

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Eur Urol. 2006; 50: 92-7; discussion 97

Objectives: The role of inflammation in carcinogenesis is unknown. To determine the relationship between cyclooxygenase 2 (COX-2) expression, inflammation, and carcinogenesis in human renal cell carcinoma (RCC), we looked for COX-2 expression in normal and pyelonephritic kidney, renal intratubular neoplasia (RIN), and RCC tissues.
Methods: COX-2 expression was assessed immunohistochemically in tissues obtained from 20 pyelonephritic kidneys, 16 normal kidneys, 19 RIN, and 75 RCC cases.
Results: COX-2 expression was found to be positive in 64% of RCCs. It was positive in 13 chronic pyelonephritic (65%), 9 normal (56%), and 15 RIN (79%) cases. COX-2 expression was significantly higher in RCC and RIN than the normal and pyelonephritic cases ($p < 0.001$ and $p < 0.001$, respectively). No statistically significant difference was noted between RCC and RIN cases.
Conclusions: Although the function of COX-2 in tumor development has not been exactly elucidated, the increased expression of COX-2 in RIN and RCC might be a factor that may play a role in the development of RIN or progression to RCC, which warrants further research.

Editorial Comment

Results of previous studies support the importance of neovascularity in tumor growth and that cyclooxygenase 2 expression may be an important regulator of neovascularity in renal cell carcinoma. The authors of this study found that there is no significant difference between cyclooxygenase 2 expression in normal and pyelonephritic kidney tissues. It is indicative of differences in the mechanism of inflammation in pyelonephritis (infectious agents) and peritumoral inflammation occurring around the tumor due to anti-tumor immune response, which could induce cyclooxygenase 2 expression. The authors pointed out that the peritumoral kidney tissue inflammation seems to have different molecular characteristics than inflammated kidney tissue in pyelonephritis, such as increased cyclooxygenase 2 expression. Although preclinical and in the experimental setting, this paper opens new avenue in the treatment of renal cell carcinoma, that is the use of cyclooxygenase 2 inhibitors.

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RECONSTRUCTIVE UROLOGY

Botulinum Toxin Injections for Neurogenic and Idiopathic Detrusor Overactivity: A Critical Analysis of Results

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Eur Urol. 2006; 50: 684-709; discussion 709-10

Objective: In recent years there has been an increasing use of the botulinum neurotoxins for the management of conditions characterised by detrusor overactivity. Early studies showed promising results in an area where few options previously existed between pharmacotherapy and surgery. This has led to an urgent need to assess the wide range of techniques and therapies available, as well as the efficacy and tolerability of the treatment. We performed a critical analysis of the numerous clinical studies for this novel treatment option in the management of neurogenic and idiopathic detrusor overactivity, with a view to directing further research and assisting urologists in the management of these conditions.
Methods: A systematic review of the literature, as well as a search for abstracts presented to relevant peer-reviewed meetings, was performed. All articles from 1988 onwards were included, prior to which no articles describing urologic use of botulinum neurotoxins had been published, although the majority of the articles have been published since 2000.
Results and Conclusions: Although many of the studies were small, overwhelming evidence supports the efficacy, safety, and tolerability of the botulinum toxins, specifically serotype A, for the management of these conditions. Before this is accepted as a widespread treatment modality, good-quality evidence from large-scale randomised controlled trials is needed. These studies should identify not only the most appropriate patients to treat but also the best dose, administration technique, and frequency for treatment.

Editorial Comment

The use of botulinum toxin in the treatment of both idiopathic detrusor overactivity (IDO) and neurogenic detrusor overactivity (NDO) is well-established clinical practice. However, as it is not an approved treatment option its use still is off label.

Schurch et al. were the first to describe the potential of botulinum toxin in the field of urology (1). In their pioneering work they were able to show botulinum toxin to be an effective, minimally invasive approach in the treatment of detrusor sphincter dyssenergy.

Two recent papers by Schulte-Baukloh et al. and by Patel et al. respectively provide the most comprehensive overview of the state of the art of the field.

Schulte-Baukloh also includes a critical assessment of Capsaicin and Resiniferatoxin (RTX) as possible alternatives to botulinum toxin. However, both drugs will probably play no more than minor roles in future long-term treatments, especially due to their limited availability as released drugs.

Patel gives the most complete overview to date of all published studies on the different types of botulinum toxin.

Both papers assess, summarize and highlight the treatment effectiveness of botulinum toxin over the past 18 years. However, emphasis must again be drawn to the fact that botulinum toxin is still unlicensed and therefore off label in the field of urology.

All studies on botulinum toxin to date have found overwhelming evidence of its efficacy, safety and tolerability. Even more, its use has demonstrably led to significant improvements in the patients' quality of life - an aspect often overlooked or forgotten. On top of that, it should be noted that NOB major surgeries, in particular, can be avoided or at least be delayed through use of botulinum toxin.

Despite of all this positive evidence a lack of worldwide, multi-center, double blind, placebo-controlled clinical trials inhibits the use of botulinum toxin from being more generally accepted. Only 3 placebo-controlled studies (2 on NDO, 1 on IDO) are mentioned by Patel attesting to the urgent need of carrying out accordingly designed studies.

Consequentially, several such trials have been initiated or are under way right now. Until they will have been completed the drug should primarily be used at designated centers to increase our understanding of its properties and applications.

Comparison of the different types of botolinum toxin is difficult because of variations in their individual molecular structures and mechanisms of action. The precise mechanism underlying the effects on smooth muscle cells and the nervous system is still not fully understood - as opposed to the well-studied effect guiding the onset of action in the striated muscle - opening further fields of study.

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Neuromodulatory Therapies in Female Pelvic Medicine and Reconstructive Surgery: Biological Agents

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In recent years, important improvements in the management of patients with neurogenic or non-neurogenic detrusor overactivity and urge incontinence have been brought about by the introduction of vanilloids and botulinum toxins in urology. In this review we introduce the new therapeutic options, provides basic information, and summarize the results experienced so far.

Neobladder Emptying Failure in Males: Incidence, Etiology and Therapeutic Options

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J Urol. 2006; 176: 1468-72; discussion 1472

Purpose: Neobladder reconstruction is considered the best option for patients requiring cystectomy. Limited information is available about incidence, etiology and therapeutic options for neobladder emptying failure in males.
Materials and methods: In a retrospective study we analyzed the data of a consecutive series of 655 male patients (age range 23 to 82 years, median 63; followup range 0 to 208 months, median 36.5) who received an ileal neobladder following radical cystectomy at our institution. All patients had a complete followup until death or until December 2003. Data on all diagnostic and therapeutic procedures performed for neobladder emptying failure were collected.
Results: Of 655 patients 75 (11.5%) had at least 1 episode of failure emptying the neobladder requiring some form of therapy during followup. Failure was due to dysfunctional voiding in 23 patients (3.5%) and mechanical obstruction in 52 patients (8%). Causes of mechanical obstruction were benign strictures of the neovesicourethral anastomosis (23 patients, 3.5%) or the anterior urethra (11 patients, 1.7%), neoplastic obstruction by local tumor recurrence (13 patients, 2.0%) or a nonurological malignancy (1 patient, 0.2%), and obstruction by mucosal valves (3 patients, 0.5%) or a foreign body (1 patient, 0.2%). In 38 of 52 patients with mechanical obstruction of the neobladder outlet emptying was fully restored with endourological procedures, while in 14 of 52 patients long-term catheterization was necessary. Catheterization was the therapy of choice for all patients with dysfunctional voiding.
Conclusions: Neobladder emptying failure is of major concern but is not an argument against orthotopic diversion. The overall rate of transient or permanent neobladder emptying failure in males is high but most of the mechanical causes can be managed endoscopically, while the rate of patients with long-term catheterization for dysfunctional voiding is relatively low.

Editorial Comment

The authors report on the emptying problems in their vast experience in male patients with an orthotopic neobladder. 75 of 655 patients (11, 5%) had problems with emptying of the neobladder requiring therapy after follow up of up to 208 months. The biggest group of patients were those with a stricture of the neovesicoureteral anastomosis (3, 5%) followed by a local tumour recurrence (2, 0%) and urethral strictures (1, 7%). In the recent literature with six major retrospective publications who analyzed this issue, a rate of outlet obstruction, mainly

as anastomotic strictures was found in 4.5 – 17.5% within 6 – 8 months after the surgery. Compared to these data, the authors have only 3.5% of anastomotic strictures, which is at the lower end.

The good message about the report of these problems is that the majority of patients did regain volitional voiding, generally after one endoscopic treatment (with the exception of pelvic tumour recurrences). This led to the conclusion by the authors that despite a fairly large emptying failure in this series most of these problems were of mechanical origin and could thus be managed endoscopically.

It is of note, too, that apparently none of the anastomotic tumor recurrences was treated either surgically or by radiotherapy. One can speculate that the anastomotic tumour recurrences were a consequence of a more cranial pelvic recurrence. It may, however, also have been possible that due to the omission of endoscopy during the follow up a recurrence was only diagnosed at a time when surgery was not a possibility anymore.

From this large series one can also see that a neobladder valve obstructing the outlet can be found in male patients as well. We have seen and published obstructing ileal valves as a possible reason of urinary retention in female patients. Obstructing ileal valves seem to be a possibility in male patients as well and are leading to the same therapeutic consequence, i.e. transurethral valve resection (1). The similar observation in male patients was seen with dysfunctional voiding: It was present in 2% of male patients and almost always led to long term catheterization.

Altogether a nice series of a not so rare problem in both male and female neobladder patients. For those performing such a procedure and those dealing with these patients during follow up it is definitely a recommendable manuscript.

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UROLOGICAL ONCOLOGY

Cystectomy for Transitional Cell Carcinoma of the Bladder: Results of a Surgery Only Series in the Neobladder Era

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Purpose: We studied the effect of radical cystectomy for transitional cell carcinoma of the bladder on survival and failure patterns when the 2 surgical standards cystectomy and neobladder were combined, when possible. Materials and methods: A consecutive series of patients undergoing radical cystectomy with pelvic lymph node dissection for transitional cell carcinoma of the bladder with curative intent was analyzed. Patients with neoadjuvant radiotherapy/chemotherapy were excluded. Pathological characteristics based on the 2002 TNM system, recurrence-free/overall survival and metastatic patterns were determined.

Results: A total of 788 patients with a mean age +/- SD of 65 +/- 10 years and a mean followup of 53.5 months who underwent surgery between 1986 and 2003 were analyzed. A neobladder was constructed in 75.4% of patients. Ten-year recurrence-free and overall survival rates were 59.1% and 44.9%, respectively. Positive lymph nodes were present in 143 patients (18%). The rate of recurrence-free survival at 5 years was 82.5% for pT2a pN0, 61.9% for pT2b and pT3a pN0, and 53.1% for pT3b pN0 disease. Local and distant failure rates were 4% and 9.5% for organ confined tumors, 15.9% and 19.2% for nonorgan confined tumors, and 20.4% and 45.1% in patients with positive lymph nodes, respectively.
Conclusions: In patients with organ confined, lymph node negative transitional cell carcinoma excellent survival data can be achieved as long as the tumor is limited to the inner half of the detrusor. These data on a large group of patients support early aggressive surgical management for invasive bladder cancer. The results of this surgery only series may serve as a reference for other treatment modalities for bladder cancer.

Editorial Comment

This impressive series of cystectomy only in all stages of transitional carcinoma is certainly a reference for other treatment modalities – as the authors themselves proudly state.
Still some aspects may be worth considering. An overall tumor-specific survival rate of roughly 60% after 10 years means that 40% of patients have died of their tumor. These 40% certainly deserve more or other therapy than cystectomy only as their disease was not cured finally. Looking more closely into the N+ group with roughly 15% recurrence-free survival after already 5 years, or into the T3bN0 group with 42 % recurrence-free survival after 10 years may support this statement. Adjuvant systemic chemotherapy, still far from ideal, might be one of such therapies to consider in these high-risk patients, as recent metaanalyses suggest.

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Safety and Efficacy of Intravesical Bacillus Calmette-Guerin Instillations in Steroid Treated and Immunocompromised Patients

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Purpose: We assessed the safety and efficacy of intravesical bacillus Calmette-Guerin instillations in steroid treated and immunocompromised patients.
Materials and methods: We retrospectively reviewed the charts of 697 patients treated with bacillus Calmette-Guerin instillations at our institution from 1991 to 2004. In 24 patients (3.5%) an underlying comorbidity directly affecting the immune system was diagnosed before bacillus Calmette-Guerin administration or steroids were administered at least 6 weeks before and at the time of bacillus Calmette-Guerin instillations. The immunosuppressive effect of steroids was assessed by the percent of lymphocytes. End points were the bacillus Calmette-Guerin response at 6 months, defined as normal cystoscopy, cytology and biopsy when available, and treatment related toxicity.
Results: Four patients (17%) had active lymphoma or chronic lymphocytic leukemia during bacillus Calmette-Guerin administration and 21 (88%) had a concurrent condition for which oral steroids (11), inhaled steroids

(14) or oral and inhaled steroids (4) were administered. Patients treated with oral steroids had a lower percent of lymphocytes than patients treated with inhaled steroids and 15 age matched patients with high risk superficial bladder cancer and no steroid treatment (12.3% vs 17.5% and 18.6%, respectively). The overall bacillus Calmette-Guerin response rate at 6 months was 58%. Ten of the 24 patients had disease recurrence and 3 had disease progression at a median followup of 63.5 months (IQR 19.5, 89). One patient treated with oral steroids had self-limited febrile disease and worsening of myalgia 48 hours after his third bacillus Calmette-Guerin cycle. No other systemic adverse event following bacillus Calmette-Guerin therapy was recorded and all patients completed scheduled treatments.
Conclusions: Intravesical bacillus Calmette-Guerin is a viable therapeutic option in patients with high risk superficial bladder cancer and concomitant lymphoma or chronic lymphocytic leukemia, treatment with low dose oral steroids or treatment with inhaled steroids. The bacillus Calmette-Guerin response rate at 6 months and the side effects profile associated with bacillus Calmette-Guerin therapy in these patients were comparable to those in patients with no evidence of immunosuppression. Further studies are warranted to assess the safety and efficacy of bacillus Calmette-Guerin instillations in critically immunocompromised patients.

Editorial Comment
Intravesical BCG is the most effective immunotherapy to date. An effective immune system is deemed necessary on one hand to transfer the local immune response against live mycobacteria into efficacy against urothelial cancer and on the other hand to restrict the more or less inevitable mycobacterial colonization of the bladder and even systemic bacteremia. So what happens if the immune system is compromized?

This paper gives an important answer to this question. According to their data, no complications occurred in immunocompromized patients and even more important, no major side effects were seen.

This experience is supported by own and others personal experience in such patients. Still, from own published experiments in mice a more effective immune ablation by steriods might results in complete ineffectiveness of BCG and the risk of systemic spread, so the good results reported here might just reflect relative low immunosuppressive dose of corticosteroids.

In conclusion after careful risk and benefit evaluation BCG might be given in individual immunocompromized cases.

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NEUROUROLOGY & FEMALE UROLOGY

The Effect of Terazosin on Functional Bladder Outlet Obstruction in Women: A Pilot Study

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J Urol. 2006; 176: 1487-92

Purpose: We assessed the effect of terazosin (Hytrin®) on functional bladder outlet obstruction in women.
Materials and methods: Functional bladder outlet obstruction was defined as a maximum flow rate of less than 12 ml per second combined with a detrusor pressure at maximum flow rate of more than 20 cm H2O in pressure

flow studies in the absence of neurological disorders or mechanical causes. In a prospective pilot study 15 women with functional bladder outlet obstruction were treated with terazosin. Terazosin was initiated at 1 mg daily and gradually increased to the maintenance dose of 5 mg daily during 2 weeks. Symptoms and urodynamic parameters were assessed before and 3 to 4 weeks after the initiation of alpha-blocker therapy.
Results: While on terazosin, voiding symptoms subjectively improved greater than 50% in 10 of the 15 women ($p = 0.002$). Median maximum urethral closure pressure at rest decreased significantly from 98 to 70 cm H2O ($p = 0.001$), median maximum detrusor pressure decreased from 45 to 35 cm H2O ($p = 0.008$), median detrusor pressure at maximum flow decreased from 34 to 27 ml per second and median post-void residual urine decreased from 120 to 40 ml ($p = 0.006$ and 0.002, respectively). There was a significant increase in the median maximum flow rate from 9 to 20 ml per second and in median voided volume from 300 to 340 ml ($p = 0.0005$ and 0.021, respectively). Storage symptoms, functional urethral length and maximum cystometric capacity did not change significantly with alpha-blocker therapy ($p > 0.05$). Overall terazosin resulted in a significant improvement in symptoms and urodynamic parameters in 10 of the 15 women (67%).
Conclusions: Terazosin had a significant symptomatic and urodynamic effect in two-thirds of our patients. These results suggest that terazosin may be an effective treatment option in women with voiding dysfunction due to functional bladder outlet obstruction.

Editorial Comment

The authors review the efficacy of terazosin on functional bladder outlet obstruction in women. In this prospective study 15 women diagnosed with functional bladder outlet obstruction (as opposed to mechanical outlet obstruction) were treated with terazosin beginning at a dose of 1 mg with gradual increase to a maximum dose of 5 mg over a two week period. Patient's symptoms and urodynamic studies were assessed at the onset of the study and approximately one month after the initiation of the terazosin therapy. The authors found that two-thirds of the women had improvement in their voiding symptoms as well as an improvement in the urodynamic studies examined. Simply stated, the investigators found that terazosin had both a subjective and objective improvement in two-thirds of the study patients.

With this paper, the authors delve into the complex world of non-neurogenic female voiding dysfunction. The difficulty of diagnosis and the relative lack of understanding of this malady has been discussed in the literature (1). That only two-thirds of the patients experienced symptomatic improvement may be secondary to the potential cause of voiding dysfunction being secondary to the failure of relaxation of the striated urethral sphincter(2) The discussion section of this paper is excellent and provides a great deal of information upon which many may expand their understanding of functional bladder outlet obstruction in women.

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Prevalence and Occurrence of Stress Urinary Incontinence in Elite Women Athletes

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Objective: 1) To assess the prevalence of stress urinary incontinence (SUI) and urge urinary incontinence (UTI) in elite women athletes versus the general female population, and 2) to analyze the conditions of occurrence of urine loss in search of etiological clues in elite athletes.
Decision: An anonymous self-questionnaire was collected transversally from women aged 18 to 35 years. The exposed group was composed of elite female athletes; the non-exposed group was made up of women in the same age range accepting to answer the questionnaire.
Results: A total of 157 answers from elite athletes and 426 from control subjects were available for analysis. Urinary incontinence prevalence was 28% for athletes and 9.8% for control subjects ($p = .001$). There was no significant difference in the relative prevalence of SUI between the athletes and control subjects. Athletes reported urine loss more frequently during the second part of the training session ($p < 0.0003$), and the second part of competition ($p < 0.05$). Urinary incontinence prevalence was 9.87% in physically-active control subjects versus 9.84% in sedentary control subjects (NS). Even a small quantity of urine loss was felt to be embarrassing. Most incontinent women did not dare to speak of their condition to anybody.
Conclusions: There is a very high prevalence of urinary incontinence in women athletes. Detailed studies of the patho-physiology of this problem are necessary to formulate preventive recommendations.

Editorial Comment

As stated by the authors, this was an epidemiologic study of the presence of urinary incontinence in female athletes and a controls. The two groups were not age matched but fairly close. The authors found a statistically significant difference between athletes and physically active women with regards to the prevalence of urinary incontinence. Parity was not found to be a risk factor in the elite athlete study group. Of note, though both groups complained of incontinence, < 5% of either group wore any incontinence protection such as pads or shields. It seemed, as noted in the figures of the paper, that swimmers had one of the highest rates of urinary incontinence thus giving support to those who value highly chlorinated swimming pools. In addition, there are few among the readership who would challenge the athletes participating in the fight category to their claim of 0% of urinary incontinence. It would have been of interest for the authors to have included the incontinence rates in the subgroup of elite athletes participating in gymnastics and weightlifting: the internet has provided ample pictures of ill-timed episodes of urinary loss during weightlifting competitions. It was interesting to see that when looking at the group of women who participated in physical exercise but were not classified as nationally competitive athletes, that physical activity did not seem to be a risk factor for incontinence. It will be of keen interest to examine the rate of response to pelvic floor exercise and therapy in the group of elite level national athletes; will this highly disciplined and physically trained group have a higher success rate than the general population of patients which are seen in our usual practice.

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PEDIATRIC UROLOGY

Augmentation Cystoplasty Rates at Children's Hospitals in the United States: A Pediatric Health Information System Database Study

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Purpose: We identified augmentation cystoplasty rates in children with spina bifida at children's hospitals enrolled in the Pediatric Health Information System database.
Materials and Methods: The Pediatric Health Information System database tabulates demographic and diagnostic patient data from 35 children's hospital centers in the United States. Between October 1999 and September 2004 we extracted data on 0 to 19-year-old patients with International Classification of Diseases-9 diagnosis codes for spina bifida. The International Classification of Diseases-9 procedure code for augmentation cystoplasty was cross-referenced with these patients to determine the total number of patients with augmentation, total population augmentation rates and individual institution rates of bladder augmentation.
Results: Staff at enrolled pediatric medical centers submitted inpatient data accounting for 9,059 beds servicing an aggregate metropolitan population of 82 million individuals. In the 5-year period 12,925 unique spina bifida patient encounters were identified, including 665 patients who underwent augmentation cystoplasty. The mean 5-year institutional number of augmentations performed in children with spina bifida was 20 (range 1 to 121) and the mean annual number of augmentations performed per institution was 4. The overall augmentation rate at 33 hospitals contributing data for the full years 2000 to 2003 was 5.4% (range 0.5% to 16.3%, $p < 0.0001$). The male-to-female ratio of those who underwent augmentation was 1:1.2. Median length of stay in children with augmentation was 7 days (mean 9). The median age of children with augmentation was 10.4 years, that is 11.3 years in boys and 9.8 years in girls. The difference in mean age was statistically significant ($p < 0.003$). At institutions where 10 or more augmentations were performed in 5 years (mean 27) mean patient age at operation was 10.1 years. This was significantly younger than the mean patient age of 12.3 years at hospitals where fewer than 10 augmentations (mean 5) were done in 5 years ($p < 0.05$). Conclusions: Clinical management for neurogenic bladder conditions has evolved to emphasize nonoperative management. Several studies suggest that aggressive early intervention improves bladder compliance and may protect renal function. However, results from the Pediatric Health Information System database demonstrate no change in augmentation rates during this time and they demonstrate significant interinstitutional variability. To our knowledge this represents the largest series of augmentation cystoplasty in children with spina bifida to date.

Editorial Comment
The authors review the PHIS database, which is a data set that includes 33 children's hospitals, about 70% of all free standing children's hospitals in the United States. They looked specifically at all children admitted to a hospital in their database with the diagnosis for spina bifida, between 10/1999 and 9/2004. There were 12, 925 admissions for the diagnosis of spina bifida and of these, 534 were for augmentation cystoplasty. They examined information about this procedure in particular. Some findings were pretty standard. The length of stay was around 7 days and the mean age of the patients undergoing augmentation was 11.3 for boys and 9.8 for girls. Interestingly, the rate of augmentation remained stable throughout the study period, but there were marked variations between hospitals. Also of note, the rate of augmentation in an individual hospital had little to do with the overall number of hospitalizations for spina bifida in that hospital.

These large data sets have the advantage of looking at actual practice patterns and allow for comparisons of different institutions. In these respects, studies like this are extremely useful. The finding of no change in the rate of augmentation over time is a bit disappointing in that the advent of aggressive neonatal medical management has been thought to reduce the need for augmentation. Moreover, as the life-long risks of augmentation become increasingly clear, one would guess that ever more caution would be exercised in the use of the procedure. Interestingly, this was not seen.

Also striking is the enormous variation between hospitals. One hospital did approximately 105 augmentations (of about 600 admissions) whereas during the same time period another did only about 7 (of about 550 admissions). Both are clearly high volume centers with significant interest in the care of these patients, yet with extreme variability in their urological management.

One major weakness of the data set is the lack of outcome information. What a terrific opportunity exists to look at patient reported outcomes in these two centers! Unfortunately, in this data set, the centers are de-identified. Maybe in the future someone will take this on. Until then, we await more information from striking studies like this.

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Nocturnal Enuresis in Adolescents and Adults Is Associated With Childhood Elimination Symptoms

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Purpose: Since nocturnal enuresis in adults and adolescents is rarely monosymptomatic, we identified the prevalence of childhood bladder and bowel dysfunction, and compared findings to those in a normative cohort.
Materials and Methods: Childhood and current bladder and bowel dysfunction were investigated in 56 consecutive adolescents and adults attending a public nocturnal enuresis service and in 293 normative adults using a self-administered questionnaire. Analysis involved descriptive statistics, the chi-square and Kruskal-Wallis tests, and regression analysis with $p < 0.05$ considered significant.
Results: Adolescents and adults attending a public nocturnal enuresis service had significantly higher childhood scores than normative adults, and significantly more childhood urgency, frequency, urge incontinence, infrequent voiding and small volume, high urge voids. Infrequent bowel action and fecal soiling in childhood were also significantly more common in those with nocturnal enuresis than in controls. Adult symptoms of urge incontinence, general bowel symptoms and nocturnal enuresis were significantly more common in adults and adolescents with nocturnal enuresis. Significant associations were found between childhood symptoms and adult overactive bladder, and childhood emptying dysfunction and adult voiding dysfunction. Higher childhood scores in adults and adolescents with nocturnal enuresis correlated significantly with current adult symptoms of urge, urge leakage, stress incontinence, hesitancy, incomplete emptying and UTI within the last year.
Conclusions: Significant childhood bladder and bowel symptoms along with more adult urge and bowel dysfunction were found in adults and adolescents with nocturnal enuresis. The association with adult urgency and urinary tract infection supports the likelihood of underlying bladder and or voiding dysfunction in unremitting nocturnal enuresis.

Editorial Comment

The authors report the results of two prospective questionnaire surveys, comparing adolescents and adults with nocturnal enuresis to those with a non-urological (ENT) problem. They find that older patients with nocturnal enuresis frequently have urge incontinence (45% vs. 8%) and may have bowel symptoms (16.4% vs. 12.6%). In addition, the adult patients with enuresis had markedly higher recollection of childhood problems like urgency, frequency and urge incontinence, as well as constipation and fecal soiling.

This study is another in a growing literature suggesting that adults with voiding problems, often have a history of childhood voiding and bowel problems. Although we do not know the number of children who outgrow their childhood issues and never recur as adults, it is clear that a large number of adults with problems had childhood symptoms. This emphasizes the critical need for new innovative and effective treatment modalities for children with voiding problems.

Also interesting is the finding that adults with continued nocturnal enuresis have a large likelihood of reporting symptoms of overactive bladder, despite often being labeled "monosymptomatic nocturnal enuresis." This has several implications. First, it suggests that clinicians should look harder for an urge component in children with this condition. It is probably underlying in many, but may not be symptomatic as children can control their voids and fluid intake during the day. Second, it suggests a mechanism by which the clinician can approach adults with this condition. Both anticholinergic and alpha-adrenergic blockers can reduce overactive bladder symptoms and should be considered as adjuncts in behavioral management.

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