gous). In the case of urethral replacement, these are commonly derived from culturing transitional epithelial cells obtained from a bladder biopsy. Still, these cells cannot simply be injected into the diseased urethra with any hope of successful implantation and generation of a normal appearing urethra. Instead, their growth and differentiation must be supported by a tissue matrix. The extracellular matrix comes in two varieties: an acellular heterologous collagen matrix or a biodegradable synthetic polymer matrix. Examples of collagen matrices include small intestinal submucosa (SIS) and bladder collagen matrix. The synthetic matrices are composed of polymers such as polylactic acid that can be degraded by enzymatic hydrolysis into non-toxic byproducts: carbon dioxide and water. The purpose of the extracellular matrix (whether collagen or polymer) is to provide mechanical and architectural support for native cellular ingrowth. These matrices are biodegradable so that as the patient generates his new urethra, the foreign material is resorbed.

These 3 articles tell the story of the principles that have been discovered to govern urethral engineering thus far. First, acellular matrices have been successfully used in an onlay fashion by themselves (without seeding them with transitional cells). It appears that as long as there is normal urethral epithelium along the edges of the onlay matrix graft, these cells can grow in from the edges and populate the graft. However, when matrix grafts have been used as a tubular graft (i.e. complete urethral replacement) only very short graft have been successful (0.5 cm in animal models). The utility of such short tube grafts is questionable as short defects can be bridged generally with primary anastomosis of the native urethra. Tubular grafts will likely serve their role in complete replacement of longer segments of severe urethral disease when onlay options are not available or feasible due to a lack of a dorsal plate. In such cases, it is clear that whether a biodegradable synthetic mesh or an acellular heterologous matrix graft is used it will be necessary to seed these grafts with epithelial cells.

Continued investigation in animal models and human trials will expand the role of tissue engineering for salvaging the devastated urethra.

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UROLOGICAL ONCOLOGY

High frequency of intracerebral hemorrhage in metastatic renal carcinoma patients with brain metastases treated with tyrosine kinase inhibitors targeting the vascular endothelial growth factor receptor

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Eur Urol. 2008; 53: 376-81

Objectives: To report the high incidence of intracerebral hemorrhage (ICH) in patients with metastatic renal cell carcinoma (RCC) treated with the tyrosine kinase inhibitors targeting the vascular endothelial growth factor receptor (VEGFR).
Methods and Results: Between October 2005 and December 2006, 67 patients with metastatic RCC were treated with sorafenib or sunitinib at the Montpellier Cancer Center in compassionate access programs. The

medical records of five (7%) patients who died of ICH during therapy were reviewed retrospectively. Four of them had known brain metastases. Previous radiation therapy had been indicated in two patients. Two patients had a history of hypertension. Death from ICH occurred in the first 2 wk following the onset of treatment. Three other patients with brain metastases who received sorafenib or sunitinib during the same period did not experience ICH.
Conclusions: The frequency of fatal ICH in RCC patients with brain metastases treated with tyrosine kinase inhibitors targeting the VEGFR seems high. Prospective clinical trials will be necessary for assessing the true incidence and predictive factors related to this toxicity.

Editorial Comment

Modern treatment of metastatic renal cancer involves tyrosine kinase inhibitors (TKI). This is an early report on possible lethal complications associated with this therapy in patients with brain metastases. Five cases with lethal brain hemorrhage while under TKI are reported and compared to 3 patients with brain metastases who did had not (yet) experienced any complications. No risk factors could be identified so far. Importantly, brain hemorrhage occurred within 2 – 14 days after onset of TKI medication. Urologists involved in the medical therapy of patients with renal cancer and brain metastases should be aware of immediate the risk of such complications and should report them to the community.

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Predictive factors for progression in patients with clinical stage T1a prostate cancer in the PSA era

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Objective: In the literature, most data regarding the outcome of patients with clinical stage T1a prostate cancer were established before the prostate-specific antigen (PSA) era. The aim of our study was to determine the predictive factors of progression in patients with T1a prostate cancer diagnosed in the PSA era.
Methods: Consecutive patients (n=144) with newly diagnosed T1a prostate cancer (tumor involving < or =5% of the resected prostatic tissue) were included. None of them was treated before evidence of tumor progression confirmed by prostate needle biopsies. The associations between tumor characteristics and time to cancer progression were assessed using Cox regression analysis.
Results: With a mean follow-up of 5.1 yr, 30 patients (21%) experienced cancer progression. Five adverse parameters were significantly associated with cancer progression: preoperative PSA> or =10 ng/ml, postoperative PSA> or =2 ng/ml, prostate weight > or =60 g, weight of resected tissue > or =40 g, and Gleason score> or =6. The 5-yr progression rate was 12% if fewer than two of these parameters were present, whereas it was 47% if two or more parameters were present ($p<0.001$).
Conclusion: In the PSA era the risk of progression associated with T1a prostate cancer can be predicted using five criteria, and two groups of patients can be defined. The patients at low risk of progression may be good candidates for surveillance. In those with a high risk of progression, a more aggressive treatment should be discussed.

Editorial Comment

Therapeutic options in pT1a prostate cancer vary from watchful waiting to immediate radical therapy. Because of (sometimes falsely) pathologically confirmed small tumor volume, conservative follow-up is not uncommon. These autors report on the clinical course of 144 patients with pT1a prostate cancer. This cohort is impressively low-risk with 71% Gleason score smaller or equal to 5. Still, a 25% 5 year progression rate was observed. The relative risk (RR) was increased in patients with initial PSA > 10 (RR 3.3, 40 % 5-year progression rate), Gleason score 6 or more (RR 2, 54 % 5-year progression rate) or postoperative PSA > 2 (RR 3.2, 44 % 5-year progression rate).

These figures caution anyone to recommend watchful waiting if more than 1 risk factor is involved.

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NEUROLOGY & FEMALE UROLOGY

Recurrent pseudodiverticula of female urethra: five-year experience

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Objectives: To report our experience of transvaginal diverticulectomy with pubovaginal sling placement in a series of 32 women with recurrent urethral pseudodiverticula.
Methods: A total of 32 women underwent surgical repair from January 2000 to June 2007. Of the 32 women, 12 had undergone other concomitant previous urethral surgery, predominantly for stress urinary incontinence. Transvaginal excision of the diverticulum and concomitant pubovaginal sling placement were performed routinely. The women were evaluated postoperatively for symptom relief, anatomic result, and postoperative continence status at 1, 6, and 12 months and annually thereafter. Pelvic magnetic resonance imaging was repeated after 1 year.
Results: The mean follow-up was 4.3 years. In all cases, the voiding urethrogram after catheter removal showed a good urethral shape with an absence of urinary leaks. At the postoperative urodynamic investigation, 27 patients had an unobstructed and 5 an equivocal Blaivas-Groutz nomogram. Three patients (20%) reported a persistent degree of stress urinary incontinence, including 2 with grade 1 stress urinary incontinence and 1 with mixed incontinence. Two patients presented with clinically evident diverticulum recurrence, and in 1 patient, an intraurethral diverticulum, was found at the 1-year magnetic resonance imaging examination.
Conclusions: A pubovaginal sling added routinely to all diverticulectomy procedures offers significant support to the urethral repair and/or prevention of urinary incontinence, including in recurrent cases, and does not increase the risk of erosion into the urethra or fistula formation.

Editorial Comment

The authors review a very large series of recurrent urethro-diverticula (32 women). Of note is that aside from performing the actual diverticulectomy all patients underwent a concomitant suburethral sling. With a good