Mazal et al. (1) reported that the sex-chromosome pattern in examples of bladder nephrogenic metaplastic lesions in the recipient reflected the pattern of the donor patient, and was different from the chromosome pattern of adjacent urothelium in the recipient patient. An additional support for nephrogenic adenomas arising from shed renal tubular cells is positivity for PAX2. Tong et al. (2) reported that 100% of a series of 39 examples of nephrogenic adenomas stained with PAX2, a renal transcription factor which is specific for tubular epithelium. Urothelium and prostate epithelium do not stain with this antibody. These studies support that nephrogenic adenoma is not of urothelial origin and most probably originates from implanted cells shed from renal tubules.

Devaraj et al. considered the possibility that nephrogenic adenomas arise from kidney stem/progenitor cells that retain the ability to proliferate and develop into renal tubule-like structures when implanted at a distant site. They investigated the expression of stem cell surface markers CD133 and CD44 as well as renal-specific transcription factors PAX2 and PAX8 by immunohistochemistry. Renal stem/progenitor cells have recently been identified in adult kidney tubules with several markers, including CD133 and PAX2. Stem cell markers CD44 (70%) and CD133 (28%) were identified in a subpopulation of cells in nephrogenic adenomas, all of which were also positive for renal-specific transcription factors PAX2 and PAX8. These findings suggest that nephrogenic adenomas may arise from transplantation and proliferation of primitive renal cells into an extrarenal stem cell niche.

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BASIC AND TRANSLATIONAL UROLOGY

Oestrogen receptor expression and neuronal nitric oxide synthase in the clitoris and preputial gland structures of mice

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Objective: To study the presence of oestrogen receptors (ER) and neuronal nitric oxide synthase (nNOS) in the mouse clitoris.
Materials and Methods: A series of sections of the pelvic area, including the preputial glands and clitoris, of 10 mice were assessed by immunocytochemical studies specific for ER-alpha and -beta, and nNOS; selected sections were also stained with Masson's trichrome.
Results: ER alpha was detected in the epithelium of the gland of the clitoris, and in the glandular tissue, preputial and apocrine gland. ER alpha was detected in the nuclei of stromal cells around the cavernous tissue and near the epithelium of the clitoris. Cytoplasm ER alpha was detected in a few cells in an area ventral to the clitoral

gland. There was also nuclear staining in the connective tissue cells surrounding the clitoris. Very light ER beta immunostaining was detected in the clitoris and in the tissue related to it. There were some cells with nuclear staining in the vessels of the cavernous tissue of the clitoris. nNOS immunostaining was detected in the clitoris, the preputial gland and the connective tissue.
Conclusion: ER alpha and beta isoforms, and nNOS, are present in the clitoris and preputial glands of female mice in different cellular locations and with differing levels of receptivity. Functional studies would further elucidate the role of receptor functions and their relationship to the neuronal expression of NO.

Editorial Comment

The authors are to be commended for this interesting study, which provided additional knowledge on the presence of estrogen receptors alpha (ERα) and beta (β), as well as on neuronal nitric oxide synthase (nNOS) and their relationships, in the mouse clitoris.

It was found a diffuse and deep immunostaining for ERα in the epithelium of the gland of the clitoris, and in the glandular tissue and prepuce. Also, ERα was detected in the nuclei of stromal cells around the cavernous tissue and near the epithelium of the clitoris. On the other hand, the authors found very few ERβ immunostaining in the clitoris and in the tissue related to it. However, there were some cells with nuclear staining in the vessels of the cavernous tissue of the clitoris.
In a similar pattern of ERα, although not too strong, nNOS immunostaining was detected in the clitoris, the preputial gland and connective tissue.

Concerning the epithelium of the vaginal wall, it was negative for the immunostaining for ERα and β. Membrane-based nNOS was found in the vaginal wall, and not along the upper vaginal wall, but only in one part, closest to the vaginal opening.

The authors proposed that the nuclear immunostaining for ERα in the stroma of the clitoris suggests a higher receptivity to this hormone. All receptors identified in the clitoris tended to be more intensely expressed in stromal than epithelial cells, suggesting that there is a stromal - epithelial interaction induced by the different sex steroids. ERβ immunostaining was only detected in a few cells in the vascular lumen of the cavernous tissue of the clitoris.

By contrast, with ERα, the study showed that there was no staining in the glandular tissue, epithelium or stroma of the clitoris. The authors speculate that these results suggest that ERβ is not essential for the normal functions that take place in the clitoris of the mouse.

nNOS was immunodetected with a similar pattern of distribution to that of ERα. Therefore, the authors proposed that NO might play a role in controlling blood flow and capillary permeability, the mechanisms of sexual lubrication due to cGMP action, induced by NO. The homeostasis of this system needs cGMP breakdown. It is possible that the physiological response to sexual arousal in the female follows the same biochemical pathway as in the male.

The new knowledge presented in this work, concerning the relationship of estrogen receptivity in the genital sensory field and clitoral vasculogenic processes, represent and important advance in the understanding of the presence and anatomical location of nNOS and ER isoforms.

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Natural orifice translumenal endoscopic surgery (NOTES) renal cryoablation in a porcine model

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Objective: To present our laboratory experience with natural orifice translumenal endoscopic surgery (NOTES) renal cryoablation.
Materials and Methods: In two female farm pigs, we performed four procedures of NOTES renal cryoablation. In each pig, NOTES was performed through a transgastric approach and a transvaginal approach for each kidney, respectively. The pig was placed in the flank position and pneumoperitoneum obtained using a transabdominal Veress needle. In the first pig, we started with the left kidney with a transgastric approach: a dual-channel video gastroscope (Olympus, Tokyo, Japan) was used, the stomach wall was punctured using a needle-knife, a guidewire was passed into the abdominal cavity and the access dilated using a controlled radial expansion balloon. The bowel was mobilized medially and the Gerota's fascia overlying the upper pole was dissected. Under direct endoscopic vision, a cryoablation probe was introduced percutaneously into the anterior upper pole of the kidney. The pig was then flipped to the right flank position and a transvaginal approach was used: the gastroscope was introduced through the posterior fornix of the vagina. For the second pig, we performed initially a transgastric right-side cryoablation then a transvaginal left-side cryoablation as described for the first pig.
Results: All four procedures were performed successfully, with no intraoperative complications. No additional laparoscopic ports or open conversions were necessary. The vision of the kidney and the ice-ball was adequate for all cases. The mean operative duration was 83 min. Stomach closure was tested watertight, and there were no abdominal or pelvic injuries found at autopsy.
Conclusions: NOTES can provide adequate minimal surgical dissection for safe and effective percutaneous renal cryoablation under direct videoscopic monitoring at kidney locations otherwise not accessible percutaneously. Both transgastric and transvaginal approaches can be used effectively for renal cryoablation providing a minimally invasive scar-less surgery.

Editorial Comment

This is an interesting bench to bedside research, demonstrating the usefulness of the pig model for research in endourology and videoendoscopy. It has been shown that the pig is the best animal model for translational research in urology, due to its renal similarities with humans, concerning intra-renal anatomy of collecting system, arteries and veins (1-3). Also, abdominal and pelvic cavities in pigs are similar to humans, both in volume and in organ position. So, it is possible to transpose the laboratory research to clinical setting very fast.

The present paper clearly demonstrated the feasibility of NOTES for videoendoscopic monitoring of percutaneous renal cryoablation both by transgastric and transvaginal approaches.

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UROLOGICAL ONCOLOGY

Prevalence and risk factors of bisphosphonate-associated osteonecrosis of the jaw in prostate cancer patients with advanced disease treated with zoledronate

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Background: In addition to other treatments, patients with prostate cancer (pCA) and bone metastasis receive bisphosphonates. Since 2003, a previously unknown side-effect of bisphosphonates-bisphosphonate-associated osteonecrosis of the jaws (BP-ONJ)-has been described, and frequency has since increased. An exact incidence is still unknown.
Objectives: The aim of this study was to assess the incidence and additional factors in the development of BP-ONJ.
Design, Setting, and Participants: From July 2006 to October 2007, patients with advanced pCA and osseous metastasis receiving bisphosphonate therapy in the Department of Urology or Haematology and Oncology at the Johannes-Gutenberg-University Mainz, Germany, received a dental examination. In all, 43 patients were included.
Measurements: Patients were checked for exposed bone, osteonecrosis, mucosal defects, inflammation, and oral hygiene. Further points were the applied bisphosphonate, co-medication, the duration of application, and possible trigger factors for BP-ONJ.
Results and Limitations: Eight of 43 patients developed BP-ONJ (18.6%). All patients had received zoledronate at least 14 times. Two patients had received bondronate, and one patient had received pamidronate before switching to zoledronate. All patients had had a previous tooth extraction or a denture pressure sore, and all patients had received additional chemotherapy and corticosteroids.
Conclusions: The reason for this relatively high incidence compared to other studies might be the prospective study design and thorough dental examination. In studies with such small numbers as have been published to date, nondetection or nonreported cases of BP-ONJ have an influence on the outcome. The incidence of BP-ONJ in patients with pCA might be an underestimated problem.

Editorial Comment

Bisphosphonates are widely given in patients with a high risk for, or manifest, bone metastases. In most patients with advanced prostate cancer, this drug is considered standard therapy. Recently, the risk for developing dental complications became evident but neither the true incidence nor risk factors are known. This paper helps to clarify the situation.

Nearly 19% of patients from this uncontrolled series suffered from some sort of osteonecrosis. Most were highly pretreated with biphosphonates and steroid and/or docetaxel therapy. Urologists should be aware