Urologists should differentiate high-grade Gleason score $4 + 3 = 7$ from $3 + 4 = 7$. They have different biological significance. Pathologists should always report grade 4/5 in radical prostatectomy specimens even if it corresponds to a tertiary grade.

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INVESTIGATIVE UROLOGY

The distribution of neuronal and inducible nitric oxide synthase in urethral stricture formation

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Purpose: The distribution of neuronal (n) and inducible (i) nitric oxide synthase (NOS) may have a role in the maintenance of normal urethral spongiosum and during the development of spongiofibrosis in urethral stricture disease.

Materials and Methods: Eight normal and 33 strictured human bulbar urethras were studied by histological and immunohistochemical techniques for the neuronal markers S-100, nNOS and iNOS. The smooth muscle-to-collagen ratio was calculated by morphometric analysis of Masson's trichrome sections. Immunohistochemical staining patterns of the neuronal markers in normal urethral tissue was compared to that in urethral stricture tissue with spongiofibrosis.

Results: The smooth muscle-to-collagen ratio was significantly lower in the strictured urethra compared to that in the control group ($p = 0.001$). In the strictured bulbar urethra nNOS immunoreactivity was decreased compared to that in normal urethral tissue. The severity of spongiofibrosis corresponded to the loss of nNOS immunoreactivity. iNOS immunoreactivity was found in strictured urethral epithelium and spongiosal tissue, whereas the control group was nonimmunoreactive to iNOS.

Conclusions: Urethral stricture formation is a fibrotic process associated with significant changes in NOS metabolism. Abnormal collagen synthesis following urethral trauma may be stimulated by inappropriate iNOS activity. A functional nerve supply to the urethral spongiosum seems to be crucial in the maintenance of the unique ultrastructure of the urethral spongiosum.

Editorial Comment

It is well known that in the strictured urethra the main changes are found in the extracellular matrix. As well as in other tissues, the normal urethra and spongiosal tissue must have an adequate blood supply and nerve innervation to maintain its elastic and compliant characteristics. To our knowledge, this is the first study to analyze the quality of the nerve supply of the urethral spongiosum in the normal and strictured urethra. The authors investigated the changes of neuronal and inducible nitric oxide synthase (NOS) immunoreactivity in strictured bulbar urethras with different degrees of spongiofibrosis.

Structural differences in spongiosal tissue were described previously stating that biomechanical properties required for normal urethral function differ in the spongiosal tissue of glanular, penile and bulbar segments. For this study, the authors consistently used the bulbar urethra in the stricture and control groups.

The authors found a decrease in neuronal NOS activity associated with a slight increase in inducible NOS activity and postulated that it could result in a decrease in total NOS activity, leading to abnormal collagen synthesis. They concluded that urethral stricture formation is a fibrotic process associated with significant molecular changes in NOS metabolism. Also, they found that a functional nerve supply to the urethral spongiosum seems to be crucial in the maintenance of the urethral spongiosum structure.

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Urethral dysfunction in diabetic rats

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Purpose: We investigated the effects of diabetes mellitus (DM) on urethral relaxation mechanisms during reflex bladder contractions in rats.

Materials and Methods: Five weeks after streptozotocin injection (65 mg/kg intraperitoneally) the effects of DM on urethral relaxation mechanisms were evaluated by simultaneous recordings of intravesical pressure under isovolumetric conditions and urethral perfusion pressure (UPP) using urethane anesthesia.

Results: In diabetic rats the UPP nadir during urethral relaxation and intravesical pressure thresholds for inducing urethral relaxation were significantly higher (199% and 92%, respectively) than in normal rats, while baseline UPPs were not significantly different. The mean rate and amplitude of high frequency oscillations of urethral striated muscle in diabetic rats were also significantly lower (17% and 64%, respectively) compared with normal rats. Following alpha-bungarotoxin treatment to eliminate striated muscle sphincter contractions intravenous administration of L-arginine (200 mg/kg intravesically), the substrate of nitric oxide (NO) synthase, decreased the UPP nadir (36% and 22%, in diabetic and normal rats) as well as intravesical pressure thresholds (49% and 22%, respectively). The effect was greater (61% to 126%) in diabetic rats than in normal rats. In each group of rats the effect of L-arginine was inhibited by Nomega-nitro-L-arginine (100 mg/kg intravesically), a NO synthase inhibitor.

Conclusions: During reflex bladder contractions streptozotocin induced diabetic rats exhibited smooth and striated muscle dysfunctions of the urethral outlet. L-arginine therapy, which could augment urethral smooth muscle relaxation by increasing NO production, may be useful for partially restoring the urethral relaxation mechanism in DM.

Editorial Comment

Cystopathy characterized by high post-void residual urine volume, weaken bladder sensations and diminished bladder contractility affects around 80% of patients with noninsulin dependent diabetes mellitus. However, as yet, little is known on the effects of diabetes mellitus on urethral function.

Previous studies showed that nitric oxide is the most important transmitter that induces urethral relaxation during voiding. It has also been demonstrated that relaxation responses to nitric oxide in urethral muscle strips were decreased in diabetic rabbits. Thus, the authors investigated if urethral relaxation during the voiding reflex would be decreased in diabetes mellitus. In addition, the authors evaluated the effects on diabetes mellitus induced urethral dysfunction of L-arginine treatment, a drug that can increase endogenous nitric oxide production.

The authors found that relaxation mechanisms of urethral striated and smooth muscle during reflex bladder contractions are impaired in diabetes mellitus. They proposed that this defect coupled with bladder hypoactivity could result in inefficient voiding and bladder overdistention in diabetes mellitus. The authors also proposed that therapy with L-arginine might be useful for partially restoring the urethral relaxation mechanism in diabetes mellitus.

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RECONSTRUCTIVE UROLOGY

Sexual behavior and sexual function of adults after hypospadias surgery: a comparative study

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Purpose: We assessed sexual behavior and sexual function in adults operated on for hypospadias.

Materials and Methods: Long-term psychosexual adjustment was assessed with a standardized questionnaire which was mailed to 57 patients with hypospadias older than 18 years and 60 age matched normal control subjects.

Results: A total of 37 patients with hypospadias and 39 controls participated. Self-reported strength of libido on a scale of 1 to 5 was shown to be similar in the 2 groups. Patients with hypospadias did not have problems in achieving erection and average self-rated quality of erection ranging from 1 to 5 was the same as that of controls (mean value 4.5). Patients with hypospadias noted curvature in a downward direction in a significantly higher proportion compared to controls (40% vs 18%, respectively). There were 13 patients with hypospadias who had ejaculation difficulties, of whom 6 had spraying and 7 had only dribbling of ejaculate. Patients with hypospadias masturbated significantly less often, were significantly less sexually active and had a smaller total number of sexual partners compared to control subjects. Control subjects were significantly more completely satisfied with their sexual life compared to patients with hypospadias (76.92% vs 51.35%, respectively).

Conclusions: Sexual function of patients who underwent surgery for hypospadias in general is not affected. However, there is clearly a difference in certain aspects of sexual behavior between patients with hypospadias and controls. Followup and adequate counselling of patients who underwent surgery for hypospadias in adult life is necessary.

Editorial Comment

This is a nice paper dealing with late functional aspects after early hypospadias repair. Most of the previous papers are dealing with the results regarding general appearance and urethral function in the first few years after the reconstruction. Few authors, however, thought about consequences on sexual behaviour and sexual function in adulthood.