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## INVESTIGATIVE UROLOGY

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### **Immunohistochemical Distribution of cAMP- and cGMP-Phosphodiesterase (PDE) Isoenzymes in the Human Prostate**

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**Objectives:** With the introduction of sildenafil citrate (VIAGRA trade mark), the concept of phosphodiesterase (PDE) inhibition has gained tremendous interest in the field of urology. Cyclic nucleotide second messengers cGMP and cAMP have been assumed to be involved in the control of the normal function of the prostate. The aim of the present study was to evaluate by means of immunohistochemistry the expression and distribution of some cAMP- and cGMP-PDE isoenzymes in the prostate.

**Material & Methods:** Cryostat sections (10µM) of formaldehyde-fixated tissue segments excised from the transition zone of human prostates were incubated with primary antibodies directed against the PDE isoenzymes 3, 4, 5, and 11. Then, sections were exposed to either fluorescein isothiocyanate- (FITC) or Texas Red- (TR) labeled secondary antibodies and visualization was commenced by means of laser fluorescence microscopy.

**Results:** TR-immunofluorescence indicating the presence of PDE4 (cAMP-PDE) was abundantly observed in the fibromuscular stroma as well as in glandular structures of the transition zone. In contrast to the distribution of PDE4, immunoactivity indicating PDE5 (cGMP-PDE) and 11 (dual substrate PDE) was mainly observed in glandular and subglandular areas. No immunostaining for PDE3 (cGMP-inhibited PDE) was detected.

**Conclusion:** Our results confirm the presence of PDE isoenzymes 4, 5 and 11 in the transition zone of the human prostate and present evidence that these isoenzymes are not evenly distributed. These findings are in support of the hypothesis that there might be a rationale for the use of PDE inhibitors in the pharmacotherapy of BPH and LUTS.

**Editorial Comment**

Lower urinary tract symptoms (LUTS) and erectile dysfunction (ED) association is a very much discussed theme in urology practice and many papers have been published during the last few years. Prostatic obstruction may be clinically treated either by alpha-blockers (effect on bladder neck) or by 5-alpha-reductase inhibitors (reducing effect on gland volume) (1). Recent research (2,3) suggests that the combination of an alpha-blocker and a phosphodiesterase type 5 inhibitor may be useful in patients with (LUTS) associated with erectile dysfunction. The present paper demonstrates the pharmacological background for previous clinical findings.

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**Is Pelvicaliceal Anatomy a Risk Factor for Stone Formation in Patients with Solitary Upper Caliceal Stone?**

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**Objectives:** To investigate the effect of pelvicaliceal anatomy on stone formation in patients with solitary upper caliceal stones.

**Methods:** The records of patients with solitary upper caliceal stones between 1996 and 2004 were reviewed. After the exclusion of patients with hydronephrosis, major anatomic abnormalities, noncalcium stones, metabolic abnormalities, history of recurrent stone disease, multiple stones, and previous renal surgery, 42 patients (24 male, 18 female) and 42 healthy subjects (22 male, 20 female) with normal results on intravenous pyelography (IVP) were enrolled into the study. With a previously described formula, upper pole infundibulopelvic angle (IPA), infundibular length (IL) and width (IW), and pelvicaliceal volume of the stone-bearing and contralateral normal kidney of patients and bilateral normal kidneys of healthy subjects were measured from IVP.

**Results:** Forty-two stone-bearing and 126 normal kidneys (42 contralateral, 84 healthy) were assessed. The mean stone size was 153.47 mm<sup>2</sup> (range, 20 to 896 mm<sup>2</sup>). There were no statistically significant differences in terms of upper caliceal specifications between stone-bearing and normal kidneys. The mean (+/- standard deviation) pelvicaliceal volume of 42 stone-bearing and 126 normal kidneys was 2455.2 +/- 1380.2 mm<sup>3</sup> and 1845.7 +/- 1454.8 mm<sup>3</sup>, respectively (P = 0.019). These values were 2114 +/- 2081.5 mm<sup>3</sup> (P = 0.34) and 1709.5 +/- 989.1 mm<sup>3</sup> (P = 0.001) for contralateral normal kidneys (n = 42) and normal kidneys of healthy subjects (n = 84), respectively.

Conclusions: Explanation of the etiology of the upper caliceal stone by the anatomic features is very difficult, and these caliceal anatomic variables (IPA, IL, IW) seem not to be a significant risk factor for stone formation in the upper calyx.

#### **Editorial Comment**

The study is interesting and demonstrated that there is any statistically significant difference between the stone-bearing and the normal kidneys of patients with upper caliceal stones and healthy individuals in terms of infundibulopelvic angle (IPA), infundibular length (IL) and width (IW) of upper caliceal system. Previous anatomical findings on pelvicaliceal features are well presented and discussed.

The mean pelvicaliceal volume of 42 stone-bearing was  $2455,2 \pm 1380,2$  mm<sup>3</sup> and contralateral kidneys was  $2114 \pm 2081,5$ , with no statistical difference between stone-bearing and contralateral normal kidneys ( $p=0,34$ ). When comparing to bilateral kidneys of healthy individuals not bearing stones the difference was significant. Nevertheless, as the authors stated, these finding must be viewed with caution.

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## **UROLOGICAL ONCOLOGY**

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### **Is A Second Transurethral Resection Necessary For Newly Diagnosed Pt1 Bladder Cancer?**

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Purpose: We evaluated the potential benefit of a second transurethral resection in patients with newly diagnosed pT1 transitional cell carcinoma of the bladder.

Materials and Methods: Between January 2001 and May 2003, 80 patients with stage T1 bladder cancer were included in this protocol in which all patients prospectively received second TUR within 2 to 6 weeks following the initial resection. Patients with incomplete resections were excluded from study. The pathological findings of the second TUR were reviewed.

Results: Of the 80 patients who underwent second resection, 18 (22.5%) had macroscopic tumors before resection. However, with the addition of microscopic tumors, overall residual disease was determined in 27 (33.8%) patients. Of the 27 patients 7 had pTa, 14 had pT1, 3 had pT1+pTis and 3 had pT2 disease. Residual cancers were detected in 5.8%, 38.2% and 62.5% in G1, G2 and G3 tumors, respectively. The risk of residual tumor directly correlated with the grade of the initial tumor ( $p = 0.009$ ).

Conclusions: Although second TUR dramatically changed the treatment strategy in a small percentage of cases, we strongly recommend performing second TUR in all cases of primary pT1 disease, especially in high-grade cases.

#### **Editorial Comment**

This paper highlights the usefulness of a second transurethral resection in superficial bladder cancer by providing own data and a review of the meanwhile large body of literature evidence.