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Effect of transforming growth factor ß1 and ß2 on human prostatic epithelial proliferation in culture

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Introduction: The peptide growth factors, TGF-ß1 and ß2 may have a role in the development of prostatic disease. TGF-ß1 has been described as an inhibitor of prostatic epithelial and stromal proliferation. This study aimed to determine the effects of TGF-ß1 and ß2 on epithelial proliferation directly and indirectly in co-culture with prostatic stroma.
Patients and methods: Primary cultures of human prostatic epithelium were cultured with exogenous TGF-ß1 and neutralizing antibodies (NAbs) to TGF-ß1 and ß2. The effect of varying initial cell density and varying experimental time on epithelial response to TGF-ß1 was also measured. Epithelial cells were co-cultured with stroma in the presence of TGF-ß1 NAbs. Proliferation was measured by thymidine incorporation.
Results: Exogenous TGF-ß1 (> 0·01 ng/mL) inhibited proliferation of prostatic epithelium and stroma. However, at low concentrations (< 0·01 ng/mL) TGF-ß1 stimulated epithelium up to 1·5x control. Stimulation increased with increasing initial cell density and experimental time. Addition of NAbs directly to epithelial cells caused a 3-fold increase in proliferation with TGF-ß1 NAbs ($P = 0·05$) and a 3·5-fold increase with TGF-ß 2 NAbs ($P = 0·0015$). Epithelial proliferation increased ($P = 0·008$) when co-cultured with stroma. Addition of TGF-ß1 NAbs to stroma in co-culture caused a significant increase in stromal proliferation ($P = 0·05$). However, there was no effect on the epithelium.
Conclusion: TGF-ß1 has a biphasic effect on prostatic epithelial proliferation. Epithelial secretion of TGF-ß1 and 2 has an autocrine effect on epithelial proliferation; however, stromal secretion of TGF-ß1 has no significant effect on epithelial proliferation. Such findings may be important in the development of prostatic disease.

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Normalized obstruction and contractility coefficients for detailed analysis of voiding function

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Introduction: Different algorithms for the analysis of pressure/flow studies yield different obstruction and contractility parameters. Although these parameters are highly correlated, they often rank patients differently as more or less obstructed, so that standardization is needed. Commonly used are the Abrams/Griffiths (A/G) nomogram for the definition of obstruction, and the Schäfer nomogram for grading the severity of obstruction. We show how these two algorithms can be combined to provide an easy graphical and numerical analysis, either manually or by computer. This new method has been compared with all other methods (A/G, Schäfer, URA, OBI, DAMPF) on a large patient database.
Methods: A simple algorithm is used to describe the Schäfer nomogram numerically, with respect to its grading of outlet obstruction and detrusor strength, using the separation lines between *grade II* and *III*, and between *weak* and *normal* contraction strength as reference levels. This results in two simple coefficients, which for urodynamic data above and below these reference lines are > 1 and < 1, respectively. The detrusor coefficient 0·5 differentiates between *very weak* and *weak*, and 1·5 between *normal* and *strong* contractility. The outlet coefficients corresponding to the separation lines between obstruction grades in the Schäfer nomogram are approximately: 0·5 for O/I, 0·75 for I/II, 1·5 for III/IV, 2 for IV/V, and 2·5 for V/VI. In this way, a simple continuous grading of voiding function is achieved, specific to outlet and detrusor function. These new coefficients were tested on an extensive database from more than 2000 patients.
Results: Mean values in patients with clinical 'BPH' were 1·26 for the outlet and 1·06 for the detrusor — for unobstructed and obstructed 0·82 and 1·61 for the outlet and 0·9 and 1·16 for the detrusor, respectively. Other examples were (diabetes), outlet 0·6, detrusor 0·5 = definitely unobstructed/hypocontractile detrusor; (prostatis) outlet 0·95, detrusor 1·05 = no significant obstruction/normal detrusor; (BPH, urge incontinence) outlet 2·5, detrusor 1·75 = severely obstructed/strong detrusor.
Conclusion: Our new coefficients are consistent with standard methods, but more specific and easier to determine and interpret.

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Wives notice 'prostatism' too!

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Introduction: Symptom scores have become important in the assessment of men with bladder outflow obstruction (BOO). It is well known that men may make light of their symptoms and may delay seeking medical advice. Perhaps wives or partners are a better judge of symptom severity?
Patients and methods: Four hundred men with symptomatic BOO were referred for consideration for TURP. Objective assessments included pre-and post-operative flow rates and bladder residual volume. AUA symptom scores, quality of life and bother scores were completed by patients pre-operatively and at 3 and 6 months post-operatively. Similar questionnaires were completed by the patients' partners at home, with the help of a research nurse.
Results: Pre-operatively, the mean AUA score was 18 and this decreased to 5·8 at 6 months. This corresponded to an increase in maximum urinary flow rate (Qmax) from 10·4 mL/s to 21·6 mL/s. Mean bother scores recorded by the patients fell from 16·0 to 4·8, and the quality of life score improved, with mean scores falling from 8·4 to 2·5. Similar improvements were recorded by the partners; bother scores fell from 17·4 to 3·3 and quality of life scores from 9·6 to 2·0. Generally, partners scored pre-operative symptoms more severely than their husbands, but symptom improvement following TURP was greater with lower post-operative scores.
Conclusions: The partners' perception of voiding symptoms attributable to BOO has not been studied previously. This prospective study has shown that partners regard their husbands' pre-operative symptoms as being more severe, but report a greater improvement in their post-operative symptoms. Therefore, partners are able to provide useful additional information about the symptoms suffered by men with BOO.

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A pilot study for a prostate assessment clinic for symptomatic men

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Introduction: In an attempt to relieve the workload of the general urology clinic and provide a more streamlined service for patients, a prostate assessment clinic has been set up. It is hoped that this clinic will be run by a nurse practitioner in the future.
Patients and methods: Experience of the first 100 patients was assessed (age range 22–89 years, mean 89). GP referral letters were screened by the consultants, and patients with lower urinary tract symptoms were sent for. At the clinic, patients arrived with a completed frequency/volume chart. Multiple flow rates and bladder residuals were measured, a blood sample taken for PSA + creatinine and a full history and examination performed.
Results: Of the 100 patients, 89% completed their frequency/volume chart and had complete data available. The most common main complaint of the patients were frequency and nocturia. The mean PSA

level was 4·1 ng/mL and two cases of prostate cancer were detected from the patient group: 33% of the group were eventually listed for surgery, 22% were reassured and discharged back to their GP and 23% were started on medication for their symptoms. A diagnosis of nocturnal polyuria was made in 23%.
Conclusion: The new system has made a considerable impact on the general clinical workload in the reduction of lists and the greater availability of medical staff. In all cases, a treatment decision was made within two visits. The results of this pilot study suggest that this would be an ideal area of the clinical workload that could be taken over by a nurse practitioner.

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Urodynamic grading of obstruction can predict the outcome of transurethral prostatectomy

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Introduction: A significant proportion of patients (> 25%) undergoing TURP are dissatisfied with the treatment outcome. We investigated whether the use of a urodynamic grading system for prostatic bladder outflow obstruction (BOO) can predict the outcome of TURP.
Patients and methods: Forty patients with an AUA symptom score > 12, peak flow rate (Q_{max}) < 13 mL/s and a significant residual urine volume underwent routine pressure flow studies (PFS) before undergoing TURP. The PFS data were analysed to record $p_{mu\sigma}$ (the lowest detrusor pressure at which flow starts or ends) and pdet Q_{max} (the detrusor pressure at peak flow rate). These results were used to grade the degree of obstruction into three groups: unequivocally obstructed (OB), equivocally obstructed (EQ) and unobstructed, using a modification of Schäfer's linear passive urethral resistance relation classification. Post-operative outcome was assessed at 3 months by symptom score, uroflowmetry, ultrasonography (residual urine) and PFS.
Results: The results are presented as mean (SEM) with the % change after TURP.

	OB group (n = 22)			EQ group (n = 18)		
	Pre-TURP	Post-TURP	% Change	Pre-TURP	Post-TURP	% Change
Symptom score	20·3 (1·5)	5·5 (0·4)	73	17·8 (1·1)	11·6 (0·7)	35
Q_{max} (mL/s)	9·1 (0·5)	18·2 (1·1)	100	10·2 (0·3)	13·4 (0·8)	31
Residual urine, mL	118 (8·8)	33·3 (3·2)	72	111·7 (7·2)	68·8 (3·7)	38
$p_{mu\sigma}$ cmH_2O	50·9 (2·1)	20·8 (1·5)	60	27·1 (0·9)	18·3 (0·7)	32
p_{det} Q_{max} cmH_2O	76·3 (4)	35·3 (1·8)	53	36·5 (1·5)	24·5 (1)	32

Pre-operatively, there was no significant difference (ANOVA) in the symptom score, Q_{max}, residual urine and prostatic volume between the OB and EQ groups. Weak detrusor contractility (without significant obstruction) accounted for the voiding dysfunction in 40% of the patients. Post-operatively, the improvement in all parameters was significantly better (ANOVA) in the OB group than in the EQ group. Furthermore, a subgroup of OB patients with weak detrusor contractility had a significant poorer treatment outcome.
Conclusion: The results of this study suggest that the precise grading of BOO in patients with symptomatic BPH can predict the outcome of TURP.

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Who needs follow-up after TURP? The telephone can help

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Introduction: The need for follow-up after TURP is controversial. Most patients experience a good result and will not need review; however, a significant number will suffer from persistent lower tract symptoms which require further assessment. A retrospective study was performed which agreed with previous reports, indicating that unfavourable outcome could not be predicted at the point of discharge by any pre- or post-operative parameters. Could the telephone help in reducing the number of unnecessary post-operative visits?
Patients and methods: One hundred consecutive patients undergoing TURP comprised the study. A screening telephone call was made by a urological research nurse at 3 months after the operation using a standard questionnaire. Patients requesting follow-up at this time and those with malignancy or admitted with high-pressure chronic retention were reviewed in the outpatient department.
Results: Telephone review was carried out in 23 patients; 14 had malignancy, eight were not on the 'phone and one was unable to be contacted after seven attempts. Of the remaining 77 contacted by 'phone, 61 (79%) declined further clinical review and 16 (21%) requested follow-up for persistent problems. A mean of two calls was made per patient before contact, and the mean time of each call was 6·3 min.
Conclusion: Telephone screening at 3 months successfully identified the 20–25% of patients who require out-patient review following TURP, enabling resources to be targeted towards this difficult group of patients.

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A TURP simulator – further developments

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Introduction: The evolution of fast, relatively low-cost computer graphics techniques has allowed realistic simulation in many different areas of medicine. The teaching of skills associated with TURP is likely to become a very important example of these virtual training methods.
Methods: We have developed a preliminary version of an interactive system in which a mock resectoscope may be manipulated within a simulated prostate, allowing resection and cauterization. There is provision for a degree of force feedback to the operator and the simulated interactive images are displayed on a monitor screen in a similar way to a modern video TURP.
Results: Initial results with fixed vessel walls were very encouraging. We have now added a simulation of the elastic motion of the tissues under simulated pressure from the resectoscope. The provision of suitable force feedback is felt to be important to realistic training, but requires approximate methods in a simple low-cost system. The relevant position and orientation of the resectoscope are measured using a sensing system. Generation of high-quality realistic images of the bladder wall is possible when this structure is not required to be cut or moved.
Conclusion: The system has shown teaching potential for several skills involved in TURP. The ability to display cross-sections of the prostate to assess the surgery performed is a feature not available from the real procedure but invaluable to the trainee.

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Urodynamic, ultrasonographic and cystoscopic findings: correlation with irritative symptoms following laser prostatectomy

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Objective: To prospectively correlate the results of cystoscopy, urodynamics, and symptomatology with findings of TRUS of the prostate in the evaluation of problems after laser prostatectomy.
Patients and methods: Thirty-six patients with symptomatic BPH who underwent transurethral evaporation of the prostate (TUEP) form the subjects of this study. Inclusion criteria for this study included patients with BPH with a peek flow rate (PFR) <12mL/s and IPSS score > 7. All patients underwent pre-operative evaluation with the IPSS symptom questionnaire, sexual function questionnaire; uroflowmetry and synchronous pressure-flow, EMG study, post-void residual urine (PVR) measurements. TRUS using a sector scanning probe (Sonoline SI-200, Siemens, Inc., Issaquah, WA), and cystoscopy were repeated at 1, 3,

and 6 months. TRUS lesions were classified as ***Type I***: Multiple cystic areas with no well defined channel. ***Type II***: Multiple cystic areas, some of which coalesced to form a channel defect. ***Type III***: Clearly defined channel defect which may include all or part of transition zone; rest of the prostate is normal, the channel defect may extend the entire length of prostatic urethra from bladder neck or a part of it, most often near the bladder neck. Cystoscopic lesions were classified as Type I: Large bulk (> 75%) yellow coagulated adenoma still present. Fossa still close. Type II: < 50% of yellow coagulated adenoma present. Fossa irregular but open. Partial area of reepithelization. Type III: > 5% of fossa open, clean, smooth epithelialized mucosa.
Results: (a) Laser prostatectomy at 6 months resulted in a 45% reduction in total prostate volume, 74% in IPSS score, 52% in Pdetmax, 122% improvement in PFR and 39% in bladder capacity. (b) TRUS and cystoscopic findings at various times correlated with each other and with clinical and urodynamic parameters: (c) at 1 and 3 months there was an increased incidence of detrusor instability which tended to occur more commonly with Type I TRUS lesions and correlated significantly with post-laser prostatectomy irritative voiding symptoms. (d) Type I TRUS lesions dominated in the initial month while Type II and III lesions were more common at 3 and 6 months. (e) TRUS can be used in lieu of cystoscopy and invasive urodynamics to determine status of the prostatic fossa and amount of residual tissue following laser prostatectomy.
Conclusion: This study shows that during the healing phase after prostatectomy there is a high incidence of detrusor instability which results in the irritative voiding symptoms, and that TRUS can be used in the follow-up of such patients.