Bladder Dysfunction (Paper session)

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Urological and sexual dysfunction following nerve-sparing anterior resection

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Introduction Both urological and sexual dysfunction are well documented after pelvic surgery for cancer of the rectum. In this study we used validated symptom questionnaires to assess the level of bladder and sexual dysfunction in men and women undergoing a novel method of nerve-sparing anterior resection for low rectal carcinoma.
Methods Nineteen men (age range 43–76 years) and 16 women (age range 59–78 years) undergoing anterior resection for low rectal carcinoma (height of tumour from anal verge < 10 cm) completed validated symptom questionnaires before and 3 months after surgery. Men completed the ICS-'BPH' and the International Index of Erectile Function (IIEF) questionnaires. Women completed the BFLUTS questionnaire, including questions 21–24 relating to sexual matters. Oncological results of resection were analysed for intention to treat (including curative and locally advanced disease). Patients underwent nerve-sparing anterior resection by one general surgeon, with meticulous pelvic nerve preservation and total mesorectal excision.
Results There were no significant changes between the ICS-'BPH' scores in men before and after undergoing nerve-sparing anterior resection of the rectum; the mean (SD) scores were 56 (7) and 52 (12), respectively. Two men had postoperative urinary retention which resolved before discharge. Four men reported a significant deterioration in the IIEF score after surgery. There were no significant changes between the BFLUTS scores before and after surgery, including those questions relating to sexual matters, for women undergoing nerve-sparing anterior resection of the rectum; the mean scores were 49 (6) and 51 (7), respectively. Local recurrence of rectal carcinoma occurred in one patient.
Conclusion Symptomatic bladder dysfunction following standard techniques of anterior resection is documented in half of patients 3 months after surgery. Sexual dysfunction is reported in 75% of male and 47% of female patients. Careful autonomic nerve preservation during pelvic surgery for rectal cancer reduces genitourinary morbidity without compromising the short-term oncological results.

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AUS implantation in the irradiated patient: safety, efficacy and satisfaction

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Introduction Whilst the AUS remains unsurpassed for treating urinary incontinence after prostatectomy, implantation in patients with prostate cancer and a previous history of irradiation may prove problematical. We compared the long-term outcomes of AUS implantation in patients after prostatectomy with and with no history of previous irradiation.

Patients and methods The study comprised 101 men (mean age 69 years) with urinary incontinence after prostatectomy for prostate cancer (91 radical prostatectomy, 10 TURP) who had an AUS implanted (AMS 800 model). The study subgroup comprised 24 patients (mean age 67 years) who had received adjuvant EBRT before the sphincter was implanted (a mean of 14.2 months since cancer surgery). The 77 control unirradiated patients (mean age 68 years) had the AUS implanted a mean of 13.4 months after cancer surgery. Co-morbidity was similar between the groups. Over the mean (range) follow-up of 47 (5–118) months, complication and surgical revision rates were documented, and compared between irradiated and unirradiated patients. The resolution of incontinence and patient satisfaction (assessed by a questionnaire) were also compared.
Results A total of 27 (27%) patients required AUS revision; there were no significant differences in overall revision rates between the control and study patients. However, urethral atrophy was more frequent in irradiated patients than unirradiated patients (four of 24, 17% vs seven of 77, 9%, $P = 0.01$). Infection and erosion were also more common in irradiated patients (six of 24, 25%, vs two of 77, 2.6%, $P = 0.006$). Late mechanical complications were equally common in both groups. Of 93 responding patients, 66 (71%) reported a significant improvement in continence after surgery, regardless of previous irradiation. Complete resolution of incontinence was more common in unirradiated patients (15 of 74, 20%, vs two of 19, 10%, $P = 0.03$) and incontinence remained unchanged more often in the irradiated group (three of 19, 16%, vs seven of 74, 10%, $P = 0.03$). Of the 74 unirradiated patients, 68 (92%) were satisfied with their surgical result, compared with 17 of 19 (90%) irradiated patients ($P = 0.4$). Sixty-seven (91%) unirradiated patients would have an AUS implanted again, compared with 17 of 19 irradiated patients ($P = 0.5$); 66 (89%) unirradiated patients would recommend AUS implantation to a friend, compared with 16 of 19 irradiated patients ($P = 0.2$). Of the 27 patients who required AUS revision, 24 (89%) were satisfied with the end result, 23 (85%) would undergo the procedure again and 23 would recommend the procedure to a friend, compared with 63 (95), 57 (86%) and 56 (85%) of 66 patients, respectively, who had not undergone revision ($P > 0.05$).
Conclusion Despite higher surgical complication and revision rates in patients undergoing AUS implantation with a history of previous irradiation, long-term continence and patient satisfaction appear not to be adversely affected.

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Tension-free autologous sling; early analysis of a randomized trial to compare two sling techniques in treating female stress incontinence

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Introduction The tension-free pubovaginal sling is becoming more widely adopted as a first-line therapy for genuine stress incontinence (GSI) in women. A randomized trial in two centres over 2 years compared the conventional full-length autologous sling (group A) with the short, suspended sling or 'sling on a string' (group B). We

present the early results (6 months after surgery) for 165 evaluable patients; the 1-year follow-up data will be completed in February 2000.

Patients and methods Over 2 years, 168 patients were randomized to the study. Patients with GSI were included regardless of previous surgery but patients with detrusor instability were excluded. All operations were undertaken by one of the investigators (two urologists and one gynaecologist, who standardized the operative procedures) or under their strict supervision. Evaluations before and after surgery (by an independent research team) included a 1-h pad test, pain and symptom scores, together with validated quality-of-life questionnaires (UDI and IIQ), and video-urodynamics. All adverse events during admission and after discharge for up to one year are being collected.

Results

Variable	*Group A*	*Group B*
Number	81	84
Cured of GSI (%)	83	87
Urge syndrome		
Before surgery (%)	83	87
After surgery (%)	46	40
de novo (%)	5	1
Overall satisfaction (%)	72	80
Mean improvement in		
UDI	122	114
IIQ	140	160

Conclusions These results show no significant clinical difference in outcome between the procedures (using the 95% CI). However, the shorter sling procedure is easier and marginally quicker to perform. These early results justify the adoption of the tension-free, short suspended 'sling on a string' as first-line treatment for women with GSI. This trial used independent evaluation to exclude observer bias. The results of this study should only be compared with other studies that have used similar methods of independent evaluation.

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SPARSI: an implant to empty the bladder and control incontinence without posterior rhizotomy in spinal cord injury

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Introduction The Finetech-Brindley sacral anterior root stimulator implant (SARSI) with S2–4 posterior rhizotomy (PR) for preventing detrusor hyper-reflexia (DH) is a very successful method for emptying the bladder in patients with spinal cord injury (SCI). However, PR causes loss of reflex erections and may contribute to stress urinary incontinence such that many young male patients believe that these disadvantages outweigh the benefits of SARSI. Neuromodulation through pudendal sensory nerves in the posterior sacral roots is known to profoundly suppress DH and significantly increases bladder volume in patients with SCI [*Neurourol Urodyn* 1998; 17: 411–3]. Therefore, this study aimed to combine sacral posterior and anterior root stimulation in a single implant (SPARSI) to provide better bladder management but with no rhizotomy in these patients.

Patients and methods With local ethics approval and informed consent, three complete male patients with suprasacral SCI received an extradural SPARSI. Previous neuromodulation tests showed successful suppression of DH using dorsal penile nerve stimulation. Stimulation through the implant was optimised and differentiated for both suppression of DH and effective detrusor contraction for bladder emptying.

Results In all three patients, good detrusor pressures were produced with optimised stimulation and then adjusted for the lowest pressures consistent with the best voiding pattern. Dyssynergic activity of the urethral sphincter was reduced by, among other methods, different stimulation strategies. Conditional neuromodulation produced immediate suppression of DH and significant increases in bladder volume when given unconditionally.

Conclusion This study has shown for the first time that by combining novel programmes of neurostimulation with neuromodulation in a single neuroprosthesis, complete bladder management in SCI is possible whilst preserving sacral reflexes, including those for erection.

Funding: Board of Clinical Studies, RNOH, Finetech Medical Ltd., Neuro Control

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Long-term results of detrusor myectomy

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Introduction Detrusor myectomy has obvious theoretical advantages over enterocystoplasty. The results reported by Swami *et al.* [*Br J Urol* 1998; 81: 68–72] have been very encouraging. However, the longer-term results are unknown.

Patients and methods The medical records of 23 patients who underwent the procedure between November 1992 and December 1997 in our unit were reviewed. The median (range) age was 33 (10–59) years. Seventeen patients (74%) had idiopathic detrusor overactivity (four males and 13 females) and six (26%) had neurogenic detrusor overactivity (four males and two females). The median (range) follow-up was 49 (28–75) months. All were confirmed as having detrusor overactivity on preoperative urodynamics and 21 patients underwent urodynamics postoperatively.

Results Thirteen of those with idiopathic detrusor overactivity showed continued overall symptomatic improvement, whereas all but one of the six with neurogenic detrusor overactivity required secondary procedures. There were no major complications during or after surgery. Cystometric capacity improved by a mean (range) of 168 (18–648) mL in 15 patients (71%). The voiding detrusor pressure at maximum flow ($pdetQ_{max}$) and bladder contractility index (BCI, $pdetQ_{max} + 5\,Q_{max}$) decreased by a mean (range) of 20.6 (3–70) and 49.8 (9–146) in nine and 11 of the patients, respectively. Five patients had to commence using CISC postoperatively.

Conclusions Detrusor myectomy appears to be a successful procedure in patients with idiopathic detrusor overactivity, although detrusor contractility is affected and over a third of the effectively treated patients required CISC afterward. However, the technique requires further evaluation in neuropathic patients, as the results in our series were poor.

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Bladder augmentation cystoplasty with a novel collagen membrane

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Introduction Urinary incontinence, particularly urge or mixed incontinence, has a major impact on quality of life (QoL); it can be resistant to treatment and ileocystoplasty has been the gold standard method. For some patients, previous bowel disease or surgery make ileocystoplasty inappropriate. Permacol is a sterile flexible sheet of acellular porcine dermal collagen and elastin. It is not allergenic and is resistant to collagenase. It is licensed for permanent surgical implantation and has been used within

faciomaxillary, general, cardiothoracic and urological surgery (fistulae, slings and Peyronie's disease).
Patients and methods Cystoplasty was performed by bivalving the bladder and a 7.5 mm thick piece of Permacol was sutured into the dome of the bladder; this section was then covered by omentum. The patients returned 3 weeks after surgery for a cystogram before the suprapubic catheter was removed.
Results Five incontinent female patients (mean age 47 years) with detrusor instability were treated, with a mean (range) follow-up of 8 (5–11) months. The mean hospital stay was 10 days and the suprapubic catheter was removed at 3 weeks in all cases. Follow-up urodynamics showed a stable bladder in three patients and a reduction in unstable contraction frequency and intensity in two. Symptomatically all patients are improved. Only two patients need intermittent self-catheterization. Follow-up cystoscopy showed excellent re-epithelialization of the membrane.
Conclusions Surgically the method is straightforward and saves theatre and hospital time. It does not have the potential problems of bowel segments, but does not augment the bladder to the same degree or improve compliance. Longer term results are awaited. A comparison with ileocystoplasty will be presented.

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Outcome and effectiveness of 'clam' augmentation ileocystoplasty for detrusor hyper-reflexia in spinal cord injuries

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Introduction Bladder augmentation is a well-recognised treatment option for the management of detrusor hyper-reflexia resistant to control by conservative measures. However, it has not been thoroughly evaluated in neuropathic bladders secondary to spinal injuries. We retrospectively reviewed our experience of augmentation cystoplasty in those who wished to retain continence and were prepared to perform CISC. The review comprehensively included the clinical follow-up, histological studies, and a postal questionnaire to assess quality of life (QoL) after the procedure.
Patients and methods Between 1987 and 1998, 34 patients with spinal cord injury and confirmed hyper-reflexia and small bladder capacities on video-urodynamics, and who were unable to tolerate anticholinergic suppression, underwent clam ileocystoplasty. The standard operative procedure was followed with or without a Mitrofanoff procedure. The patients were reviewed by video-urodynamics, ultrasonography and clinically at 3, 6, and 12 months, and subsequently annually. From 5 years after surgery, annual bladder biopsies were obtained for histological assessment. Finally, a detailed postal QoL questionnaire and telephone interview assessed the patients' perceptions of outcome.
Results Thirty-two patients were followed up for a mean (SD) of 6.0 (3.6) years. All are fully continent, 28 use CISC and four chose to retain their suprapubic catheters. There was a significant ($P < 0.01$) improvement in bladder capacity (mean 578 mL, SD 204) and reduction in detrusor pressure (mean 18 cmH_2O, SD 11) after surgery (before surgery, mean 156 mL, SD 85; and 102 cmH_2O, SD 36, respectively). VUR was noted in six patients before surgery and it resolved spontaneously in five; one required an injection of Macroplastique (STING). Recurrent UTIs in seven patients before surgery improved in five after the procedure. One person (3%) had new recurrent UTIs and catheter blockages, two (6%) had recurrent bladder stones, and one (3%) takes oxybutynin for residual hyper-reflexia. No upper tract changes were detected in any patient. Thirty-one patients report an excellent QoL and would recommend the procedure to others.
Conclusion Augmentation ileocystoplasty is an excellent treatment option for uncontrolled hyper-reflexia in spinally injured patients. Complete continence and low pressures without medication are achievable with few complications.

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The long-term outcome of augmentation cystoplasty

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Introduction Augmentation cystoplasty is an established procedure for the treatment of the unstable and hyper-reflexic bladder that has failed to respond to conservative treatment. There are no long-term results available, despite considerable anxieties about the long-term risks.
Patients and methods One hundred and sixty-seven patients underwent augmentation cystoplasty > 10 years ago and are available for follow-up. Of these, 66 had detrusor instability and 107 had neuropathic bladder dysfunction.
Results Overall, 89% of patients are continent. In the neuropathic bladder group, 90% are continent; 19% have also had an AUS implanted to achieve that value and 86% are using CISC to void; 21% have suffered complications including 13% stones and 2% perforations. In the detrusor instability group the continence rate is 87% and 16% use CISC to void. Complications other than failure include 6% with stones. Overall, 19% of patients had symptoms attributable to recurrent UTI. There was no incidence of malignancy in this series. The adverse affects of metabolic acidosis have not been seen since the introduction of routine bicarbonate therapy for all children and adolescents.
Conclusions Augmentation cystoplasty is a safe and effective treatment for unstable and neuropathic bladder dysfunction that carries a significant complication rate, of which the commonest complication is urinary infection.

Prostate Cancer I (Poster session)

P1

PSA requesting: screening for prostate cancer is happening

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Introduction Universal screening for prostate cancer using PSA is not currently recommended in the UK. There is considerable anecdotal evidence that it does occur. This has obvious financial implications for laboratories and resource implications for urology departments.
Method To determine the extent of PSA screening, we developed a simple tick-box questionnaire which was distributed with each PSA report to our GPs for one month. They were asked, anonymously, to provide the reasons for requesting that PSA test.
Results Of the first 100 replies, 45% of PSA requests were for urinary symptoms, 16% were requested by the patient, 9% for the monitoring of previously increased PSA levels, 8% for the follow-up of known carcinoma of the prostate, 7% for bone pain, 6% based on the patient's age alone, 2% for a general check-up, 2% for weight loss, 2% for evidence of metastases, 2% for a family history of prostate cancer and 1% for other reasons.
Conclusions From these data, at least 24% of GP requests for PSA tests are for screening purposes, either at the patient's request or at the behest of the GP. This simple questionnaire is a useful tool to explore requesting behaviour and would be valuable for auditing the extent of counselling before screening tests or the impact of the introduction of guidelines for PSA testing.

P2

Predicted impact of age-specific PSA on referrals of men with possible prostate cancer

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Introduction Despite the absence of a national screening programme for prostate cancer, more PSA tests are being requested. Many asymptomatic men with a normal DRE are being referred for prostatic biopsy solely because of an abnormal PSA result. TRUS-guided prostate biopsy is an invasive procedure with a significant morbidity and mortality rate (3.5% and 0.4%). Age-specific PSA reference ranges are believed to reduce the number of unnecessary biopsies while identifying younger patients with early prostate cancer and otherwise normal PSA levels (< 4 ng/mL). We examined the potential impact of the application of age-specific PSA ranges on the number of referrals and potential prostate cancers.
Methods Reports of all requests for PSA tests from GPs over a 15-month period were reviewed and categorized by the patient's age in decades between 50 and 80 years. For each group, the number of abnormal values was determined using current and published age-specific ranges.
Results There were 5186 PSA reports; 932 in men aged > 80 years were excluded. Of the remaining 4254, the total number of abnormal values was lower when using age-specific ranges than the current limit, i.e. 547 (12.9%) vs 782 (18.4%), respectively. However, with the former the number of abnormal values increased by 340% (22 of 444 vs 5 of 444) and 35.4% (82 of 860 vs 65), respectively, in patients aged < 50 and < 60 years.
Conclusions The application of age-specific PSA ranges reduces the abnormality rate, and potentially referrals, in older patients, while improving the identification of younger patients at risk of prostate cancer.

P3

The effect of prostatic manipulation on serum complex PSA levels

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Introduction We studied the effect of prostatic manipulation on serum complex PSA (cPSA) levels.
Patients and methods The study included a series of 92 men (58 after prostatic biopsy, 16 after DRE and 18 after flexible cystoscopy). Blood samples were taken before and 30 min after manipulation. Total and cPSA levels were measured using the Elecsys and Bayer immunoassays, respectively. The results were analysed using the Wilcoxon signed-ranked test, with $P < 0.01$ considered to indicate statistically significant differences.
Results There was a statistically significant but minimal rise in total PSA (tPSA) levels after DRE and flexible cystoscopy, with no significant increase in cPSA levels. However, prostate biopsy caused a statistically significant but minimal rise in serum cPSA levels (Table). There was no statistically significant increase in cPSA levels after prostate biopsy in 12 patients with prostate cancer (mean level before and after biopsy 33.6 ng/mL, $P > 0.01$), although there was statistically significant but minimal rise in cPSA levels in 46 patients with benign histology (mean level before biopsy 6.35 ng/mL, afterward 8.46 ng/mL, $P < 0.01$). The mean tPSA level increased from 7.26 before to 27.05 ng/mL after biopsy in patients with benign histology ($P < 0.01$) and from 33.9 to 38.5 ng/mL ($P < 0.01$) in patients with malignant histology.

Mean PSA (ng/mL)	*DRE*	*Flexible cystoscopy*	*Prostate biopsy*
Mean tPSA			
before	8.41	2.22	13.8
after	9.13	2.56	26.56
Mean cPSA			
before	5.95	1.46	12.46
after	5.98	1.44	13.77

Conclusions Prostatic manipulation has a minimal effect on serum cPSA levels. The increase in serum cPSA levels after prostate biopsy was more pronounced in patients with benign prostates. It is likely that only free PSA is released after prostatic manipulation and forms complexes in the circulation.

P4

An evaluation of complexed PSA in the diagnosis of prostatic carcinoma

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Introduction Complexed PSA (cPSA, Bayer) can be determined

using a commercial assay which measures PSA bound to carrier proteins, principally α-1-antichymotrypsin, using a 'knockout' technique. This test has been claimed by the manufacturer to have equal or better specificity than the free/total PSA (f/tPSA) ratio in the diagnosis of prostate cancer. To investigate this claim, our study compared total PSA, cPSA and f/tPSA.
Methods The study included 160 consecutive patients attending for prostatic biopsy who had tPSA values of 2.6–20 ng/mL. Blood samples were taken from the patients before TRUS-guided biopsy. The samples were then sent for processing and the results obtained correlated with the histological results of the needle biopsy.
Results In this series, 109 (68%) of the patients had benign histology and 51 (32%) had carcinoma of the prostate. The calculated sensitivity and specificity values, with the calculated area under the ROC curves, are tabulated below.

Variable	*Bayer tPSA*	*cPSA*	*Abbott tPSA*	*fPSA*	*cPSA/ tPSA*	*fPSA /tPSA*
Area under ROC curve	0.671	0.706	0.681	0.559	0.734	0.731
95% CI:						
lower	0.585	0 624	0.595	0.463	0.651	0.647
upper	0.757	0.788	0.767	0.655	0.817	0.815
Threshold at 90% sensitivity	5.09	4.73	4.14	2.19	0.783	0.245
Specificity at 90% sensitivity	33.0	46.8	24.8	17.4	37.6	32.1
Threshold at 95% sensitivity	3.97	3.54	3.61	2.67	0.735	0.304
Specificity at 95% sensitivity	17.4	24.8	15.6	7.3	22.0	15.6

Conclusions These results suggest that the diagnostic performance of cPSA is superior to standard tPSA assays. When high sensitivity is required for screening purposes, cPSA performs better than f/tPSA.

P5

Is cancer detection by PSA serendipitous in men with BPH?

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Introduction Because PSA level is strongly affected by the volume of BPH, we examined whether the diagnosis of prostate cancer in the PSA era is affected by prostate size and therefore is serendipitous in men with larger glands.
Methods Prostate volume was examined in 265 men (from the Baltimore Longitudinal Study of Aging) with no prostate cancer, and in 720 men undergoing radical prostatectomy. Volume was determined by MRI in those with no cancer and in those with cancer from the specimen weight after adjustment for seminal vesicle volume. To exclude the influence of tumour volume, only organ-confined specimens were analysed. Prostate volume in the study groups was compared using linear regression to allow for age.
Results Prostate volume was greater in men with stage T1c prostate cancer than in men without cancer ($P < 0.001$); this difference increased with age by 0.74 mL/year ($P < 0.001$), and was significant above 47 years of age. Allowing for age, prostate volume in men with stage T2 cancer was not significantly different from that in men without cancer in the pre-PSA era. Prostates in men with stage T1c cancer were 18.7 mL larger than in men with stage T2 cancer in the pre-PSA era, after allowing for age ($P < 0.001$).
Conclusions Men with cancer detected by PSA have larger prostates than men with palpable cancer and men with no cancer. Because PSA is a surrogate for prostate volume, cancer detection may be serendipitous in men with BPH.

P6

PSA screening for impalpable prostate cancer: are biopsies driven by cancer or BPH?

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Introduction PSA thresholds of < 4.0 ng/mL have been proposed for detecting impalpable prostate cancer, particularly in younger men. This study examines the relation between the detection of impalpable cancer, PSA threshold and prostate size.
Methods One hundred and six men referred for urological evaluation were prospectively recruited into the study. Sextant biopsy was undertaken in all men after PSA determination, DRE and TRUS, irrespective of the findings. Men with a history or previous clinical suspicion of prostate cancer were excluded. PSA and PSA density (PSAD) were evaluated at thresholds of 4.0 ng/mL and 0.15, respectively, in men with a normal DRE, in relation to prostate size.
Results Seventy-eight men had normal findings on a DRE and of these 15 (19%) had cancer. Of these 15, 10 had a raised PSA level and five had an abnormal PSAD. In the 64 men with a normal PSAD, there was no correlation between PSA and cancer risk (16% overall). In men with a normal PSAD and cancer, the serum PSA level was strongly correlated with prostate size ($r^2 = 0.74$, $P = 0.001$). In men with cancer, a normal PSA level was associated with smaller prostates and all had glands of < 35 mL ($P = 0.008$).
Conclusion Lower PSA threshold detect impalpable cancer in smaller prostates. In men with a normal PSAD, PSA level correlates with gland size irrespective of the presence of cancer. Therefore, in men with BPH the effect of prostate size driving biopsies may result in the serendipitous detection of cancer in larger prostates.

P7

Has the routine use of PSA significantly changed the rate of incidental cancer at TURP?

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Introduction The introduction of minimally invasive technologies and alternatives to TURP in men with LUTS has led to concern about 'missed' prostate cancer because there are no histological specimens. While incidental rates of cancer at TURP of 10–29% [*J Urol* 1997; 158: 1849–52] are reported from the pre-PSA era, the routine use of PSA in men with LUTS may have changed the profile of incidental cancer at TURP.
Methods A consecutive series of 537 patients undergoing TURP between 1996 and 1999 for LUTS with no suspicion of cancer were reviewed. The DRE and PSA level before surgery and histological specimens from TURP were reviewed.
Results Incidental (stage T1) cancer was detected in only 17 of 537 patients (3.1%). These patients had a normal DRE and PSA level or, in a few, no PSA level was recorded. Stage T1a disease was seen in 11 of 17 patients and stage T1b disease in six.
Conclusions The incidence of unexpected cancer at TURP in patients with LUTS is markedly lower in the era of widely used PSA testing. While incidental cancer still occurs in a few patients (3.1%), most of these (65%) are stage T1a and therefore less likely to undergo cancer progression [*BJU Int* 1999; 84: 1015–20]. The use of alternative treatments to TURP in men with LUTS risks missing clinically significant cancer in only a very few patients (1%).

P8

Diagnostic yield of extended core biopsies of the lateral peripheral and transition zones of the prostate in men with suspected prostate cancer

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Introduction There is concern that the widely practised technique of TRUS-guided para-sagittal sextant needle biopsies of the prostate may sometimes fail to detect the presence of cancer because of inadequate sampling of the prostate gland. Other studies have questioned the usefulness of taking routine transition zone (TZ) biopsies in men with suspected prostate cancer. We investigated whether performing two TZ and four lateral peripheral zone (PZ) biopsies in addition to routine para-sagittal sextant biopsies would improve the diagnostic yield in men with suspected prostate cancer.
Methods Two hundred and eighty-one consecutive men (mean age 69 years, SD 8.4) with elevated serum PSA levels with or without an abnormal DRE underwent TRUS-guided prostate biopsy. In addition to sextant biopsies, six further biopsies were obtained, two from the TZ (mid-gland) and four from the lateral PZ (base and mid-gland). Pathological findings for the additional biopsies were compared with those of the sextant regions.
Results Prostatic adenocarcinoma was diagnosed in 87 of 281 (31%) patients biopsied. Patients with cancer had significantly higher median PSA levels than patients with negative biopsies (16 vs 7.25 ng/mL, $P = 0.001$). One hundred and two (36%) patients had an abnormal DRE and of these 41 (40%) had cancer. Sextant biopsies were positive for cancer in 73 of 87 (84%) patients. All three sets of biopsies were positive in 28 (32%) of patients. In 58 (67%) patients both the sextant and lateral PZ biopsies were positive while in 30 (34%) men both sextant and TZ biopsies were positive. Fourteen (16%) tumours were not detected by sextant biopsies, five (6%) where the lateral PZ biopsies alone were positive and nine (10%) where the TZ biopsies only were positive.
Conclusion The addition of extended core biopsies increases the detection rate for prostate cancer by 16% when compared with the standard sextant biopsy protocol alone.

P9

The role of analgesia in TRUS of the prostate and biopsy

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Introduction TRUS of the prostate (TRUSP) and biopsy is now a routine step in the diagnosis of prostatic disease, especially prostatic carcinoma. Although there is a well recognized association with pain, TRUSP and biopsy are routinely performed with no analgesia. We prospectively compared the use of analgesia with the standard practice of no analgesia in consecutive randomized patients undergoing TRUSP and biopsy.
Patients and methods A prospective randomized study was conducted in which 50 patients were randomized equally to receive analgesia or not. All TRUSP and biopsy were performed by the same operator (A.H.) using a B&K Medical Type 2003 Ultrasound Machine and a Bard biopsy gun with an 18 G 'Trucut' needle. Any patient who had more than the standard sextant biopsy was excluded from the study. The analgesia was rectal diclofenac 100 mg, administered with antibiotic prophylaxis (750 mg ciprofloxacin orally) 1 h before the procedure. The patients were asked to indicate on a visual analogue scale (VAS, maximum score 10) directly after the procedure the degree of pain they had experienced.
Results The mean (range) pain score for those patients who received no analgesia was 3.3 (0–7) and for patients receiving analgesia was 1.72 (0–5.1); the difference was statistically significant ($P < 0.001$).
Conclusion This study shows that patients derive significant pain relief from diclofenac given 1 h before TRUSP and biopsy, and we recommend the use of analgesia for this procedure.

Testis/Testicular Cancer (Poster session)

P10

Testicular cancer and contralateral testicular biopsy in Scotland

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Introduction Patients with testicular cancer have a 3–5% risk of developing a second testicular primary. Biopsy of the contralateral testis is advocated, but its use varies. A survey of the practice of Scottish urologists is presented.
Methods A questionnaire was sent to all Scottish urologists. The actual rate of contralateral testicular biopsy was obtained from the West of Scotland germ cell tumour database.
Results Of 50 questionnaires, 33 were returned (66% response); 97% of those responding do not routinely biopsy the contralateral testis. Although 88% stated that they took a biopsy if one of the recognized risk factors was present, $< 1\%$ of patients on the West of Scotland database between 1990 and 1998 had had a contralateral biopsy taken. Although the stated reason for not taking a routine biopsy was concern about safety, only 9% had ever experienced some complication arising from testicular biopsy; 64% had never seen a significant complication; 12% performed too few biopsies to comment; 15% did not answer this question. Recently published Scottish Intercollegiate Network Guidelines were correctly recognized by 18% of respondents.
Conclusion In Scotland most urologists favour contralateral biopsy only in higher risk patients, but $< 1\%$ of patients actually undergo biopsy. Complications of biopsy are apparent rather than real. More specific guidelines directed at increasing the biopsy rate in patients at risk are required.

P11

Bilateral testicular cancer: prevention or cure?

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Introduction Of patients with a testicular germ cell tumour, 3–5% will develop a contralateral testicular primary. We retrospectively assessed all patients treated in a large cancer centre.
Results Of 570 men, 19 (3.3%) developed a secondary primary between 1989 and 1998; the mean age at diagnosis of the first tumour 30 years. The mean (range) interval between diagnoses was 76 (11–181) months. Eleven men presented with teratoma, seven with seminoma and one had synchronous bilateral teratoma. In 10 of 18 men the second primary was teratoma and in eight seminoma. Known risk factors for carcinoma *in situ* (CIS) were present in nine, a small atrophic contralateral testis in five, a family history of testicular cancer in two, infertility in two and unilateral undescended testis in one. Two had had contralateral testicular biopsies, both negative for CIS. A pathological review is underway to evaluate CIS associated with the tumours. Chemotherapy was required in eight and 14 for their first and second primaries, respectively. Eighteen of 19 men are alive and disease-free (median follow-up 51 months), but all have undergone bilateral orchidectomy and require hormone-replacement therapy.
Conclusions Chemotherapy does not prevent a second tumour. Routine follow-up does not always detect second tumours at an early stage, with most patients requiring chemotherapy. The incidence of second tumours may not justify routine contralateral biopsy, but selective biopsy may miss half of those at risk. Improved methods for detecting patients at risk of a second primary tumour are needed.

P12

Is it possible to predict the histology of tissues removed at postchemotherapy retroperitoneal lymph node dissection for metastatic testis cancer?

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Introduction After chemotherapy for metastatic nonseminomatous germ cell tumours (NSGCTs) it is usual practice to excise residual masses of > 2 cm diameter by retroperitoneal lymph node dissection (PC-RPLND). In previously reported series the histology of resected tissue reveals only necrosis/fibrosis in 12–52% of patients. In these circumstances surgical intervention could be deemed unnecessary. We analysed our database of PC-RPLND cases in an attempt to identify predictive factors for the histology of resected tissue.
Patients and methods A consecutive series of 102 men (mean age 32 years, range 15–71) with metastatic NSGCT were found to have a residual mass of > 2 cm diameter after an intensive course of platinum-based chemotherapy. All underwent PC-RPLND. The following variables were analysed to identify predictive factors for RPLND histology: patient age, primary tumour histology, prechemotherapy tumour marker levels (AFP and hCG), rate of decline of markers during chemotherapy, marker levels after chemotherapy, residual mass volume, CT characteristics and residual mass histology.
Results No significant predictive factors were identified for necrosis/fibrosis in the RPLND specimen. The presence of active malignancy in the RPLND specimen was significantly associated with patient age ($P = 0.002$) and the postchemotherapy AFP level ($P = 0.03$).
Conclusions The patient's age and elevated AFP levels are strongly correlated with active malignancy in PC-RPLND specimens. However, we identified no factors that might predict necrosis/fibrosis. All men with metastatic NSGCT should continue to undergo PC-RPLND to remove residual masses of > 2 cm diameter, as 80% should derive benefit from the surgery.

P13

The role of postchemotherapy surgery in intermediate and poor prognosis teratoma

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Introduction A 5-year survival of 48% and 79% has been reported for poor and intermediate prognosis (IGCCC category) teratoma. The optimal use of postchemotherapy surgery should contribute to improving these outcomes.
Patients Forty-seven patients (31 with poor and 16 with intermediate prognosis disease) were treated between 1990 and 1998; 43 had a testicular primary tumour and four a retroperitoneal primary.
Results Surgery was undertaken after chemotherapy (carefully

timed for each patient) in 36 (77%), some with disease at more than one site: 29 para-aortic nodes, 13 pulmonary metastases, one with retrocrural disease and one with brain disease. There was no surgical mortality. Resection was complete in 30 patients (mature teratoma in 13, necrosis in 12, cancer in five). In six patients, all of whom had residual cancer, there was a positive resection margin. Treatment for relapse was needed in 18 of the 47; four had surgery for growing mature teratoma, and 10 after further chemotherapy, surgery to remove disease at new sites (seven pulmonary, two brain and one retrocrural). Of 31 with poor prognosis and 16 with intermediate prognosis disease, 23 (74%) and 13, respectively, remain alive (median follow-up 72 months) with 33 of 47 (70%) in complete remission. Nine deaths were from disease progression, one from neutropenic sepsis and one from ischaemic heart disease.
Conclusions The optimal delivery and timing of postchemotherapy surgery (with repeated operations if necessary) by a specialist team of urological and cardiothoracic surgeons working closely with the oncologist, plays a critical role in the treatment of these patients.

P14

Response to cisplatin in testicular germ cell tumours is associated with reduced tumour telomerase activity: evidence from a xenograft model and human tumour samples

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Introduction We previously showed that cisplatin inhibits telomerase activity in testicular cancer cell lines and proposed that telomerase inhibition is a component of the efficacy of cisplatin against germ cell tumours (GCTs). In this study, we sought animal and clinical evidence for this hypothesis.
Methods The effect of cisplatin and bleomycin on telomerase activity in human testicular cancer xenograft TXF 881 tumours grown in mice was examined. Telomerase activity was also measured in normal testes (four), testicular cancer cell lines (four), primary human tumours (21) and residual retroperitoneal masses after cisplatin therapy (21). A telomerase PCR ELISA based on the telomeric repeat amplification protocol was used to measure telomerase activity.
Results Cisplatin but not bleomycin treatment was associated with a marked reduction in telomerase activity in the xenograft tumours. Moderate to high telomerase activity was found in untreated primary human tumours and normal testes with intact spermatogenesis. However, the highest levels were in testicular tumours that reactivated after chemotherapy, or in retroperitoneal masses containing active tumour after cisplatin therapy. In contrast, postchemotherapy masses containing either mature teratoma or necrotic tissue had very low or undetectable telomerase levels.
Conclusions Cisplatin but not bleomycin treatment is associated with a reduction in telomerase activity in a xenograft model of testicular cancer. The clinical response of GCTs to cisplatin is associated with a marked decline in telomerase activity. Our findings are consistent with the hypothesis that the activity of cisplatin against testicular GCTs involves telomerase inhibition.

P15

Use of a reliable immunoradiometric assay for placental alkaline phosphatase in the management of patients with seminomatous and nonseminomatous testicular cancer

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Introduction The expression of placental alkaline phosphatase (PLAP) by seminomatous testicular tumours has been known for a long time, although its use as a serum tumour marker has never become established. The principal reason for its lack of clinical utility has been the variability and inconsistency of measurements when PLAP is assayed in serum samples. Most assays have relied on the use of solid-phase antibody capture of the enzyme, followed by detection and quantification using inherent alkaline phosphatase activity upon an artificial chromatophore substrate. Although this system works it has limitations: recent studies have shown that some tumours produce a defective PLAP with little (if any) catalytic activity which will not be detected by the solid-phase capture method. Furthermore, there are sample storage problems. It is widely recognised that although PLAP is heat stable, its activity diminishes upon freeze-thawing. Therefore, relative levels of PLAP might vary because of storage conditions and not through an actual increase or decrease in PLAP antigen production by the tumour. The obvious way to overcome this problem is to measure the antigen mass of PLAP rather than its enzyme activity. Although some PLAP radio-immunoassays were developed these were often inefficient because of the difficulty in radiolabelling PLAP, which has relatively few tyrosine residues.
Method We have developed a two-site immunoradiometric assay to measure PLAP, which uses two PLAP-specific mAbs; one solid-phase antibody for capture and the second radiolabelled for detection.
Results In *in vitro* studies 70% of both seminomatous and nonseminomatous testicular tumour cell lines expressed antigenic PLAP. This was in contrast to hCG and AFP, which these tumours failed to express *in vitro*. In this study antigenically measured PLAP levels were elevated in serum from patients with seminoma or teratoma and paralleled the course of disease. Both AFP and hCG are useful markers for specific histological types of testicular tumours. If more extensive studies confirm this initial report, antigenic PLAP may prove extremely useful in the monitoring of all types of testicular tumour.
Funding: Barts JRB

P16

Effect of delay in diagnosis upon stage of testicular germ cell tumours at presentation

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Introduction Although platinum-based chemotherapy has dramatically improved the survival of patients with testicular germ cell tumours, testicular cancer remains an important cause of cancer death in men aged 15–34 years. Prognosis is stage-related and worse for those with metastatic disease. The impact on disease stage of a consultant-lead clinic offering rapid diagnosis of scrotal swellings is reported.
Method The clinical records of 926 patients attending a rapid-access testicular clinic between 1 January 1996 and 31 December 1998 were reviewed. Clinic waiting times, duration and type of symptoms, clinical findings, ultrasonography findings and interventions for all clinic attendees was recorded on a computer database by the clinic urologist at the time of attendance.
Results Thirty (3.2%) testicular germ cell tumours were diagnosed among 926 patients with testicular symptoms. The median (range) age of the patients was 27.8 (16–65) years. Nine patients (30%) had metastasis at presentation, in all cases limited to the retroperitoneum. The median (range) duration of symptoms at clinic attendance was 58 (6–720) days and the delay between referral and orchidectomy (hospital delay) 16 (6-73) days. There was no

difference in the median duration of symptoms or hospital delay between those patients with metastasis and those without. However, significantly more patients with metastasis had a wait of > 56 days from developing symptoms to orchidectomy ($P < 0.05$).
Conclusions Delay in presentation remains problematic in men with testicular cancer and may have a significant effect upon disease stage and prognosis.

P17

Intratesticular calcification is a risk factor for testicular cancer

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Introduction Calcification in the testis is encountered infrequently; it is most often a marker of benign disease but occasionally is an indicator of the presence of malignancy. The objective of this study was to evaluate the association of testicular calcification and microcalcification with testicular tumour.
Methods Over a 4-year period testicular ultrasonography performed by experienced sonographers was digitally recorded on a PACS system (Amersham, Bucks, UK); 2742 images from 2924 examinations were retrospectively reviewed by two sonographers for the presence and types of distribution of testicular calcifications. Scrotal abnormalities, if any, were also recorded.
Results The overall incidence of testicular calcification was 6.5%. The distribution was: microlithiasis 75 (2.7%); 'scrotal pearl' 50 (1.8%); epididymal calcification 34 (1.1%); extratesticular 22 (0.8%) and not microlithiasis (0.4%). There were 27 testicular tumours in this group (0.98%), of which only three were found in conjunction with microlithiasis. The association of microlithiasis with testicular cancer was statistically significant (odds ratio 4.90, Fisher's exact test $P = 0.03$). The association of testicular calcification and testicular tumours was also significant (odds ratio 45.1, Fisher's exact test $P < 0.001$).
Conclusion The association of any form of intratesticular calcification with a testicular tumour is highly significant. Patients with testicular calcification and microcalcification should be followed up.

P18

Testicular assessment ultrasonography clinic: 1000 cases

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Introduction Testicular pain or swelling is common. In December 1995, a nurse-supervised assessment service was established using ultrasonographic screening for scrotal disease.
Patients and methods Patients considered likely to have testicular cancer were given urgent clinic appointments. The remainder attended a dedicated scrotal ultrasonography session. Significant pathology was reported by the nurse specialist to the consultant in charge. Patients with 'benign' ultrasonography reports were given routine outpatient review appointments and a copy of the report sent to their GP; 1000 men (78% $<$ 50 years old) attended for assessment over a 42-month period.
Results Complete data are available for 85% of patients; 68% underwent ultrasonography within a month but 6% waited > 4 months. Forty-four patients defaulted completely and a further 207 from outpatient review after their scan. In all, 52% were discharged at the first outpatient appointment. The diagnoses were:

Finding	*Number*
Normal scan	387
Epididymal cyst	241
Varicocele	86
Hydrocele	79
Epididymitis	20
Tumour	14
Microcalcification	9
Testicular cyst	7
Intermittent torsion	5
Granuloma	4
Atrophic testis	4

Subsequently, 72 men underwent scrotal surgery.
Conclusions Demand delayed many scans beyond the 3 weeks originally intended. Most tumours seen in this period were accurately identified for urgent consultant assessment and are not included in these figures. Ultrasonography provides immediate reassurance for those with benign disease and identifies unsuspected tumours. This is an efficient way of assessing the large number of men now referred with these conditions.

P19

One-stop testicular clinic: a rapid and efficient service

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Introduction 'One-stop' clinics have been applied successfully to a variety of urological problems. We report the experience of a consultant-lead one-stop QED (Quick Early Diagnosis) testicular clinic offering scrotal ultrasonography.
Method Patients referred to the clinic between 1 January 1996 and 31 December 1998 were identified from computer records and clinical records reviewed.
Results In the period assessed, 1025 patients were referred (mean age 39 years, SD 14); 945 patients attended, of whom 926 were new presentations, and 726 (78.5%) were referred by a GP. The median (range) duration of symptoms was 60 days (7 days to 20 years). The median time from referral to the clinic visit was 10 days. Indications for referral were testicular swelling in 532 (55%), testicular pain in 158 (16%), and pain and swelling in 205 (21%). Testicular tumours were found in 32 patients (3.2%), benign scrotal lesions in 743 (80%) and normal findings in 193 (20%). After assessment, 777 patients (81%) were discharged or referred back to the GP with advice (with no further follow-up), 132 (14%) were admitted for surgery, and 58 (6%) required further follow-up or investigation.
Conclusion Scrotal swellings are a common urological problem, most of which may be managed conservatively. A one-stop testicular clinic provides efficient use of resources and patients' time, promotes early referral and reduces delays in diagnosis through immediate access to imaging facilities. Criteria for urgent referral of testicular lesions will require guidelines based on evidence from clinics such as this.

Prostate Cancer II (Poster session)

P20

Update on high- and low-penetrance genes in prostate cancer

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Introduction Prostate cancer is associated with a genetic predisposition in ≈10% of cases. Both high- and low-penetrance genes are thought to be involved. The search for these genes through linkage and association studies continues. The UK Familial Prostate Cancer study has collaborated with other centres worldwide to form the ACTANE consortium. We report the results of a linkage study at chromosome 1q42.2-43, a proposed locus for a high-penetrance prostate cancer gene, and secondly the association between polymorphisms in the low-penetrance glutathione-S-transferase (GST) genes and young onset prostate cancer.
Methods One hundred and thirty-one prostate cancer families from the ACTANE Consortium were genotyped for markers in the candidate region of 1q42.2-43 and the linkage analysed. In all, 275 young-onset prostate cancer cases (< 55 years old) and 280 controls were genotyped for polymorphisms in the GSTM1, GSTT1 and GSTP1 genes.
Results Linkage analysis yielded negative two-point and multipoint LOD scores with no support for linkage to 1q42.2-43. For the GST genes, there was no association between the GSTM1 and GSTT1 polymorphisms and the development of prostate cancer. However, the GSTP1 genotype had a significant association with prostate cancer risk: valine/valine homozygotes had maximal risk (odds ratio 1.8, 95% CI 0.04–3.06, *P*trend = 0.026.
Conclusion These data do not support the possibility of a high-penetrance gene in the 1q42.2-43 region and there are still other major susceptibility loci to be identified. Polymorphisms within low-penetrance genes such as GSTP1 may be important in the predisposition to young-onset prostate cancer, conferring a relative risk of 1.8.
Funding: CRC and PCTT

P21

Androgen-dependent regulation of MUC1 expression in prostate cancer

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Introduction MUC1 mucin over-expression is associated with poor clinical outcome in many human adenocarcinomas. This has been correlated to its anti-adhesive properties, i.e. inhibition of cell-cell, and cell-matrix adhesion. Oestrogen, progesterone and glucocorticoid responsiveness of the MUC1 gene promoter is well established but androgen-dependent regulation of MUC1 is not currently reported. MUC1 expression in prostate cancer remains virtually unexplored, and the aims of this project were therefore to define MUC1 expression in a model of prostate cancer and to investigate the effects of androgenic steroids.
Materials and methods Cancer-derived cell lines from two androgen-sensitive organs were used: (a) prostatic; LNCaP and LNCaP-r (androgen receptor, AR+), DAR17 and 19 (AR+ transfectants of the DU-145 cell line); DZeol (vector control) and DU-145 (both AR–); (b) breast: ZR-75-1, MDA-MB453, T47D (AR+); MDA-MD231 and MCF7 (AR–). These cell lines were characterised for the expression of MUC1, cytokeratin 18 and AR, using immunocytochemical immunoprecipitation and automated cell cytometry. Sex steroid-dependent changes in expression were investigated by adding DHT or R1881 (a non-metabolised androgen), oestradiol or medroxyprogesterone acetate (MPA). Receptor specificity was confirmed by the addition of 4-hydroxy-flutamide (4-OHF), a nonsteroidal AR antagonist.
Results Of the prostatic cell lines, LNCaP and LNCaP-r were MUC1 negative, as were MDA-MB231 and -MB453 of the breast lines. The addition of the AR agonists (DHT, R1881) or partial agonist (MPA) to DAR17 and 19 was associated with marked up-regulation of membranous MUC1 protein expression. Similar changes were seen in MUC1+ AR+ breast cell lines (ZR-75-1 and T47D) but not AR– (MCF7) cell lines. Androgen responsiveness of MUC1 was abolished by the addition of 4-OHF.
Conclusions This is the first report of androgen-dependent expression of MUC1 in any organ system and the first *in vitro* investigation of MUC1 in prostate cancer. Given that over-expression of MUC1 is associated with a poor prognosis in many human adenocarcinomas, the findings reported here potentially represent an important new contribution to our understanding of the mechanisms surrounding the change from noninvasive to invasive prostate cancer.
Funding: Smith & Nephew Foundation, MRC

P22

Conformational analysis of exon 9 of the Fas gene in hormone-resistant prostate cancer

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Introduction Fas is a cell-surface receptor involved in inducing apoptosis. Alterations of the Fas gene can lead to the loss of its apoptotic function and contribute to the pathogenesis of some cancers. The role of Fas-mediated apoptosis in prostate cancer is unclear. The aim of this study is to detect Fas gene alterations in hormone-resistant prostate cancers.
Materials and methods Components of the Fas/FasL apoptotic pathway were examined by immunohistochemistry in 20 paired samples from patients with prostate cancer, both before treatment with androgen withdrawal and after relapse into an androgen-resistant state. Student's *t*-test for equality of means and Pearson's correlation were used to analyse the data. The malignant cells were selectively microdissected from sections stained with haematoxylin and eosin. Conformational changes in a 150 bp segment of exon 9 (which codes for the functionally critical death domain) was analysed by PCR-single strand conformational polymorphism.
Results There was no difference in the expression of the factors of Fas apoptotic pathway between the paired samples. The conformational analysis of exon 9 of the samples so far reviewed has shown no detectable conformational changes.
Conclusions This is the first report on Fas gene alterations in prostate malignancy. The results suggest that expression of the Fas pathway is unaltered after androgen resistance, and no conformational changes were noted in the exon critical to the induction of apoptosis suggesting a functional Fas receptor which may be exploited therapeutically.

P23

Suicide gene therapy in prostate cancer

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Introduction We explored the role of suicide gene therapy using the herpes simple virus thymidine kinase (HSVtk)/ ganciclovir (GCV) system in two rat models of prostate cancer. As current gene-transfer technologies allow only a limited proportion of tumour to be transfected, we have investigated the 'bystander effect' of tumour killing both *in vitro* and *in vivo*.
Methods MATLyLu and PAIII cells were retrovirally transfected with the HSVtk gene. To assess the bystander effect *in vitro*, mixtures of the transfected and wild-type cells were exposed to GCV and cell viability assessed at 5 and 7 days. To assess the bystander effect *in vivo*, the wild-type and transfected cells were mixed in various percentages and administered subcutaneously to Copenhagen and Lobund Wistar rats (the syngeneic hosts of MATLyLu and PAIII cells, respectively). The animals were treated with a 5-day course of GCV. Tumour volume and animal survival was recorded.
Results *In vitro* there was a slight bystander effect with PAIII but none with the MATLyLu model. *In vivo* there were clear differences in the growth and survival of animals with transfected tumour present compared with fully wild-type tumour, even when the proportion of wild-type tumour was taken into account. In addition, the eradication of transfected cells led to a degree of protection from rechallenge with wild-type tumours.
Conclusions The limited bystander effect *in vitro* suggests that there are no significant intracellular communications in either of these two cell lines. The bystander effect shown *in vivo* suggests that a significant immune response was initiated by the death of the transfected tumour cells. Further work is underway to examine the immune response generated by transfected tumour cell killing.
Funding: The Swire Group plc

P24

Expression of the developmental control gene PAX2 in prostate cancer

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Introduction In recent years there has been increasing evidence for the involvement of PAX genes in oncogenesis. PAX genes encode nine nuclear transcription factors, which are essential for embryogenesis and are proto-oncogenes in mice. The class III PAX genes (PAX2, 5 and 8) are the most likely candidates for a role in oncogenesis because they are expressed in highly mitotic undifferentiated cells during development and their inappropriate expression in several human tumours. PAX2 is expressed at high levels in the developing cells of the urogenital system and is down-regulated upon terminal differentiation with no expression in normal adult cells. Furthermore, PAX2 is located on 10q25, which is frequently implicated in prostate cancer.
Methods Using RT-PCR combined with southern blot analysis, PAX2 expression in three prostate cancer cell lines, five normal, 10 BPH and 27 prostate cancer specimens was investigated. The presence of PAX2 protein was investigated using immunofluorescence and western blotting. The effect of demethylation on PAX2 expression was studied using 5-aza-2'-deoxycytidine (2 μmol/L).
Results PAX2 was expressed in all three prostate cancer cell lines and 14 of 27 primary prostate cancers. There was no expression in the benign specimens. Using immunofluorescence and western blotting, all three cell lines expressed PAX2 protein; this expression was not altered by DNA demethylation.
Conclusions The difference in PAX2 expression between the benign and malignant specimens was significant ($P = 0.003$, Fisher's exact test). PAX2 expression in prostate cancer cells may contribute to the pathogenesis of prostate cancer by supporting cellular proliferation in the de-differentiated state.
Funding: Royal College of Surgeons/ Prostate Cancer Research Campaign UK

P25

Detection of circulating prostate cells after TURP

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Introduction Studies have shown that prostate cells are detectable in the circulating blood of men with prostate cancer and that prostate surgery causes release of cells into the blood. However it has proved difficult to extract and characterize these cells. We have used an immunomagnetic separation technique to detect prostate cells in peripheral venous blood during and after TURP, both to characterize the cells and to determine their fate.
Patients and methods The cell extraction system was first tested with volunteer blood samples to which known numbers of LNCaP cells had been added. Blood samples were then taken from patients before, during and 30 and 120 min after TURP for both prostate cancer and benign disease. Blood was also taken from patients with advanced prostate cancer at rest. After collection samples were subjected to density gradient centrifugation followed by immunomagnetic separation with anti-human epithelial antigen. The resultant extracted cells were air-dried on a slide, examined morphologically and immunostained for PSA and cytokeratin markers.
Results Half of the LNCaP cells added to blood were retrieved by the assay. Circulating prostate cells were detected in four of five patients with advanced prostate cancer. Blood was taken from 12 patients undergoing TURP; none had circulating prostate cells before TURP, whilst five had detectable circulating cells during surgery (1–10 cells). Three of these five patients had prostate cancer and two had benign disease. Of seven patients sampled after TURP, one had detectable prostate cells at 30 min and none at 2 h.
Conclusions This method detects half of all intact prostate cells in blood samples. Most patients with advanced prostate cancer have extractable circulating prostate cells. Few cells are detectable in the peripheral circulation during TURP and these cells are almost undetectable after 30 min.
Funding: BUF

P26

A study of the enzymes involved in the invasion of bone marrow stroma by prostatic epithelial cells

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Introduction The ability of prostate cancer to invade and grow in the bone marrow stroma (BMS) is thought to be partly because degradative enzymes break down the surrounding extracellular matrix (ECM).
Methods To study the role of these enzymes, the formation of prostate skeletal metastases was mimicked *in vitro* by growing co-cultures of prostate cell lines PC-3, DU145, LNCaP-FGC (metastatic), PNT2-2C (not malignant) and primary tissue samples of prostatic adenocarcinoma and BPH in long-term bone marrow cultures. The expression of urokinase plasminogen activator (u-PA), matrix metalloproteinase 1 and 7 (MMP-1 and -7) by prostatic cells was identified using immunocytochemistry. To establish the role of these enzymes in colony growth, inhibitory antibodies directed against

u-PA, MMP-1 and -7 were added daily (for 7 days) into co-cultures of primary BPH cells and BMS. The mean epithelial colony size was then calculated.
Results Metastatic prostate epithelial cell lines showed greater MMP-7, u-PA and MMP-1 immunocytochemical staining than nonmalignant prostate epithelial cells. The mean epithelial colony size within the BMS co-cultures was reduced by 47%, 62% and 65% compared with the control when inhibiting antibodies against u-PA, MMP-7 and MMP-1 were added.
Conclusion These data suggest that certain types of prostate cancer cells express higher levels of the degradative enzymes; primary adenocarcinoma cells particularly showed higher MMP-7 levels than did BPH cells. Growth studies also indicate a reduction in the size of developing epithelial colonies in BMS when these enzymes were inhibited, suggesting that these enzymes may play an integral role in cell colony growth and hence metastatic development in prostate cancer.
Funding: Surgical Research Fund, Christie Hospital and the Cancer Research Campaign

P27

Modulation of mechanisms controlling cell proliferation in prostate cancer by fatty acids

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Introduction While the incidence of latent cancer of the prostate is uniform across the world, the incidence of clinically significant cancer of the prostate is high in the west. This indicates that modifiable lifestyle factors such as diet and nutrition could play a significant role in the progression of prostate cancer. As 40% of the total energy intake in a traditional western diet is derived from dietary fat, attention has been focused on the role of dietary fat in prostate cancer. The n-6 fatty acids (FAs) appear to be procancerous and the n-3 FAs appear to be anticancerous in their effects. However, the mechanisms by which FAs modulate the cellular growth control mechanisms in prostate cancer are unclear. Thus we analysed *in vitro* the effects of different FAs on the proliferation of normal and malignant prostatic cells, the effects of FAs on the expression of PSA by malignant prostate cells, and the effects of FAs on the total protein kinase C (PKC) activity in prostate cancer cells.
Materials and methods Cell culture methods using human prostate cell lines PNT2 (normal), LNCaP (hormone-sensitive) and PC-3 (hormone-resistant) were used. Cells were treated with n-6 linoleic acid, n-3 eicosapentaenoic acid and n-9 oleic acid using a wide range of concentrations (3–400 μmol/L) for 48 h, with appropriate controls. Cell proliferation was assessed using the standard MTT (tetrazolium dye) assay. Changes in the expression of PSA and the total PKC activity in the LNCaP cells were estimated using an ELISA (Hybritech-Tandem MP and Calbiochem, respectively).
Results At concentrations of FAs that can be achieved *in vivo* at the cellular level (< 100 μmol/L), the growth of human prostatic cells is stimulated. At concentrations that can be obtained *in vivo* only by using pharmacological doses (200, 400 μmol/L) the growth of these cells is inhibited. However, at 100 μmol/L, although cell proliferation increases, the expression of PSA in the cell culture supernatants appears to decrease compared with the control. In keeping with the effects on cell proliferation, the total PKC activity was increased in LNCaP cells treated with FAs at 100 μmol/L. Future work will elucidate which of the 12 known isoforms of PKC could possibly be modulated by FAs. Early results indicate that PKC-i (iota) could be modulated by FAs in prostate cancer cells (LNCaP).
Funding: RCSEd, NHS Trust

P28

Interactions of primary human prostatic epithelial cells with bone marrow-derived endothelium

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Introduction Prostate cancer shows a predilection to form secondary tumours within the bone marrow. We have developed an *in vitro* system to investigate interactions between prostate epithelial and bone marrow endothelial cells.
Methods Prostate epithelia and fibroblasts were prepared from men with prostate cancer or BPH. Primary bone marrow endothelial (BME) cultures were established and characterized. Epithelial cells were seeded onto human umbilical vein endothelial cells (HUVEC), prostatic fibroblasts, a lung microvascular cell line (Hs888Lu), bone marrow stroma (BMS) and BME, then allowed to bind. Binding of the prostate cell lines PC3 (metastatic) and PNT2-C2 (not malignant) were also assessed. Adhesion is reported as optical density for cytokeratin fluorescence. Studies using antibodies against various cell adhesion molecules were then performed to try to inhibit binding.
Results Primary prostatic epithelial cells from both malignant and benign tissue showed significantly greater binding to BME and BMS than to HUVEC; they bound to a lung microvascular cell line at an intermediate level. Comparable data were obtained with PC3 and PNT2-C2 cell lines. PC3 binding to BME was inhibited by 64% after pre-incubation with a β1 integrin antibody. Antibodies against β4, α2, α4, α5, P-selectin, CD31, VCAM-1 and sialy Lewis X showed no effect on blocking PC3 binding.
Conclusion Prostate epithelial cells showed preferential adhesion to BME and BMS compared with controls and binding to BME cells could be substantially inhibited by blocking the integrin β1. This suggests that the initial binding step in the metastatic process in bone marrow is mediated by the β1 integrin.
Funding: Association for International Cancer Research, and the CRC

P29

Prostate cancer vaccine trial: allogeneic whole-cell vaccine phase I/II study in men with hormone-relapsed prostate cancer

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Introduction Allogeneic vaccines, using stored cultured cancer cells, are an efficient and practical form of immunotherapy. We investigated the possibility of using this form of allogeneic triple-cell vaccine in metastatic prostate cancer.
Methods Four prostate cell lines were mixed into four triplet groups. Sixty patients with hormone-relapsed prostate cancer and a rising PSA level of > 30 ng/mL were recruited; there was no placebo. Patients were vaccinated with cells and the adjuvant *Mycobacterium vaccae* every 2 weeks for the first 6 weeks. The triple-cell vaccine was given monthly thereafter. Patients were monitored by PSA level, serum immunological markers, clinical progression and quality-of-life scores.
Results The vaccine was very well tolerated; minor adverse effects were 'flu-like symptoms in one patient and transient local skin reactions at the site of injection. Immune responses were seen in all patients and tended to correlate with PSA changes.
Conclusions This preliminary study shows that the use of allogeneic whole-cell vaccines in prostate cancer is efficient, safe and well tolerated. That these patients were able to mount immune responses even with end-stage, high-volume disease implies that the potential for immunotherapy in lower volume disease is very promising.
Funding: BUF, Onyvax Ltd

P30

Cyclo-oxygenase-2: a novel therapeutic target in prostate cancer

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Introduction Cyclo-oxygenases (COXs) are important enzymes involved in the formation of PGs. Two isoforms of COX have been recognised; COX-1 is constitutively expressed and COX-2 is inducible and has been suggested to play a role in cancer development. Our aims were to determine the expression of COX-1 and -2 in human prostate, and to study the effect of COX-2 inhibition on prostate cancer cell growth.
Methods COX-1 and -2 protein expression was assessed in 30 cases of BPH and 82 prostatic adenocarcinomas, using standard three-layer immunohistochemistry (IHC) and immunoblotting in 13 of these cases. Three prostate cancer cell lines (DU-145, LNCaP and LNCaP-r) were used to assess the effect of the COX-2 inhibitor NS-398 on cell proliferation, as assessed by the MTT cell proliferation assay and direct cell counting.
Results IHC showed significantly greater ($P = 0.008$) COX-2 expression in tumour cells than in benign glands, which correlated with tumour grade ($P = 0.01$), and with an appreciable change in cellular location, from membranous in benign glands to cytoplasmic in tumour cells ($P = 0.001$). On immunoblotting, significantly greater levels of COX-2 were detected in prostate cancer than in BPH. NS-398 produced a dose-dependent inhibition of cell proliferation (up to 70%) in all the cell lines tested.
Conclusion We have shown for the first time that COX-2 is over-expressed in human prostate cancer and that COX-2 inhibition may be useful in the chemoprevention and therapy of prostate cancer.
Funding: Friends of Hammersmith Hospital

Andrology (Poster session)

P31

MUSE™: failed expectations

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Introduction Intraurethral alprostadil (MUSE™) was designed as a less invasive means of administering PGE1 than the injection system (Caverject™). Its early promise has been tempered by some recent reports questioning its efficacy. This study compares the efficacy in two groups, i.e. those started on MUSE as the initial treatment and a cross-over group transferring from Caverject to MUSE.
Patients and methods Patients (231) treated with MUSE were assessed retrospectively using a specially designed questionnaire adapted from the International Index of Erectile Function. All patients had at least 6 months of follow-up.
Results Of the 231 patients, 154 (65%) returned their questionnaires; only 40 of these (26%) were still using MUSE at 6 months. In patients who had discontinued MUSE the predominant reason (58%) was 'failure to work'; 21% stopped because of pain and 10% because of the advent of sildenafil (Viagra). Erections were considered firm enough for penetration in 28% and 86% of those who attempted intercourse found it difficult to maintain their erection to completion. Only 18% were satisfied with their sex life when using MUSE. Side-effects were reported by 63% of patients, the commonest being localized pain. In the cross-over group, 30% were still using MUSE and 33% reported satisfaction with their sex life; of those expressing a preference, 14 of 33 (42%) said they would like to resume using Caverject.
Conclusion Although patients found MUSE easy to use, after 6 months many patients had discontinued because it was ineffective and caused side-effects. Even of those patients continuing to use MUSE, most had unsatisfactory erections. Patient dissatisfaction is common with MUSE and its lower efficacy than Caverject must be considered.

P32

Tolerance to sildenafil (Viagra™) after long-term use: possible mechanisms

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Introduction Orally administered sildenafil is effective in 72–86% of patients with erectile dysfunction (ED). However, its ability to maintain long-term efficacy remains to be fully established. Follow-up data for up to a year indicates that in 2.6–4% of patients the efficacy diminishes. The factors contributing towards the lack of maintenance of long-term efficacy in these patients are unclear.
Patients and methods A prospective study was carried out to evaluate the long-term (3.6 years) efficacy and side-effects of sildenafil in 40 patients.
Results Ten (25%) patients stopped using sildenafil after a mean period of 2.4 years. In a further four patients (10%) the efficacy diminished, requiring an increase in dose from 50 mg to 100 mg to maintain a similar quality of erection. Furthermore, with time, the increased sildenafil dose also became less effective.
Conclusions The decrease in efficacy may be caused by the progression of ED or, more importantly, by the development of tolerance to sildenafil. Could the tolerance be analogous to that seen in patients treated for angina with nitroglycerine? Both nitroglycerine and sildenafil enhance the nitric oxide/cGMP signal transduction pathway, albeit through different mechanisms. The mechanisms that may contribute sildenafil tolerance will be discussed.

P33

Sildenafil in the treatment of erectile dysfunction in parkinsonism

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Introduction Erectile dysfunction (ED) is common in men with parkinsonism. Multiple system atrophy (MSA) is a cause of parkinsonism often associated with autonomic failure. Postural hypotension has been infrequently reported with the use of sildenafil. Our aim was to evaluate sildenafil in men with parkinsonism and ED.
Methods Patients were randomized to receive either sildenafil or placebo for 10 weeks, followed by the alternative therapy for 10 weeks. Assessments included the International Index of Erectile Function (IIEF) questions 3 (ability to achieve erections) and 4 (ability to maintain erections), and an erectile problem question (EPQ). Responses were scored from 1 (almost never/never) to 5 (almost always/always) for the IIEF, and from 1 (no erection problem) to 4 (severe erection problem) for the EPQ. Lying, sitting and standing BP was measured before and 1 h after dosing.
Results Ten patients with Parkinson's disease (PD, mean age 59 years) and six with MSA (mean age 54 years) were recruited. All had ED for a mean of 48 (PD) and 58 months (MSA). The mean scores at baseline, on placebo and on active treatment for the PD group were 1.8, 2.2 and 4.2 (IIEF Q3), 1.1, 2.0 and 4.3 (IIEF Q4), and 3.5, 3.6 and 2.2 (EPQ), respectively. The respective mean scores in the MSA group were 0.8, 1.3 and 3.8; 0.5, 1.3 and 3.8, and 3.8, 3.5 and 2.0. In three patients with MSA and coexisting postural hypotension, there was a significant decrease in mean BP (on placebo, 109.2 mmHg lying to 80.2 mmHg standing; on sildenafil, 87.0 mmHg lying to 47.5 mmHg standing).
Conclusions Sildenafil was an effective therapy for ED in patients with parkinsonism. However, these results also suggest that caution should be exercised when using sildenafil for treating ED in patients with postural hypotension secondary to autonomic failure in MSA.
Funding: Pfizer independent grant

P34

General urological practice experience with oral sildenafil in men with erectile dysfunction

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Introduction Recently, oral sildenafil (Viagra™) has been introduced as an effective treatment for male erectile dysfunction (ED). In a prospective study we evaluated the efficacy and safety of oral sildenafil in a busy general district hospital.
Patients and methods The study included 161 consecutive patients with ED (mean age 56 years, range 21–79) who completed a baseline International Index of Erectile Function (IIEF) questionnaire (questions 3, 4 and 14), underwent a physical examination and hormone profile; the cause of their ED was identified. Each patient was initially given 50 mg sildenafil (four tablets) to use at home, with instructions to increase or decrease the dose to 100 mg or 25 mg depending on the response, and then reviewed after one month. The patients who had good results were reviewed at 3, 6 and 12 months.
Results The mean (range) duration of ED was 40 (6–120) months

and the mean follow-up 6 (6–12) months. After treatment, 135 patients (84%) had good erections sufficient for penetration, which was maintained over the follow-up period. The most common causes of ED in these patients were mixed in 43 (32%), psychological in 38 (28%), unknown in 14 (10%) and diabetes in 13 (10%). There was a poor response to treatment in 26 patients (16%), 10 of whom had mixed aetiology (diabetes and vascular in half), six had diabetes and four a vascular aetiology. Side-effects were headache in 14 patients (9%), flushing in nine (6%) and rhinitis in two (1%).
Conclusion Oral sildenafil significantly improved the quality of erection and sexual satisfaction, making it the first-line management of ED for most patients in general urological practice.

P35

Intracavernosal injection with phentolamine during dynamic colour Doppler ultrasonography can abolish apparent venous leakage in young patients

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Introduction The diagnosis of venogenic impotence in young patients by colour Doppler ultrasonography (CDUS) may be misleading because of the sub-optimal response to PGE1 injection. Some men with either anxiety or increased sympathetic tone may not respond to PGE1 or sildenafil. The objective of our study was to evaluate the CDUS variables and objective erectile response, and to determine whether phentolamine can abolish this venous leak remaining after a full dose of PGE1.
Patients and methods Dynamic CDUS was undertaken in 21 young patients (mean age 28.4 years, range 17–39, SD 5.34) with 10 and 20 µg of PGE1; 17 of them were found to have venogenic impotence. Venous leak was defined as the presence of an end-diastolic velocity (EDV) of > 5 cm/s when the peak systolic velocity (PSV) was at $\geqslant 35$ cm/s with a suboptimal erection. These patients were then given 2 mg of phentolamine. The diameter, PSV, EDV and clinical response were assessed. Five older men (mean age 53 years) with the same diagnosis were studied as controls.
Results The venous leak reversed in 15 of the 17 patients, but the grade of erection improved in all patients and was unmodified in the controls.

Variable	*Change*	*95% CI*	*P*
Diameter	−0.04	−0.09, 0.01	0.14
PSV	−6.52	−13.6, 0.5	0.06
EDV	7.2	4.3, 10.1	< 0.001
Grade	1	Mean rank 8.5	< 0.001

Conclusions Alpha blockade is mandatory before diagnosing venous leakage. Phentolamine may be a treatment option for these patients.

P36

Difference in penile blood flow during bicycling in an upright or lying position

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Introduction Perineal compression during bicycling appears to be responsible for some cases of impotence.
Methods In 35 healthy athletic men, the transcutaneous penile oxygen pressure (tpO_2) at the glans of the penis was measured using a transcutaneous device. Several authors have shown that the tpO_2 levels correlate with the arterial pO_2 levels. The tpO_2 was measured before, during and after cycling in an upright and lying position, in a cross-over study.
Results The mean (SD) tpO_2 at the glans when standing before cycling was 60.5 (8.1) mmHg; it decreased after sitting on the saddle in an upright position to 17.9 (3.9) mmHg. Continued cycling while seated in the upright position showed tpO_2 levels of 18.3 (5.2) mmHg and there was a full return to normal tpO_2 values after a 10 min recovery period while standing. Cycling while lying down produced tpO_2 levels of 59.4 (4.2) mmHg, similar to the levels before and after exercising.
Conclusion These results support the hypothesis that as there is compression of the penile arteries against the pubic bone by the saddle during cycling, the tpO_2 values are decreased. Additionally, cycling while lying, where there is no perineal compression, produced penile blood oxygenation values similar to those before and after exercising. Therefore, we suggest that cycling while recumbent avoids the health hazards of penile numbness and hypo-oxygenation.

P37

The penile oxygen pressure during cycling

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Introduction Perineal compression during bicycling appears to be responsible for some cases of impotence. We evaluated the blood supply to the penis by measuring the transcutaneous oxygen pressure (tpO_2) during cycling.
Methods In 50 healthy athletic men, the penile tpO_2 at the glans of the penis was measured using a transcutaneous device. The tpO_2 correlates with tissue pO_2 and the peripheral blood supply. The tpO_2 was measured while subjects cycled in various positions and before, during and after cycling.
Result The mean (SD) tpO_2 at the glans when standing before cycling was 61.4 (7.2) mmHg; it decreased after 3 min cycling to 19.4 (4.7) mmHg. After 1 min cycling in a standing position it increased significantly to 68.0 (7.6) mmHg. Cycling was then continued while seated; after 3 min the tpO_2 decreased to 18.4 (4.2) mmHg and there was a full return to a normal tpO_2 value after a 10-min recovery period.
Conclusion The tpO_2 seems to correlate with the blood supply to the penis. These results support the hypothesis that as there is compression of the penile arteries against the pubic bone by the saddle during cycling, tpO_2 values are decreased. Changing from a seated to a standing position significantly improved the tpO_2 values of the penis and there was improved penile blood oxygenation. We suggest frequent changes in body position during cycling. Correcting the handlebars or the height of the saddle, tipping the nose of the saddle to be more horizontal or even pointing down slightly, and attention to the design of the saddle, may be the only required precautions.

P38

Plaque excision and Permacol grafting for Peyronie's disease

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Introduction Plication or excision of the normal tunica albuginea to correct penile curvature in Peyronie's disease produces unacceptable penile shortening in some patients. Plaque incision or excision and tunical grafting are alternative techniques. A variety of tissues and materials have been used with success, but associated consequences such as herniation and impotence are not uncommon.
Patients and methods We present the technique and results of plaque excision and tunica grafting with Permacol™ (Tissue Science Laboratories Ltd) in five patients with severe Peyronie's disease. Permacol™ is porcine dermal collagen, which has been fully approved for permanent biological implantation.
Results The short-term results of the patients treated are encouraging. It is hoped that further experience will be obtained before the meeting.
Conclusion Permacol™ is strong, has low immunogenicity, and is integrated into surrounding tissues, promoting local angiogenesis. Plaque excision and Permacol grafting should be considered in all men requiring surgical correction of Peyronie's disease. Although the procedure takes longer than a standard Nesbitt procedure, the advantage of preserving penile length and function is a worthy outcome.

P39

Corporeal plication for penile curvature caused by Peyronie's disease: a patient's perspective

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Introduction Peyronie's disease is estimated to affect up to 1% of the male population. Corporeal plication (CP) is a common and simple surgical procedure for this condition.
Methods A postal questionnaire was sent to 69 patients and their sexual partners who had undergone CP for Peyronie's disease between 1992 and 1999.
Results Of the 69 patients, 68% returned the questionnaire. The mean follow-up period was 4.1 years and the mean age of patients was 54.6 years; 55% of patients are currently sexually active. Before CP, 18% of patients complained of significant erectile dysfunction (ED); after surgery, 32% reported marginal ED and 18% significant ED; 16% of patients continue to have significant penile discomfort and 34% felt nodules at the suture site; 57% reported a mild and 13.6% a severe persistent penile deformity; 90% noticed a decrease in penile length, of whom 55% thought that this was significant; 32% observed a 'numbness' of the glans penis. Overall, only 52% of patients would recommend this surgery, with 57% reporting a deterioration in their quality of life. Of the evaluable patients, 86% of their partners responded; 35% suggested a significant deterioration in sexual performance.
Conclusions Overall, the long-term results of CP are disappointing in this study. These poor results could be related to a current lack of understanding of the natural history and progression of the disease, case selection, or surgery. We intend to use these results to counsel our future patients so they have a more realistic perception of the outcome.

P40

An evaluation of the efficacy of percutaneous epididymal sperm aspiration for intracytoplasmic sperm injection in unobstructive compared with obstructive azoospermia

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Introduction The simple technique of percutaneous epididymal sperm aspiration (PESA) pioneered by our group has been established as a safe and effective procedure. We compared its use in patients with unobstructive and obstructive azoospermia.
Methods The study comprised 234 therapeutic PESA/intracytoplasmic sperm injection (ICSI) cycles carried out in patients with obstructive or unobstructive azoospermia. Retrieval of epididymal sperm was successful in 170 of 191 patients (89%) with obstructive azoospermia (group 1) and 30 of 47 patients (64%) with unobstructive azoospermia (group 2).
Results In group 1, 1610 oocytes underwent ICSI; 963 fertilised (59.8%) and 758 cleaved (78.7%). Fertilization failed in six patients (3.5%) and one patient had all her embryos frozen; 163 patients (96%) received 444 fresh embryos (2.7 embryos/cycle). The outcome of treatment was unknown in two cycles (excluded); 55 patients achieved clinical pregnancy (34.2% per embryo transfer, ET). The implantation rate was 16.9%. Eight patients miscarried and 47 gave birth (28.8% per ET). In group 2, 271 metaphase II oocytes underwent ICSI; 161 fertilised (55.7%) and 133 cleaved (88.6%). Fertilization failed in one patient (3.3%); 29 patients (96.7%) received 63 fresh embryos (2.2 embryos/cycle). The outcome of treatment was unknown in three cycles (excluded). Clinical pregnancy was diagnosed in 10 patients (34.5% per ET). The implantation rate was 22.8%. Three patients later miscarried and seven patients gave birth (24% per ET).
Conclusion PESA, as expected, is more successful in obstructive than unobstructive azoospermia (89% vs 63.8%). This might be because there is no epididymal sperm in unobstructive cases. The procedure is technically easier in obstructive azoospermia because the epididymis is distended. It is worth trying PESA first in unobstructive azoospermia to retrieve, if possible, epididymal sperm which are more mature and tolerant of cryopreservation than testicular sperm. PESA is also less traumatic than testicular sperm aspiration, which should be the reserve procedure to retrieve testicular sperm if PESA is not successful.

Bladder Cancer (Poster session)

P41

Bladder cancer in patients with spinal cord injury: is it as common as we think?

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Introduction The crude incidence of bladder cancer in patients with spinal cord injury is reported to be 0.28–10%. Studies quote up to a 20-fold increase compared with the general population. This varying incidence among different centres prompted a retrospective study of bladder cancer in our spinal injury centre.
Methods The case-notes of 1324 patients who were injured between 1960 and 1998 were reviewed to collect information about the level of injury, bladder management, complications (stones, infections), bladder histology if available and causes of death of deceased patients. Data were cross-checked with that of Regional Cancer Registry. The length of follow-up was calculated as the time elapsed between the dates of entry and exit from the study. The age-specific incidence rates (ASR) were calculated using 5-year age bands and these were used to calculate an overall incidence rate for the cohort, using direct standardisation with the European standard population. All pathology slides were reviewed by one pathologist and immunohistochemically stained using cytokeratin 14 and 20.
Results The mean age of the population assessed was 47 years and the male to female ratio 7 : 3. Half of the population were managed using chronic indwelling catheters and 35% by CISC. The remaining subjects were on either penile sheath drainage or had undergone urinary diversion. The 1324 patients included four with bladder cancer and contributed a total of 12 444 person-years of follow-up, giving an ASR of 30.7 per 100 000 person-years (95% CI 0.4–61.1). The ASR for invasive bladder cancer in the general population of Yorkshire was 14.4 per 100 000 person-years (95% CI 13.9–14.9), rate standardised to the European standard population. The incidence among patients with spinal cord injury increased slightly with increasing follow-up. Immunohistochemical analysis confirmed all four tumours to be squamous cell cancers.
Conclusions The ASR of bladder cancer in patients in our spinal injury unit is similar to that of the general population. The risk of bladder cancer increased with the length of follow-up and these tumours tended to be of squamous cell phenotype.

P42

The risk of urethral recurrence is low with radical radiotherapy for bladder cancer

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Introduction Previous series report a lower rate of urethral recurrence with orthotopic reconstruction than for cutaneous urinary diversion. It has been suggested that continued exposure to urine may reduce the risk of urethral disease. This study reports the rate of urethral recurrence after radical EBRT.
Patients and methods The study comprised a review of 217 men (median age 69 years, range 39–86) undergoing radical radiotherapy at one centre (1990–1995). Men undergoing chemotherapy were excluded.
Results The stage and grade of tumours were: T1 (7%), T2 (41%), T3 (42%), T4 (10%), G1 (1%), G2 (32%) and G3 (67%). The median (range) follow-up was 32 (1–101) months. The 5-year survival was 30%. Six of 217 men (2.8%) developed urethral recurrence: five were found within 2 years (median 10 months, range 3–60). Sixty-five men completed the 5-year follow-up, with a rate of recurrence of 3.1%. Two men with urethral recurrence had bladder neck involvement at diagnosis, one had concurrent carcinoma *in situ*. No identifiable risk factors were noted in the other four.
Conclusions The risk of urethral recurrence after radical radiotherapy for TCC of the bladder is lower than that reported after cystectomy and external diversion (10%) and is comparable with that after orthotopic reconstruction (3%). It is not possible to completely exclude selection bias, but the data are consistent with the suggestion that continued contact with urine may be protective.

P43

Phase I and phase IIa studies of the novel intravesical chemotherapeutic agent, meglumine γ-linolenic acid

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Introduction γ-Linolenic acid is known to be cytotoxic to a wide range of tumour types in tissue culture. However, difficulties have been encountered in delivering the potential drug to its target site in solid-organ tumours. In superficial bladder cancer, the tumour is readily accessible and high concentrations of potential therapeutic agents may be delivered to their site of action with minimal side-effects. This has been shown by the use of the anthracyclines in the bladder at much higher concentrations than would normally be used systemically. Earlier studies have shown meglumine γ-linolenic acid (MeGLA) to be cytotoxic to urothelial cell lines and tumour explants at concentrations as low as 10 μg/mL. This is a relatively immediate effect, not seen with the other intravesical agents. Studies in rodents have shown minimal systemic absorption of the drug and no adverse effects after instillation of MeGLA at 2.5 mg/mL.
Patients and methods Ten patients about to undergo cystectomy had a single instillation of 50 mg of MeGLA in 50 mL water (1 mg/mL) for up to one hour. Side-effects and the duration tolerated were recorded, and a consultant histopathologist reviewed the histology results. Patients with superficial recurrent urothelial cancer were recruited at flexible cystoscopy clinics and then had a single intravesical dose of 50 mg MeGLA in 50 mL water 1–2 weeks later. The patient then returned for rigid cystoscopy and a comparison of the bladder appearance recorded using bladder maps. Patients were categorized into those with a complete response, partial or indeterminate response or no response. If a lesion was thought to have changed in appearance, or there were fewer, it was labelled as indeterminate.
Results Seven of the 10 patients in the tolerability study had minimal side-effects and tolerated one hour of instillation. Two patients tolerated the drug for < 1 h, one because of a feeling of accumulating pressure and the other because of an urgent need to defecate. One patient only held the drug for 2 min because of pain, and this patient had eosinophilic cystitis. There were no consistent histological results suggestive of collateral damage to normal urothelium. Twelve patients received instillations as part of the efficacy study and none had any significant side-effects. There were two complete responses, six partial responses and four patients with no response. The partial responses were either as fewer tumours or a change from a papillary, fronded lesion to a flatter appearance, or even to an erythematous patch suspicious in two cases of carcinoma *in situ*, although neither were confirmed as such on biopsy.
Conclusions MeGLA is well tolerated when given intravesically and there is no evidence of significant collateral damage to normal urothelium. The results of the uncontrolled Phase IIa efficacy study show that this novel agent has similar efficacy to conventional intravesical agents. Further dose and frequency escalation studies

are needed, followed by a definitive randomized controlled trial, with time to recurrence and progression as end-points.
Funding: Scotia Pharmaceutical

P44

Over-expression of metallothionein predicts resistance of TCC of the bladder to intravesical mitomycin therapy

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Introduction Metallothionein is a low molecular weight intracellular protein which binds to mitomycin with high affinity, protecting tumour DNA. We studied prospectively the relationship between metallothionein expression in TCC of the bladder and resistance to intravesical mitomycin therapy.
Patients and methods A series of 44 patients (mean age 69.9 years, range 44–89) with superficial TCC who were treated with intravesical mitomycin were assessed. Resected tumour tissues were stained with metallothionein mAb E9. The staining intensity was scored by two pathologists. All patients were followed up by regular flexible cystoscopy. The results were analysed using the Mann–Whitney *U*-test with $P < 0.05$ taken to indicate statistical significance. Spearman's correlation coefficient (r) was calculated for tumour grade (G) and staining intensity.
Results Most tumours (29) were G2, with six each of G1 and G3; 15 patients (34%) developed recurrent tumour after mitomycin therapy. The mean cytoplasmic staining scores for recurrent and non-recurrent tumours were 14.7 and 3.4, respectively. The mean nuclear staining scores for recurrent and non-recurrent tumours were 10.13 and 2.7, respectively. The mean follow-up for patients with no recurrence was 10.5 months (95% CI 7.96–13.14). The r values for tumour grade and cytoplasmic and nuclear staining were 0.27 ($P > 0.05$) and 0.3 ($P < 0.05$). Both the nuclear and cytoplasmic staining score were significantly higher in recurrent tumours ($P < 0.05$) than in non-recurrent tumours.
Conclusion Over-expression of metallothionein predicts the resistance of TCC of the bladder to intravesical mitomycin therapy. There was a weak positive correlation between tumour grade and nuclear metallothionein content.

P45

Combination chemotherapy with epirubicin and mitomycin C against the bladder tumour cell lines EJ138 and T24/83

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Introduction Epirubicin is an anthracycline which inhibits topoisomerase type II and is effective in the aerobic tumour fraction, whilst mitomycin C is the prototype bioreductive alkylator activated by one or more bioreductive enzymes and hypoxic conditions. The aim of this study was to investigate this combination of drugs *in vitro* for additive, synergistic and antagonistic effects.
Methods The cell lines EJ138 and T24/83 were plated into 96-well cluster plates and exposed to the drugs on the following day. Individual dose–response curves for each drug were compared with the combinations mitomycin + epirubicin or mitomycin followed by epirubicin, or epirubicin followed by mitomycin. The overall concentration × time parameters were identical for all exposures through nine consecutive two-fold serial dilutions in all the groups. Cells were washed and incubated for 4 days in RPMI medium. Cell survival was determined using the MTT assay.
Results The IC_{50} analysis showed that all combinations of mitomycin C and epirubicin were additive against both cell lines. No synergism or antagonism was detected.
Conclusion The combination of these two agents *in vitro* is at least as effective as using either agent alone. *In vitro* data may not translate directly to a clinical setting where synergism may exist because of physiological differences in the microenvironment (e.g. oxygen tension, pH) of different parts of the same tumour or between different tumours in the same patient.
Funding: Kyowa Hakko UK Ltd

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Detection of upper tract TCC using the BTA Stat™ test

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Introduction The clinical diagnosis of upper tract TCC (UTTCC) currently relies on upper tract imaging followed by invasive ureteric washing cytology and/or ureteroscopy. The BTA Stat™ test (Bion Diagnostic Sciences, Inc., CA) is a rapid, qualitative immunoassay for detecting human complement factor H and related proteins in voided urine, and has been shown to be a sensitive method for detecting bladder cancer. We evaluated the efficacy of the BTA Stat test in the noninvasive detection of UTTCC from voided urine specimens.
Patients and methods This was a prospective, blinded study where voided urine and ureteric washing samples were obtained from a total of 81 patients (mean age 65 years; 61 male, 20 female) before surgery or treatment. Cystoscopy was negative in all patients at the time of sampling. Twenty-seven patients had histologically confirmed UTTCC, most of which were renal pelvic or upper ureteric TaG2 tumours. Twenty-eight patients had microscopic haematuria but no evidence of urological disease and 26 had upper tract calculi. These samples were subjected to the following tests: (i) voided urine BTA Stat test; (ii) voided urine cytology; and (iii) ureteric washing cytology.
Results The BTA Stat test had a diagnostic sensitivity of 82%, compared with 11% for voided urine cytology and 48% for ureteric washing cytology. The BTA Stat test specificity was 89%, compared with 54% for voided urine cytology and 33% for ureteric washing cytology. Negative predictive values for the BTA Stat test, voided urine cytology and ureteric washing cytology were 91%, 55% and 55%, respectively, and the corresponding positive predictive values were 79%, 11% and 28%.
Conclusions The BTA Stat test was better than voided urine cytology and ureteric washing cytology in detecting UTTCC. These results may support adopting a less aggressive follow-up policy when monitoring for UTTCC when the BTA Stat test result is negative. Conversely, if cystoscopy is negative and the BTA Stat test is positive, then upper tract investigations should be expedited.
Funding: Bion Diagnostic Sciences, Inc.

P47

A new *in vitro* chemosensitivity assay in TCC of the bladder

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Introduction The response of TCC to intravesical chemotherapy is poorly understood. *In vitro* chemosensitivity in TCC has previously been reported using a complex technique of inhibition of thymidine LI. We carried out a pilot study to assess the feasibility of a simple chemosensitivity method in TCC using an ATP bioluminescence assay.

Patients and methods Twenty-eight samples from 26 patients with bladder TCC of different grades and stages were disaggregated to produce a cell suspension which was exposed to a range of concentrations of mitomycin C for 48 h. Cell viability was assessed using the ATP assay.
Results Values were obtained in 22 of the 28 samples. The reasons for failure included too few cells isolated or low cell viability. The median (range) LC_{50} (concentration required to kill half the cells) was 11.5 (0.34–123.5) μmol/L. There was some variability within each pathological stage (TA, 0.34–39.9; T1, 9.5–123.5; T2–4, 1.88–58.9 μmol/L) and grade (grade I, 0.34–39.9; grade II, 13.5–123.5; grade III, 1.88–58.9 μmol/L).
Conclusions The *in vitro* ATP assay for chemosensitivity in TCC showed a marked variation in the effect of mitomycin C between patients, with a 300-fold difference between the most sensitive and most resistant samples. It may have a place in the prediction of treatment response, recurrence and progression.

P48

Further experience with the detection of TCC with DNA pre-replication proteins from urinary cellular extract

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Introduction The formation of pre-replication complexes (PRCs) is essential for DNA replication before the onset of the S phase of the cell cycle. PRCs are present throughout the cell cycle of proliferating cells but are absent in non-proliferating cells. We have raised monoclonal antibodies to PRCs, superseding our previous polyclonal antibodies, to attempt to detect urinary tract TCC more reliably than with urine cytology.
Method Urine from 47 patients with haematuria or a past history of bladder TCC was analysed. Cells were isolated by centrifugation and subjected to hypotonic dounce and salt extraction. Cellular extracts were applied to an immunofluorometric assay using affinity-purified mAb against PRC proteins. All patients had upper tract imaging and cystoscopy within 12 h of producing the urine samples.
Results TCC was found in 15 patients (14 bladder, one renal pelvis). In 14 of them, PRC was detected in the urine. There were 32 patients with negative cystoscopy and upper tract imaging. Of these, no urinary PRC was detected in 31, but one (with a past history of TCC) had urinary PRCs. Whether this is a true- or false-positive remains to be determined. The assay had a sensitivity of 93% and a specificity of 97%.
Conclusion The presence of PRCs in urinary cellular extracts is highly predictive for TCC within the urinary tract, and may prove more useful than standard cytology.

P49

Endoluminal ultrasonography of the ureter with a reusable catheter: early results

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Introduction Endoluminal ultrasonography (US) has been used in a variety of fields, including gastrointestinal, vascular surgery and urology. Until now, the ultrasound catheters have been disposable, making their regular use costly. We describe the technique and preliminary results of a reusable endoluminal US catheter for examining ureteric anatomy.
Methods Retrograde ureteropyelography is undertaken initially to define the renal anatomy. The 2.4 mm (7.2 F) or 3 mm (9 F) catheter (Olympus Keymed, Southend, UK) is then passed up the ureter retrogradely. No intraoperative preparation of the catheter is needed. Either 12 or 20 MHz systems are available. An axial image as small as 1 cm or as large as 10 cm around the ureter can be obtained. Proper orientation is essential and 4–15 min are required to perform the procedure. Over the last 6 months, 41 patients underwent endoluminal US in our unit. Twenty-six (63%) were for PUJ obstruction, 10 (25%) for upper tract TCC and the remaining five (12%) were for ureteric strictures.
Results Endoluminal US detected crossing vessels and a septum at the PUJ in 18 (69%) and six (23%) of the cases, respectively. In those with upper tract TCC, images correlated well with the nephroureterectomy specimen. There were no recorded complications after the procedure and the catheter had to be replaced once.
Conclusions This endoluminal US catheter system produces superb images of the ureteric and peri-ureteric anatomy, with no artefacts. The reusability of this endoluminal US catheter removes an important obstacle from its common use for evaluating a variety of upper urinary tract abnormalities.

P50

Long-term results of open and endoscopic treatments for PUJ obstruction

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Introduction Patients with PUJ obstruction are faced with several treatment options. However, there are no randomized studies and very few series reporting a long-term follow-up. We report the results of open and endoscopic treatments for PUJ obstruction at one centre over a 6-year period.
Methods Patients were only included in the study if renograms were available before and after surgery; 63 patients (aged 17–85 years) underwent 65 procedures, with open pyeloplasty in 31, Acucise™ endopyelotomy in 24 and percutaneous endopyelotomy in 10. The median follow-up was 13 months. Open pyeloplasty (Hynes-Anderson) was performed by a range of consultants and trainees (40% of cases). All percutaneous endopyelotomies were performed in conjunction with percutaneous nephrolithotomy (PCNL).
Results Of the 31 patients, 81% had a successful outcome (relief of symptoms and obstruction) after open pyeloplasty, as opposed to 63% after Acucise endopyelotomy and five after percutaneous endopyelotomy and PCNL.

Group	*Open pyeloplasty*	*Acucise endopyelotomy*	*Percutaneous endopyelotomy*
Total	31	24	10
Relief of symptoms:			
unobstructed	25	15	5
residual obstruction	4	3	2
Symptomatic obstructed	2	6	3

Conclusion Pyeloplasty is the most successful long-term treatment for PUJ obstruction. Endoscopic treatments may be appropriate in selected cases to reduce perioperative morbidity.

P51

Laparoscopic dismembered pyeloplasty: 30 consecutive cases

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Introduction The best long-term results for the treatment of PUJ obstruction are obtained by dismembered pyeloplasty. The loin incision which usually accompanies open pyeloplasty is painful, prolongs hospitalization and prevents a return to normal activities and/or work for several weeks. The wound is also unsightly and can lead to morbidity. Laparoscopic dismembered pyeloplasty aims to reproduce the same excellent results as open surgery without the disadvantages of the wound.
Methods Thirty consecutive consenting patients presenting with PUJ obstruction underwent laparoscopic dismembered pyeloplasty by one surgeon. Three patients (10%) had failed previous surgery (one each for open pyeloplasty, antegrade endopyelotomy and balloon rupture). The mean (range) patient age was 39.4 (17–70) years and weight 76.7 (52–110) kg. A four-port balloon-dissecting extraperitoneal laparoscopic technique was used in all cases. Interrupted 4/0 polyglactin sutures were used for the pelviureteric anastomosis and the same material as a continuous suture to close the renal pelvis, when appropriate.
Results The conversion rate to open surgery was two in 30 (7%). The mean operative duration was 180 (120–240) min. Eight (26%) patients had their ureter transposed anterior to a crossing lower-pole vessel. Eleven (37%) patients had a separate renal pelvic suture line. The mean postoperative parenteral analgesic requirement was 16.5 (0–60) mg of morphine sulphate. The mean duration of hospital stay was 2.8 (2–7) days. Two (7%) patients had complications: one patient had subendocardial myocardial infarction diagnosed 6 h after surgery, following chest pain, and was discharged after 7 days; one patient developed a renal pelvic calculus, which was treated by percutaneous nephrolithotomy 18 months after surgery. The mean renographic follow-up was 11.8 (3–24) months. Normal upper tract drainage was noted in 24 of 30 (80%) patients. Equivocal excretion curves were obtained in the remaining six (20%) patients, all of whose anastomoses were widely patent on retrograde ureteropyelography and/or ureteroscopy. All patients were symptom-free.
Conclusion A longer renographic follow-up of more patients, preferably in the setting of a randomized controlled trial, is necessary to definitively determine whether a loin wound is necessary for a successful outcome after dismembered pyeloplasty. These results suggest that it is not.

P52

Outpatient ureteric procedures using flexible cystoscopy and sedoanalgesia

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Introduction Retrograde ureteric stenting became established in the 1960s and is usually performed under general anaesthesia in the operating theatre. Since 1996 we have performed retrograde ureteropyelography and ureteric stent insertion with sedoanalgesia in the radiology department, and now report our experience with this technique.
Patients and methods Data were collected prospectively from 1996 to 1999. Procedures were undertaken using sedoanalgesia with antibiotic cover. A flexible cystoscope was used to identify the ureteric orifice and a straight 0.035 inch hydrophilic guidewire inserted under fluoroscopic control. A 4 F general-purpose catheter was then passed over the wire and ureteropyelography performed. If stenting was required, an ultra-stiff guidewire was placed via the catheter and a stent passed over it.
Results In all, 601 procedures were performed on an outpatient basis in the 40-month period. The clinical indications were ureteric obstruction (50%), haematuria (18%), unexplained hydronephrosis (17%) and other (15%); 531 procedures (88%) were technically successful. Failure was most commonly caused by not visualizing the ureteric orifice; 53% of successful procedures involved stent placement or replacement. Immediate complications occurred in 17 patients (3%), including sepsis (0.5%), pain (0.8%), ureteric perforation (0.3%), collecting system rupture (0.3%) and incorrect stent position (0.3%); 94% of patients reported the procedure as acceptable.
Conclusion Retrograde ureterography and ureteric stenting can safely be performed without general anaesthesia on an outpatient basis and both are well tolerated by patients. This technique can reduce costs, hospital admissions, demands on theatre time and complication rates.

P53

Initial experience with the MemoKath™ thermo-expandable ureteric stent

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Introduction Double-pigtail stent placement is the established method for the palliation of benign and malignant ureteric strictures. Complications include trigonal irritation, loin pain, encrustation and blockage. Stents have a limited life-span and regular exchanges are required to avoid obstruction. The use of expandable metallic ureteric stents may avoid complications related to kidney and bladder irritation, encrustation and reflux, as peristalsis is maintained in those parts of the ureter not in contact with the stent. We report our experience with the MemoKath ureteric stent.
Patients and methods Over an 18-month period, nine stents were placed in eight patients (five men and three women, mean age 62.8 years, range 38–69). All stents were placed retrogradely using a flexible cystoscope and C-arm digital fluoroscopy. Local anaesthetic and sedoanalgesia were used as necessary. Complications, further interventions, time to blockage and outcome were determined.
Results Stent insertion was technically successful in all cases; there were no immediate complications. Early complications (five) included obstruction (five), migration (four) and septicaemia (two). Long-term patency (mean 8.3 months) was achieved in three patients. There were no problems with irritative symptoms. In five patients the stent blocked after a mean of 3 days (range 0–7). In two patients successful drainage was established by re-positioning the stent. In the remaining three patients a double-pigtail stent was inserted through the MemoKath.
Conclusions Long-term drainage of the upper urinary tract is possible using thermo-expandable ureteric stents. Patients tolerate the stents well but there is a high risk of stent migration in the first week after insertion; this problem must be solved before the MemoKath can be recommended.

P54

Duration of steroid therapy for treatment of idiopathic retroperitoneal fibrosis

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Introduction Steroid therapy is now an established treatment for idiopathic retroperitoneal fibrosis (IRF). The optimum dose and duration of treatment has not been agreed. In this prospective study we assessed the optimum duration of steroid usage for effective treatment of IRF and its side-effects.
Methods Between 1990 and 1998, 13 patients (10 men and three women, mean age 43.9 years, range 23–78) were treated with prednisolone after a histological diagnosis of IRF; the total duration of treatment was 24 months, with 60 mg on alternate days for 2–3 months, gradually reduced to 5 mg over the next 2 months. Percutaneous nephrostomy or JJ stents were used until the upper tract was free from obstruction. Progress was monitored by changes in ESR, renography and CT. All the patients were given H2-blockers and calcium replacement as prophylaxis against complications of steroids; they were followed up for 23–110 months.
Results Pain relief was noticed within a week of starting the treatment, and leg swelling and renal obstruction were relieved over a few weeks. CT showed regression of the retroperitoneal mass in all patients. At 9–85 months from discontinuing steroids eight patients have had no recurrences requiring treatment. Two patients needed further low-dose steroid treatment for recurrence of pain, with no re-growth of the retroperitoneal mass. No patient developed any serious side-effects from steroid use.
Conclusions Steroids may be used to treat IRF effectively; from this prospective study, 24 months seems to be the optimum duration of treatment of IRF with no serious side-effects.

P55

Malignant ureteric obstruction: antegrade or retrograde stent placement?

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Objective To determine the optimum route for double-pigtail stent placement for malignant ureteric obstruction.
Method A consecutive series of 25 patients (15 male and 10 female) with malignant ureteric obstruction were studied prospectively over a 20-month period. Retrograde stent placement was attempted on 41 ureters in these patients, carried out using a flexible cystoscope and digital C-arm fluoroscopy, under intravenous sedation and analgesia in the uroradiology suite. If retrograde placement was unsuccessful the stent was placed antegradely.
Results Retrograde stent placement was successful in 23 of 41 ureters (56%) attempted; antegrade stent placement was successful in 17 of the remaining 18 ureters. Causes of failure to place the stent retrogradely included failure to identify the ureteric orifice (16),

impassable stricture of the vesico-ureteric junction (one) and impassable ureteric stricture caused by pyeloureteritis cystica (one).
Conclusion If imaging studies identify ureteric orifice involvement by tumour, the antegrade approach should be the initial method of choice. Nephrostomy followed by antegrade stent placement is the preferred method of treatment for patients presenting with acute renal failure and malignant obstruction. The retrograde route is preferred for patients presenting less acutely with elevated serum creatinine values or pain.

P56

JJ stents cause less pain than full-blown renal colic – but only just

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Introduction JJ stents are an essential adjunct to the urological armamentarium but recent studies have stressed the symptoms associated with their placement. We have followed patients through from acute obstruction to stent placement and assessed their subsequent postoperative state.
Methods Fifty patients were assessed at the time of their acute obstruction, again when the stent was *in situ* and then after stent removal. Pain (in the loin and suprapubic region) was measured on a visual analogue scale (VAS). Irritative symptoms were analysed using the IPSS. Any limitation of daily activities was recorded, including sexual activity and return to work.
Results The pain from a stent (mean 5.7 on the VAS) was considered to be less severe than full-blown colic (mean 8.5 on the VAS). Insertion of a stent increased the IPSS by a mean of 9 points and the quality-of-life score by 1.5 points. A third of the patients were able to carry on with their normal level of sexual activity; 40% returned to work (mostly those self-employed). Symptoms decreased with time while the stent was *in situ*.
Conclusion JJ stent insertion is associated with severe symptoms. A prospective study is now underway, with randomization, into long-tailed nonrefluxing and conventional stents.

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Antegrade stent placement for malignant ureteric obstruction

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Introduction Double pigtail stent placement is an established technique for treating ureteric obstruction. A consecutive series of 157 patients with malignant ureteric obstruction treated by antegrade stent placement is reviewed.
Method Purpose-designed catheters with a straight hydrophilic-coated guidewire were used for crossing the stricture. Combined 'rendezvous' procedures and a Nd:YAG laser were used rarely for difficult cases. All stents were delivered through a 'peel-away' sheath, to limit buckling and reduce stent misplacements. Malfunctioning stents were removed and replaced either percutaneously or retrogradely using fluoroscopic guidance or a flexible cystoscope. Stent placement was attempted in 237 ureters in 157 patients over a 7.5-year period.
Results Stent placement was successful in 228 of 237 (96%) ureters. Complications included UTI, trigonal irritation, haematuria, stent obstruction, misplacement, encrustation, ureteric perforation and string retention.
Conclusion Recent advances in equipment for crossing ureteric strictures, and in stent design and delivery, have led to improved technical success rates for antegrade ureteric stent placement, making it a highly successful alternative to retrograde ureteric stent insertion for the palliation of malignant obstruction.

Renal Cancer (Paper session)

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Tumours of the kidney – analyses of the 1999 Section of Oncology Registry

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Introduction The newly formed BAUS Section of Oncology has established a register of newly presenting tumours. After testing in a 6-month pilot study, a minimum dataset has been agreed with the membership. The first 6 months of data are available for this abstract, but all 1999 data will be presented.
Method and results Between 1 January and 30 June 1999, 287 Consultants from 138 centres provided data on 8164 newly presenting urological tumours. Of these, 771 (9.2%) were tumours of the kidney. The male to female ratio was 468 : 296 and the mean (range) age 64.5 (21–97) years. The source of referral was a GP in 58%, another urologist in 5% and other specialists in 31%. There were more referrals from other specialists than for any of the other urological tumours studied. The median time from referral to diagnosis was 39 days, with the delay being > 1 year in eight patients. Histological confirmation of the diagnosis was obtained in 88% of patients and the histology suggested an origin from the renal parenchyma in 598 (78%). Transitional cell tumours were found in 70 (9%). Staging could be estimated in 92% but missing data on clinical T and pathological N categories hampered this process. Most patients were treated by radical ablative surgery, with only 20 having 'organ-conserving' surgery. Systemic palliative therapy was used as sole therapy in 27 patients.
Conclusion The database will be a valuable resource in planning future renal cancer trials and will act as a baseline for monitoring of the delay between referral and diagnosis.

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Renal cell cancer clinic: the first 15 months of a subspecialized clinic dedicated to patients with RCC

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Introduction Increasing subspecialization within both oncology and urology units in our University Teaching Hospital led to the creation of a clinic run by a consultant urologist and a medical oncologist dedicated to patients with RCC.
Method Urologists and oncologists within the region were notified about the clinic and asked to refer complex surgical cases or patients requiring immuno/chemotherapy. A renal cancer database has been established and patient data entered prospectively.
Results In all, 149 patients have been referred in the first 15 months; 29 patients were referred for complex surgical reasons (caval extension, partial nephrectomy, excision of metastases) and 24 patients have been entered into clinical trials. A prospective follow-up protocol for patients after nephrectomy has been developed, including quality-of-life measurement. Four families with Von Hippel–Lindau disease have also been identified.
Conclusion The specialized clinic has demonstrated its success in the number of patients entered into clinical trials. The database and prospective follow-up data should yield useful information in the future. Further clinical trials are planned and a Research Registrar post with funding for basic science projects is to be created.

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Staging of RCC: do we stage the pathology report correctly?

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Introduction Appropriate postoperative planning and prediction of prognosis, as well as comparative studies of RCC, depend on accurate staging. Differences amongst pathologists in reading histology slides are well documented, but the differences in staging pathology reports are not known. This pilot study was conducted to assess the differences in interpreting and staging RCC based on histology reports.
Methods Four consultants (two urologists and two pathologists) were given printed pathology reports of 40 patients who had undergone radical nephrectomy, and were asked to stage the tumours according to the Robson and TNM classifications. None of the consultants was aware of the staging designated by the others. For each patient, the designated stages by the different consultants were compared.
Results Overall, there was unanimous agreement in only 24 (60%) for TNM and 30 (75%) for Robson staging. Discrepancies in staging were 10–30% in TNM and 12.5–22.5% in Robson classifications; 81% of these discrepancies involved higher stages ($\geqslant$ T3). To date, we do not know if these staging differences have influenced our patient follow-up care or not, but this is currently being assessed.
Conclusion Correct staging of RCC is essential for the reliable prediction of prognosis and comparison of results between different centres. Clearly, staging differences as high as 30% between different consultants, as shown in this study, highlight the need to apply agreed protocols for reporting renal tumour histology.

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Pretreatment haemoglobin level as a predictor of response to subsequent treatment

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Introduction Although polycythaemia caused by erythropoetin production from renal cancer is a rare clinical presentation, immunoreactive erythropoetin sequences can be detected in up to a third of patients. Prompted by reports that the rare patients with florid polycythaemia had a better than average response to cytokine therapy, an analysis has been undertaken to investigate the influence of pretreatment haemoglobin level of outcome in patients treated in the recently completed MRC renal cell cancer randomized trial REO1 comparing medroxyprogesterone acetate and IFN-α.
Methods Pretreatment haemoglobin level and response at 6 months was recorded in 251 of 350 (72%) patients in the trial [*Lancet* 1999; 353: 14–7]. Haemoglobin levels (g/L) were grouped into three equal categories; low (< 118 in males and < 110 in females); medium (118–132 in males and 110–126 in females); and high (> 132 in males and > 126 in females). The response at 6 months was grouped into two categories, either (i) complete response (CR), partial response (PR) or stable disease (SD), and (ii) progression (including deaths before 6 months). The association between haemoglobin levels and response was investigated before and after adjustment for other variables using a logistic regression model.
Results There was evidence of an association between pretreatment haemoglobin and response at 6 months ($P < 0.001$). A response

(CR/PR/SD) occurred in six of 84 (7%) patients in the low haemoglobin group, 14 of 82 (17%) of those in the medium and 28 of 85 (33%) of those in the high haemoglobin group. This association between pretreatment haemoglobin level and response was also present after adjustment for age, sex, WHO performance status, single or multiple metastases, time since diagnosis and time since metastases ($P < 0.001$).
Conclusion Further examination of this risk factor in other datasets is required. Examination of the molecular biology responsible for the observation could lead to a better insight into improved strategies for the best responding group and into alternative therapeutic strategies for the poorly responding haemoglobin group.

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Magnetic resonance angiography assessment of inferior vena caval thrombus in the choice of surgical approach to renal carcinoma

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Introduction Renal carcinoma may extend into the inferior vena cava (IVC) and reach the right atrium. Infrahepatic caval extension can be removed by an abdominal approach, with control of the vena cava. More extensive involvement may require cardiopulmonary bypass with hypothermic circulatory arrest, but this more complex approach introduces other potential complications. The selection of the correct surgical approach is therefore of vital importance.
Patients Amongst 34 patients with RCC and IVC extension operated on during the past 15 years, nine have recently undergone preoperative magnetic resonance angiography (MRA) to assess the extent of the tumour thrombus. The tumour thrombus was classified as infrahepatic, hepatic, suprahepatic or right atrial. The findings on MRA were correlated with those at surgery.
Results MRA showed that four patients had infrahepatic tumour thrombus, two hepatic, two suprahepatic and one had extension into the right atrium. These findings were confirmed intra-operatively. Cardiopulmonary bypass was necessary for three patients with suprahepatic or right atrial thrombus. Tumour thrombus below the hepatic veins was removed from below, whereas in patients with tumours above this level, the tumour was cleared with cardiopulmonary bypass, including hypothermic circulatory arrest in two cases.
Conclusion MRA reliably detected the extent of tumour thrombus within the IVC in all patients, and thus facilitated the choice of surgical approach. Obstruction of the hepatic veins appeared to mark the watershed above which circulatory arrest was desirable.

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The role of embolization in the treatment of advanced RCC

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Introduction The role of embolization for patients with locally advanced or metastatic RCC remains controversial; we reviewed our experience with this technique.
Patients and methods Between 1991 and 1999, 30 patients underwent embolization for RCC; 25 patient records were retrieved (11 men, 14 women, mean age 76 years, range 57–93). Twelve presented with haematuria, four with symptomatic metastases, two with loin masses and seven as incidental findings. The diagnosis was made on ultrasonographic and CT appearances. The mean (range) tumour size was 8.4 (4–14) cm. Indications for embolization were local symptoms and metastases in seven, locally advanced disease in patients with poor performance status in 10 and abortive open surgery in two. Six elderly patients, (mean age 81 years) declined nephrectomy after informed consent and were offered embolization. Using a transfemoral approach, the feeding vessels were identified and embolized with steel coils and/or ethanol. Pethidine (mean 60 mg) and midazolam (mean 6.3 mg) were administered peri-operatively.
Results There were no immediate complications. Initially nine patients required parenteral opioid analgesia but after 24 h, 22 were comfortable with oral medication. Fever was seen in 20 patients and lasted for a mean (range) of 2.2 (1–5) days. The median (range) hospital stay was 5 (1–15) days. Eight patients died (mean survival 7.5 months); the mean follow-up of the 17 survivors was 32 (1–89) months. Twenty (80%) of all patients remained free of local symptoms; five patients reported haematuria, three required hospitalization, two a blood transfusion and one re-embolization. Fourteen patients have undergone imaging to assess disease progression. The tumour volume decreased in five, increased in two and remains unchanged in seven.
Conclusions Embolization is safe, with minimal morbidity and provides effective long-term palliation for patients with advanced renal cancer. The procedure should be included as an alternative to nephrectomy in clinical trials evaluating treatment options in these patients.

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En bloc adrenalectomy as part of radical nephrectomy for RCC: is it justified?

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Introduction The potential benefit of en bloc adrenalectomy during radical nephrectomy for RCC has been a controversial issue. Some argue that the best chances of cancer cure will be achieved by wide en-bloc excision of the kidney, perinephric fat and adrenal glands. Others are more conservative and express concerns about the potential necessity for subsequent contralateral nephrectomy for RCC and adrenalectomy, and the risk, albeit extremely small, of there being no adrenal gland on the contralateral side. Our aim was to identify the potential benefits of en-bloc adrenalectomy in all patients with RCC undergoing radical nephrectomy.
Patients and methods A consecutive series of 110 patients (36 women and 74 men, age range 32–87 years) with RCC underwent radical nephrectomy between 1992 and 1999. A 12th rib approach was used in 78 and a thoraco-abdominal approach in 32 with large tumours. In each patient the kidney, perirenal fat, the adrenal gland and all lymph nodes along the ipsilateral inferior vena cava (IVC)/aorta were widely excised. In seven patients there was tumour extension into the IVC, which was also removed, and the IVC over-sewn. Bilateral tumours were removed by radical nephrectomy of the larger tumour and partial nephrectomy (with adrenal preservation) of the smaller tumour.
Results Histological examination confirmed the diagnosis of RCC in all cases. Four patients had metastases within hilar lymph nodes. Histology revealed adrenal metastases in two patients (age 42 and 74 years), a previously undiagnosed phaeochromocytoma in one and an adrenal cortical adenoma in one. On follow-up, nine patients (8%) have died from metastatic disease. The two patients with adrenal metastases are alive with on evidence of recurrent disease at 68 and 66 months. No patients have developed hypo-adrenalism.
Conclusion In this series, excision of the adrenal gland en bloc with the kidney during radical nephrectomy did not increased the morbidity of the procedure and is likely to have cured the 2% of patients with solitary RCC metastases within the adrenal. A further 2% were found to have incidental benign tumours within the adrenal. We recommend en-bloc adrenalectomy in all patients undergoing surgery for RCC. In patients with bilateral tumours the adrenal can be preserved on the side with the smaller tumour.

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Microvascular invasion in RCC

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Introduction Recent publications have suggested that microvascular invasion might be a reliable and useful independent prognostic indicator in RCC, with a reported incidence in renal tumours of $\approx 25\%$. We have attempted to assess the incidence and the prognostic value of microscopic vascular invasion in patients with no macroscopic or microscopic renal vein invasion.

Methods In all, 111 nephrectomies for primary RCC were retrospectively assessed to determine the presence of microscopic vascular invasion. Gross or microscopic renal vein invasion and/or lymph node metastases were present in 27 patients who were excluded from the study. Details of the follow-up (at least 18 months) were obtained in all patients.

Results Of the remaining 84 patients, microscopic vascular invasion was identified in eight (10%); four of these died from metastatic disease within 3–8 years. The remaining four patients were alive and well at the last follow-up (6–12 months ago). Of the 76 patients with no microvascular invasion, 18 (24%) developed metastatic disease; 14 have died from their disease and four are currently alive with metastatic disease.

Conclusions Our findings support the adverse prognostic implications of microscopic vascular invasion that have been reported previously. However, the incidence in our series (10%) is lower than in other reports, possibly because we applied rigid criteria for accepting the presence of definite microvascular invasion, or variability of sampling and exclusion of cases with renal vein invasion.

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Laparoscopic adrenalectomy: an evaluation of 100 consecutive procedures

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Introduction We have prospectively evaluated the feasibility and safety of performing laparoscopic transperitoneal adrenalectomy in a consecutive series of surgical patients. During the study period our technique and selection criteria have developed with accumulated experience.
Method From November 1993 to August 1999, 100 laparoscopic adrenalectomies were attempted in 90 patients (median age 50 years, range 18–77, 63% female) who presented with symptomatic adrenal masses or who had an incidental large mass diagnosed during investigation for other complaints. Lesions were left-sided in 44% of patients and bilateral in 11%. Indications for resection were: Conn's syndrome (30), phaeochromocytoma (22), Cushing's disease (12), nonfunctioning adenoma (eight), congenital adrenal hyperplasia (six), cortisol-producing adenoma (five), metastatic disease (four), and others (13). The median (range) size of the lesions was 3.5 (0.5–20) cm and the median operative duration 65 (40–170) min.
Results Conversion to an open procedure was necessary in eight patients (9%). Minor morbidity occurred in seven patients (8%) and major morbidity in twos (pancreatitis, peritonitis). The median hospital stay was 3 (1–16) days. At a median follow-up of 26 (1–69) months no patient has evidence of recurrent hormonal excess.
Conclusion Laparoscopic adrenalectomy is a safe and effective alternative to open surgery. Postoperative analgesic requirements are reduced, resulting in a shorter convalescence period. It requires a high degree of technical expertise and should remain within the remit of the advanced laparoscopist.

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Retroperitoneoscopy in the first 300 patients: a single-centre one-person experience

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Introduction Since the introduction of the balloon technique of retroperitoneoscopy by Gaur in 1992, this modality is being used worldwide for various urological procedures. Although multicentre experiences have been reported earlier, the individual contributions have been too small to provide any definite conclusions. This report details the experience of one surgeon in one centre to provide a better perspective of the efficacy, efficiency and safety of this new modality.
Methods The study included 300 retroperitoneal laparoscopic (RLP) procedures using the balloon technique during the last 9 years in 290 patients (age range 4–74 years). The lumbar approach was used for 264, the iliac approach for 29 and the suprapubic approach for seven procedures. However, in nine of these, where extensive retroperitoneal dissection was required, the approach was later converted into a combined retroperitoneal approach. The mini-open access was used for 145 and the closed percutaneous access for the remaining 155 procedures. Most patients were of average build and only 14 were mild to moderately obese. The male to female ratio was 3 to 1 and 14 of these were children. Most patients had a 'virgin' retroperitoneal space, except for five who had a percutaneous nephrostomy and seven who had abdominal surgery performed earlier on the ipsilateral side. Thirty-one patients were in renal failure and two of these had acute renal failure because of calculus disease. The RLP included 138 renal, six adrenal, 82 ureteric, 50 gonadal, 13 lymphatic system, three vesical, two autonomic nervous system and six vertebral procedures. Thirty-four were minor, 236 major and 30 supra-major operative procedures. The supra-major procedures included nephroureterectomy in seven (two with excision of a cuff of bladder), live donor nephrectomy (nine), adrenalectomy (seven), ureteric reimplantation (one), correction of retrocaval ureter (one), retroperitoneal lymph node dissection for metastatic disease (two), bladder diverticulectomy (one) and total lymphatic disconnection of the upper urinary tract for intractable chyluria (two). Nitrous oxide was used for pneumo-insufflation in 103 procedures, instead of the commonly used carbon dioxide.
Results The retroperitoneal laparoscopic procedure was successful in 269 of the 300 procedures (≈ 90%). There were five failures during nephrectomy, one during renal biopsy, six during pyelolithotomy, three during pyeloplasty, three during adrenalectomy, two during varicocelectomy, eight during ureterolithotomy, one during ureteric reimplantation, one during bladder diverticulectomy and one during vertebral biopsy. These were converted into a mini-open procedure, mostly by joining the port incisions. The operative duration was 0.5–5.5 h, depending upon the type of the procedure and the presence or absence of adhesions. The total incidence of complications was 14%, but only four were major, all intraoperative and during the early part of the series, e.g. avulsion of the ureter, torn renal pelvis, colonic injury and severe hypotension. Blood transfusion was not required in any patient for operative blood loss. The mean duration of analgesic intake was 2.5 days, of hospital stay 2.6 days and for return to work 13.5 days.
Conclusion Retroperitoneal laparoscopy using the balloon technique is a reasonably safe, efficient and reliable minimally invasive operative procedure.

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Prospective comparison of standard open-flank vs laparoscopic nephrectomy in 249 patients with benign renal disease

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Introduction We report the results from a prospective comparison between standard open-flank vs laparoscopic nephrectomy for benign renal disease.
Patients and methods Between 1993 and 1998, we performed a total of 249 nephrectomies for benign renal disease. There were 118 patients in the standard open-flank nephrectomy group (median age 58.5 years, range 8–89) and 131 patients in the laparoscopic nephrectomy group (median age 40 years, range 16–73). Various clinical data were compared among both groups.
Result The median (range) operative duration in the standard group was 90 (30–240) min and was also 90 (41–210) min in the laparoscopic nephrectomy group. In the laparoscopy group eight patients were converted to open surgery (6.1%). There were 27 complications (21%) in the laparoscopic nephrectomy group, compared to 30 (25%) in the standard group. Postoperatively, patients in the laparoscopic nephrectomy group required less morphine sulphate equivalent (median 12 mg vs 20 mg) for pain control and they had a shorter hospital stay (4 vs 10 days) and shorter duration of convalescence (24 vs 36 days). These results were statistically significantly different.
Conclusion Laparoscopy nephrectomy gives similar operative

results but within a significantly briefer postoperative course than with standard open-flank nephrectomy. Laparoscopy is an attractive treatment option in patients with benign renal disease and an appreciated supplement to the spectrum of operative techniques for nephrectomy.

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Cost-effective use of the URF-P3 endoscope

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Introduction The consensus amongst endourologists is that the life expectancy of a flexible ureteroscope is as little as 15–20 procedures. Knowledge of the pitfalls and the cost of repair may encourage endourologists to increase the longevity of the ureteroscope.
Method We illustrate our use of the URF-P3 endoscope, the versatility in 35 consecutive cases, and common pitfalls with reference to the use of laser fibres, guidewires and maintenance. We also summarise the URF-P2 endoscope repairs carried out by Keymed over the last 2 years on the 14 endoscopes in the UK.
These cases show the versatility, with 13 diagnostic procedures, eight laser ablations of upper tract TCC, five laser fragmentations of lower-pole stones, four laser ablations of calyceal diverticular necks and stones, two stones in horseshoe kidneys and three complex stones. Using our protocol no scope damage has been recorded, but UK repairs were:

Reason for repair	*Repair price (£)*
Insertion damage	5404
Angulation damage	5404
Corrosion in LG probe	165
Insertion damage	5042
Leaking at tip	305

Conclusion The Olympus P3 flexible ureteroscope is a highly versatile instrument, which is cost-effective if the user is aware of common pitfalls.

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Computer-assisted surgical training system for TURP

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Objectives To develop a realistic and reusable computer-assisted surgical training system for TURP.

Methods A disposable prostate model is housed in a mock-up abdomen. A software program that provides a 3D illustration of the prostate model has been developed. The position of the resectoscope with reference to the model is tracked by infrared-emitting diodes attached to it and these in turn are monitored by an optical tracker. The movement of the loop in relation to the resectoscope is measured by a potentiometer attached to the working element.
Results The position of the resectoscope is shown on the monitor, superimposed on a 3D image of the prostate model in real time. A 2D image shows the amount of tissue resected and the proximity of the loop to the capsule. A series of thumbnail images are shown and the highlighted image represents the current position of the scope. An *in vivo* system is being researched simultaneously and this system will use ultrasonography to recognise and reconstruct 3D images of the corresponding prostate. This system will provide real-time input of the resection in progress and act as an interactive training aid.
Conclusions This system can exist as a stand-alone training aid and is to be tested. The potential application of the *in vivo* system in routine TURP has enormous implications for training and quality control.
Funding: EPSRC

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Surgical aptitude: are urologists different? A virtual study

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Introduction Specific objective investigations of surgical skill have included manual dexterity, spatial ability, personality and decision-making ability. Are urologists or endourologists a self-selected group with an innate spatial awareness ability? The MIST VR system (Ethicon Ltd, Edinburgh) is a computer-based virtual reality system which objectively tests spatial awareness, and its success has been validated in south-east Scotland.
Methods In all, 120 volunteers in three cohorts (30 consultant urologists, 30 urological trainees and 30 who are not surgeons) will undergo psychomotor testing, performing an identical series of standard exercises using the MIST VR surgical trainer to determine spatial awareness. Testing will take place during the first part of the annual BAUS meeting in June 2000; data will be collated on a database and presented from the podium on the final day. ANOVA will be used to determine statistical differences among the groups. Individuals will be given a score with which they will be able to compare their individual spatial awareness ability to the mean score of each cohort. The outcome of the study will determine whether urologists have inherent spatial awareness compared with the general population and if so whether this skill can be acquired. These results may have implications for the selection process of the next generation of urological trainees.

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A prospective randomized placebo-controlled double-blinded study of electromagnetic therapy in the treatment of chronic abacterial prostatitis and prostatodynia

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Introduction Chronic pelvic pain syndrome is a common condition where treatment has been unsatisfactory. Although the aetiology is uncertain, there is evidence that this symptom complex may result from muscular dysfunction of the pelvic floor and/or neural hypersensitivity. We hypothesised that the application of electromagnetic therapy may improve pelvic floor spasm and neural hypersensitivity.
Patients and methods Twenty-one patients (mean age 47 years) were randomized to receive either the active treatment or placebo. Full Stamey localization studies were performed on all patients to exclude the presence of micro-organisms. Treatments consisted of 15 min of 10 Hz energy, followed by a further 15 min at 50 Hz, twice a week for 4 weeks. The placebo arm was identical to the active treatment in all respects except that no energy was applied; instead, a speaker under the device replicated the sounds created during active treatment. Patients were evaluated at baseline, 4 weeks and 3 months after treatment using validated visual analogue scores, quality-of-life scores and the recently described MH-chronic prostatitis symptom index. Success was defined as an improvement in at least four of eight categories (i.e. $> 50\%$ improvement) which was maintained at the 3-month follow-up.
Results Five of eight patients receiving active treatment had a successful outcome, whereas one of eight patients responded to placebo ($P < 0.05$). There were no serious adverse events and one patient reported minor transient symptoms of paraesthesia of < 48 h duration.
Conclusion The use of electromagnetic therapy represents a promising new therapy for the treatment of chronic pelvic pain syndrome which is refractory to medical therapy. Further follow-up will determine the durability of the response.

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VEGF expression in BPH-related haematuria and its modulation by finasteride

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Introduction A bleeding prostate is the final diagnosis in 10% of patients presenting to walk-in haematuria clinics. We have seen that haematuria in this setting is associated with increased suburothelial vascularity, a finding which is reversed by finasteride [*BJU Int* 2000; 85: 70–3].
Patients and methods In this study, we examined the expression of VEGF by prostatic urethral urothelium in patients with haematuria and its modulation by treatment with finasteride. We examined TURP specimens from three groups of patients: 26 control patients with BPH but no haematuria, 13 patients with untreated BPH-related haematuria and 10 patients who had been treated with finasteride. We examined VEGF expression using anti-human VEGF immunohistochemistry. A VEGF index was calculated using the following formula: [(% urothelial cells staining strongly $\times$ 2) + (% cells staining weakly $\times$ 1)]/2
Results Bleeding prostates showed strong urothelial cytoplasmic staining, with a mean (SD) index value of 57.5 (26.3). There was also endothelial cytoplasmic positivity in the same cases. Patients with uncomplicated BPH (mean index value 7.5, SD 11.6) or those treated with finasteride (mean index value 27.5, SD 10.7) showed significantly less staining (haematuria vs obstruction $P = 0.001$, haematuria vs finasteride $P = 0.02$).
Conclusions Increased vascularity in BPH-related haematuria may be caused by increased expression of VEGF in the prostatic urothelium. Treatment with finasteride is associated with down-regulation of VEGF, in common with other studied growth factors [*Minerva Urol Nephrol* 1997; 49: 63–72].
Funding: Merck UK Ltd

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Prostate volume as a predictor of urodynamically defined BOO

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Introduction The conventional assessment of men with LUTS includes the peak flow rate (PFR) and DRE of the prostate. TRUS has been proposed as a more accurate method of measuring prostate volume (PV). Several different TRUS variables have been used to describe the prostate, e.g. the transition zone index (TZI). The relative place of each of these investigations is uncertain. We have used ROC statistics to determine their ability to predict urodynamically defined BOO.
Methods The study included 299 men with LUTS assessed in our prostate centre, investigated with DRE, PFR and TRUS (PV and TZI). BOO was diagnosed by pressure-flow study, using the Abrams-Griffiths nomogram. ROC analysis was conducted using MedCalc software.
Results There was a statistically significant relationship between PV and obstruction. The area under the ROC curve for PV by DRE was 0.67, PV by TRUS 0.68, TZI 0.63 and PFR 0.87. A threshold value for PV by DRE of 40 g, PV by TRUS of 50 g and PFR of 8 mL/s gave a specificity and positive predictive value of $> 95\%$. A TZI value of 0.6 gave a specificity of $> 95\%$ but a sensitivity of only 10%.
Conclusions TRUS volume and TZI alone are no better at predicting the presence of obstruction than simple clinical examination and were inferior to the PFR. There seems to be no advantage in calculating TZI in the determination of obstruction. Other calculated variables, e.g. the presumed circle area ratio from transrectal imaging, may yet hold the key to easier prediction of obstruction and should be investigated in the same way.

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Peripheral zone biopsy at TURP; what are we missing?

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Introduction This prospective study aimed to determine whether transrectal biopsies after TURP would increase the detection of incidental prostate cancer in men undergoing TURP for BOO. This is of particular importance because of the increasing use of ablative procedures in the treatment of BOO, where histology is not obtained.
Methods Ethical committee approval was obtained; 131 men

undergoing TURP for BOO had a transrectal biopsy of the residual prostatic tissue taken immediately after the resection.
Results Ninety-two patients had a palpably benign gland with either an unknown PSA level (they presented in acute retention) or a PSA level of < 10 ng/mL. Of these patients nine (7%) had prostate cancer, two (2%) were detected by biopsy only and a further three (3%) in the resected specimen only. Eighteen men with a PSA level of > 4 ng/mL underwent preoperative TRUS and biopsy which revealed BPH only. However, four men were subsequently found to have prostate cancer after a repeat biopsy at the time of surgery. The cancers detected were all Gleason score $\geqslant 5$ and occurred in men with a mean (range) age of 69 (58–78) years.
Conclusions The study detected a 10% incidence of prostate cancer in men who either had a normal PSA level, who presented in retention or who had undergone preoperative TRUS and biopsy. The implications should be considered in patients undergoing treatment for BOO where the histology is not obtained.

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Randomized, placebo-controlled study of alfuzosin (slow-release) in patients undergoing a trial without catheter following acute urinary retention

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Introduction Acute urinary obstruction caused by BOO resulting from prostatic enlargement is one of the commonest causes for acute admission to urology wards. Traditionally patients are catheterized and put on the first available operating list for TURP. More recently there has been a trend to commence treatment with α-blockers after catheterization followed by a trial without catheter (TWOC), in the hope that surgery may be avoided in a significant proportion of the patients. There is no conclusive evidence of the efficacy of this treatment. We conducted a trial to evaluate the efficacy of using the α-blocker alfuzosin in patients with acute urinary retention.
Patients and methods All patients presenting with acute urinary retention to our hospital were included in the trial. Exclusion criteria included patients with known bladder or prostate malignancy, bladder calculi, obvious UTI, urethral stricture or those already on α-blockers. In all, 81 patients gave their consent and were randomized and had their blood taken for biochemistry and PSA assay before catheterization. The retention volume (RV) was recorded. Trial medication was started on a twice daily dose and the first TWOC carried out after a minimum of three doses or 36 h after admission. TWOC was considered successful if the patient voided > 150 mL with a bladder scan recording a residual of < 200 mL. Patients who failed the TWOC were re-catheterized, discharged home on trial medication and called for a second TWOC after 2 weeks. Failure at the second TWOC meant they were put on next available operating list for TURP.
Results For various reasons 19 patients were excluded from the study; 62 patients remained for analysis, 34 in the active and 28 in the placebo group. The two groups were well matched for all variables except serum PSA level. The results were:

Mean (range) variable	*Placebo group*	*Alfuzosin group*
Number	28	34
Age, years	67.7 (46–84)	69.5 (56–88 9)
Retention, mL	998 (400–2000)	60 (400–2000)
Serum PSA, ng/mL	9.25 (0.3–63.6)	19.5 (0.5–62.3)
Successful TWOC, n (%)	16 (57)	17 (50)
Failed TWOC, n (%)	12 (43)	17 (50)

Conclusion Although there were few patients in the study sample there was no significant difference in voiding on TWOC after acute urinary retention in the two groups ($P = 0.575$).
Funding: Lorex Synthelabo Pharma

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Doxazosin vs alfuzosin in BPH

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Objective To assess, in a double-blind trial, the efficacy and tolerance of doxazosin and alfuzosin in the treatment of moderate-to-severe symptoms of BPH.
Methods The study included 210 men with BPH who were randomized to double-blind treatment with doxazosin (1–8 mg/day) or alfuzosin (5–10 mg/day) for 14 weeks in an escalating-dose fashion. Primary variables assessed for efficacy were the IPSS and maximum urinary flow rate (Q_{max}). The endpoint of efficacy was analysed using an analysis of covariance with baseline values as the covariate.
Results Both doxazosin and alfuzosin significantly ($P < 0.001$) relieved total, irritative, and obstructive symptoms, and significantly ($P < 0.001$) increased Q_{max} compared with baseline. Doxazosin (mean dose 6.1 mg/day) produced significantly ($P < 0.05$) greater improvements in total and irritative IPSS than alfuzosin (mean dose 8.8 mg/day). Differences between the groups were marginally significant ($0.05 < P < 0.10$) for improvements in obstructive IPSS but were not statistically significant for improvements in Q_{max}. Both treatments were similarly well tolerated. The least-squares adjusted mean (SEM) [n] changes from baseline at endpoint were:

Efficacy assessment	*Doxazosin*	*Alfuzosin*	P*
Change in:			
total IPSS	−9.2 (0.6) [92]	−7.4 (0.6) [87]	0.036
irritative IPSS	−3.5 (0.2) [92]	−2.8 (0.3) [87]	0.049
obstructive IPSS	−5.7 (0.4) [92]	−4.7 (0.4) [87]	0.069
Q_{max} (mL/s)	2.8 (0.4) [88]	2.5 (0.4) [81]	0.675

*Doxazosin vs alfuzosin

Conclusions Doxazosin (at mean dose of 6.1 mg/day) was significantly more effective than alfuzosin (at mean dose 8.8 mg/day) in relieving total and irritative urinary symptoms in patients with moderate-to-severe BPH, and with a clinically similar safety profile.
Funding: Pfizer Inc

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The changing face of TURP over a 10-year period

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Introduction TURP remains the gold standard surgical treatment for patients presenting with BOO secondary to prostatic enlargement. Recently a combination of the increasing profile of prostatic disease, the availability of α-receptor blocking agents and the expansion of urological departments may have lead to changes in the practice of TURP. We compared TURP as currently performed with that carried out 10 years ago at one UK centre.
Patients and methods The notes of patients undergoing TURP at a UK district general hospital throughout a 6-month period in 1988 and then 1998 were reviewed retrospectively. In 1988 the operations were performed by one consultant urologist, whereas in 1998 surgery was shared by two consultants, one staff-grade surgeon and a specialist registrar.

Results During the period 1 January to 30 June 1988, 88 patients underwent TURP, compared with 120 over the same period in 1998; 74% of these patients' notes were available for review in the first period, compared with 85% in the last. In the 1998 series, 17% of patients had tried initial α-receptor blocking treatment; the results were:

Variable	*1988*	*1998*
Mean (SD) age, years	72 (7.6)	72 (7.7)
Percentage of patients		
with urinary retention	46	32
with LUTS only	26	63
Mean (SD)		
weight (g) of tissue resected	32.9 (25.8)	21.9 (16.5)
length of stay, days	7.2 (4.9)	5.3 (1.8)
catheterization, days	2.8 (2.0)	2.6 (1.1)
No. requiring transfusion	12	3
% of inpatient complications	34	30
% prostate cancer	18	14

Conclusion The practice of TURP has changed considerably in 10 years. Currently fewer patients are undergoing TURP for urinary retention; as only 17% of patients had tried α-blockers before surgery it is difficult to argue that this decrease is caused by the use of these drugs. More patients are being treated for LUTS alone and the volume of the prostate resected has decreased. It is possible that the higher profile of prostatic disease has led men to be treated earlier.

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Long-term follow-up after presentation with a first episode of acute urinary retention

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Introduction We reported that slow-release (SR) alfuzosin improves the chances of a successful trial without catheter (TWOC) after acute urinary retention (AUR) [*BJU Int* 1999; 84: 622–7). We report the long-term outcome of these patients.

Patients and methods Eighty-one patients presenting with painful AUR were enrolled in a prospective, randomized, placebo-controlled trial of the effect of SR alfuzosin on the outcome of TWOC. All patients were followed to the time of prostatic surgery or continued in open follow-up.

Results Overall, 34 patients (42%) voided successfully, 22 of 40 (55%) with SR alfuzosin and 12 of 14 with placebo ($P = 0.03$). Of the 34 patients who had a successful TWOC 11 (32%) had a further episode of AUR, a mean of 4.1 months (range 1 day to 1.2 years) after discharge. Eleven patients have undergone bladder outlet surgery (seven after a further episode of AUR) a mean (range) of 8.2 (0.5–18) months after discharge. Nineteen patients (56%) have had neither further AUR nor bladder outlet surgery; of these two have been diagnosed and treated for prostate cancer, one patient failed to attend follow-up and three were discharged 3–6 months after AUR. According to hospital records they required no further urological intervention. Fifteen of 19 patients remained under follow-up for a mean (range) of 1.5 (1–2) years, none of whom have required any further urological intervention, 12 being managed with α-blockers. When compared with those who experienced further AUR or required surgery, the group who did not require further intervention had significantly smaller post-void residual volumes after their successful TWOC (mean value 44.7 vs 92 mL, $P = 0.025$); no other significant differences between these groups were identified.

Conclusions High post-void residuals after successful TWOC predict further AUR or the need for TURP, facilitating urgent intervention in the absence of a urinary catheter. In open follow-up, 19 of 34 (56%) patients who had a successful TWOC avoided surgical intervention in the longer term, justifying a TWOC after an episode of AUR.

Funding: Synthelabo

Imaging (Paper session)

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A comparison of virtual nephroureteroscopy and flexible ureteroscopy in the assessment of upper tract pathology

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Introduction Computerized endoscopy involves helical CT imaging being used to acquire data to generate high-quality 3-D images. 'Fly-through' technology then allows the reconstructed interior of the ureter and collecting system to be navigated as a virtual ureteronephroscopy. Our pilot study assesses the feasibility of virtual ureteronephroscopy in comparison with flexible ureteroscopy in upper tract pathology.
Patients and methods Seven patients with a variety of upper tract pathologies underwent CT; a fly-through software program then constructed a virtual ureteronephroscopy. The patients then underwent flexible ureteroscopy and the two examinations were compared.
Results No pathology was missed by virtual ureteronephroscopy. Analysis shows the quality of information acquired is equal if not superior to flexible ureteroscopy, with additional staging information being gained. The cost and morbidity profiles of virtual ureteronephroscopy are superior.
Conclusions Virtual ureteronephroscopy is a promising method of non-invasive imaging of the upper urinary tract which may allow the endourologist to evaluate upper tract pathology more accurately.

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Testicular microlithiasis: a benign or premalignant condition?

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Introduction Testicular microlithiasis (TM) has been described as a benign condition with a malignant association, but a few reports suggest that TM may be a premalignant condition. We reviewed our experience with TM to determine whether this claim could be substantiated.
Patients and methods All patients with classic TM diagnosed by high-frequency testicular ultrasonography (US) between 1994 and 1999 were included in this study. Over this 5-year period, 3003 testicular ultrasonograms were taken. Information including the indication for testicular US, diagnosis, management and any histological specimen reports were obtained from medical records. Patients with TM had an annual follow-up by US unless they had testicular cancer, when the follow-up with clinical reviews were more frequent.
Results TM was found in 54 patients (mean age 37 years, range 11–84). The mean (range) follow-up was 33 (1–70) months. The incidence of TM was 1.8%; 16 of these patients had testicular malignancies at diagnosis, comprising six seminomas, five teratomas and five mixed tumours. Fourteen patients had hydroceles/epididymal cysts, seven had varicoceles, two epididymitis, eight small testes and 14 patients had no pathology. Two patients developed interval tumours (seminomas) diagnosed by US, one at 2 and the other at 4 years. The overall incidence of germ cell tumours in this group was 33%.
Conclusions TM can no longer be regarded simply as a benign condition with a malignant association. In our series two patients developed interval testicular cancers, which strengthens the claim that TM may be a premalignant condition and supports the practice of annual testicular US as a standard management for these patients.

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A comparison of power and colour Doppler in TRUS of the prostate

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Introduction We evaluated the role of power (PD) and colour Doppler (CD) ultrasonography in detecting abnormal hypervascularity in patients undergoing TRUS for suspected prostate cancer.
Patients and methods The study included 148 patients with suspected prostate cancer (on the basis of an elevated serum PSA level, median 18.5 μg/L, or an abnormal DRE) who underwent TRUS using a Combison 420 (Kretz Technik) 7.5 MHz probe. The CD and PD findings were documented. Sextant biopsies were taken in 140 patients, with additional biopsies guided by abnormal Doppler findings.
Results Of the 140 patients biopsied, 62 had prostate cancer, 43 prostatitis, 33 BPH and two further patients had high-grade prostatic intraepithelial neoplasm. Abnormal findings on imaging were:

Histological diagnosis	*Grey-scale*	*PD*	*CD*
Prostate cancer (n = 62)	45	50	43
Prostatitis (n = 43)	27	35	28
BPH/normal (n = 33)	18	21	19

The sensitivity of PD was 81% (vs 69% with CD). The correlation between grey-scale TRUS and PD abnormalities for cancer was 81% (vs 73% with CD). Ten patients with abnormal PD findings and a normal grey-scale pattern had prostate cancer. Only seven of these patients had CD abnormalities.
Conclusions PD is more sensitive than CD in the assessment of patients with suspected prostate cancer, with a sensitivity of 81% but with a low specificity of 28% because findings in patients with prostatitis and BPH were similar. PD is a useful adjunct to grey-scale imaging in patients undergoing TRUS for suspected prostate cancer and may increase the overall detection rate of prostate cancer.

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Magnetic resonance urography in patients with spinal deformity

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Introduction Serial imaging of the upper urinary tract is important in patients with neuropathic bladder dysfunction. Patients with spinal deformity can be difficult to image and ultrasonography (US) is often inadequate. The disadvantages of serial IVU in such patients include poor visualization, difficult intravenous access, repeated radiation exposure and contrast allergy. We have assessed the

relatively new technique of magnetic resonance urography (MRU) in patients with spina bifida.
Patients and methods Patients with spina bifida and neuropathic bladder dysfunction were scanned using a rapid-acquisition heavily weighted T2 MRI technique. No contrast medium was given but patients received 20 mg of intramuscular frusemide. Cross-sectional, coronal and three-dimensional views were obtained. The quality of image for each component of the urinary tract and the overall quality was graded from 0 (poor) to 5 (excellent). The degree of spinal deformity was assessed by Cobb's angle.
Results To date, 20 patients (median age 33 years, range 19–52) with a median (range) Cobb's angle of 70° (0–180) have undergone MRU. Seventeen patients had undergone previous US, in only six of whom was it possible to visualise both kidneys. Of the 39 renal tracts, MRU visualised all kidneys, 34 ureters fully, three incompletely and two not at all. Twelve kidneys were scarred, and 19 pelvicalyceal systems and 17 ureters were dilated. A colonic conduit stricture was identified. The mean (range) overall quality score of the MRU was 4.6 (3–5).
Conclusion MRU provides excellent noninvasive upper tract imaging for a group of patients who were previously difficult to investigate. The potential complications of invasive techniques are avoided.

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IVU is the investigation of choice in renal colic in pregnancy

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Introduction There has traditionally been resistance to performing IVU during pregnancy to investigate loin pain, because of the perceived risk of radiation exposure to the fetus. We believe this risk is minimal and that IVU yields such valuable information as to determine management more successfully.
Patients and methods All patients presenting in pregnancy with symptomatic unilateral renal colic underwent IVU. This consisted of an initial plain film and a final postmicturition film 30 min after an injection of contrast medium. Some patients had undergone ultrasonography before IVU.
Results Over the 24-month study period, 12 patients presented with renal colic that failed to respond to conservative means. All were mid-trimester at presentation and 73% were right-sided. IVU confirmed upper tract dilatation on the side of pain in all cases. The level of obstruction was defined by IVU in all patients. Two patients had an obstructing ureteric calculus that was defined by the urogram; these were not detected by ultrasonography. All patients with persisting symptomatic hydronephrosis or a severely obstructed system underwent percutaneous drainage via a nephrostomy, followed by antegrade stenting in a proportion (29%) of patients.
Conclusion IVU is an invaluable investigation in the management of severe unilateral renal colic in pregnancy. It provides more precise information regarding the presence or absence of obstructive uropathy and, where present, the site and aetiology. This allows for safer and more precise management of the patient and fetus, and we believe that this outweighs the minimal theoretical risk to fetal well-being.

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Randomized study of unenhanced spiral CT vs IVU in patients with suspected renal colic

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Introduction We report the initial results of the diagnostic utility of unenhanced spiral CT vs IVU for patients presenting with suspected renal colic. This is part of a larger study comparing the cost-effectiveness of unenhanced spiral CT with IVU for these patients.
Patients and methods All patients presenting with suspected renal colic were randomized to undergo either unenhanced spiral CT of the renal tract or IVU. Diagnosis, alternative diagnoses, requirement for further imaging and follow-up were analysed. One hundred and seventy consecutive patients presenting with suspected renal colic were randomized into the study over a 10-month period; 81 underwent IVU and 89 unenhanced spiral CT.
Results A definitive diagnosis was made at the initial investigation in 64 (72%) patients undergoing CT and 34 (42%) IVU ($P < 0.01$, chi-square). Normal imaging was reported in 17 patients undergoing CT and 31 patients undergoing IVU, with alternative diagnoses being made in three patients (CT two, IVU one; $P < 0.01$, chi-square). Incidental calculi were seen in 46 patients (CT 35, IVU 11; $P < 0.01$). Thirteen additional plain abdominal films were taken in the CT group to assess whether the calculi were opaque.
Conclusion Unenhanced spiral CT is significantly more often able to provide a definitive diagnosis in patients with suspected renal colic.

Bladder Cancer (Paper session)

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Orthotopic bladder reconstruction in bladder cancer: something for everyone?

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Introduction Previously, patients with invasive bladder cancer were offered either radiotherapy or cystectomy with an ileal loop conduit and stoma. There is now evidence that in selected cases it is safe to preserve the urethra and perform orthotopic bladder reconstruction. There have been calls for more centres to offer this surgical option to patients.
Patients and methods A retrospective review of the clinical notes of 25 male and six female patients who underwent radical surgery (27 patients) or radiotherapy (four patients) for bladder cancer during 1998 was planned to assess who would have been suitable for reconstruction.
Results Three case-notes (10%) could not be traced and therefore 28 patients were studied. Three patients referred for radiotherapy were unfit for cystectomy and one patient, known to have metastases, had a palliative cystectomy for bladder symptoms. All four were unsuitable for reconstruction. Of the rest, only two would have been suitable for reconstruction (one of whom was aged 76 years) using currently accepted criteria. Of the 22 fit but unsuitable patients, 13 had more than one contra-indication. Fourteen had carcinoma *in situ* within the bladder distant from the tumour, 15 had multifocal tumour, nine had TCC in the prostatic urethra, three women had bladder neck involvement, and three had previously received pelvic irradiation, which we feel is a relative contra-indication, but only one of the patients had this as the sole contra-indication.
Conclusion Accreditation to perform radical pelvic surgery will in part be based on the number of cases per year dealt with by a unit. We feel justified in performing radical cystectomy. However, at present we feel that we lack sufficient suitable cases to offer orthotopic reconstruction within the unit and will continue to discuss this option with patients, offering tertiary referral if requested. We expect to review this decision regularly, as the eligibility criteria for reconstruction crystallize and radical treatment is offered to more patients.

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Quality of life after radical cystectomy is not dependent on the type of urinary diversion performed

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Introduction Little is known about psychosocial adjustment and general state of health after radical cystectomy and different types of urinary diversion. A detailed informative education process after diagnosis is said to be paramount in maintaining quality of life (QoL). We have attempted to assess the impact on QoL after cystectomy and urinary diversion.
Patients and methods Of 49 patients identified over a 2-year period, 38 were alive, 15 had neobladders, 12 continent diversions and 11 ileal conduits, with mean ages of 58, 58 and 59 years, respectively. To assess quantitative and qualitative aspects of QoL, the SF-36 Questionnaire was administered, followed by a series of semi-structured interviews.
Results The overall response rate was 70%. The three groups did not differ significantly in the mean percentage scores of the SF-36. Both the neobladder and continent diversion group had above-average scores for social function, mental health, energy/vitality, pain and health perceptions. State of general health was perceived as improved or the same compared with one year ago by 65% of individuals. Assessment of detailed interview statements showed that QoL is maintained. The importance of detailed information and support to facilitate the individual's decision making was stressed.
Conclusion The effect of cystectomy and urinary diversion on life-style is not related to the type of diversion. Adaptation back to normal life is an individual-led process and is helped by a good supportive network.

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Holmium:YAG laser ablation of superficial TCC of the bladder

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Introduction The cystoscopic electrocautery of tumours is standard practice for superficial TCC and usually requires a spinal or general anaesthetic. We present our experience ablating these tumours using the holmium:YAG (Ho:YAG) laser via the flexible cystoscope with topical anaesthesia.
Patients and methods Patients with histologically confirmed superficial TCC of the bladder found to have recurrences at surveillance flexible cystoscopy underwent Ho:YAG laser ablation of these at the same time. The laser beam is delivered through a 365 μm bare fibre inserted via the instrument port. The power output is set to 10 W with 1 J being delivered per pulse. The pattern of recurrences was carefully mapped in all patients. Patients were then asked to report their discomfort during the procedure using a visual analogue pain scale (score 0–10).
Results During 86 patient visits (mean age 70.5 years) over 14 months, 192 superficial tumours were ablated. The mean (range) energy used was 47.76 (12–153) J. The mean (median, range) pain score was 2.58 (2, 0–6). Of the 86 episodes, 85 patients reported a preference for this procedure in the event of future recurrence, instead of standard electrocautery under a general or spinal anaesthetic. The recurrence rate was comparable with tumours treated by electrocautery ($< 9\%$).
Conclusions Recurrences in superficial bladder cancer are easily and safely treated with the Ho:YAG laser. Discomfort is low and this procedure was accepted by 99% of patients. It is highly cost-effective and we recommend it as the standard treatment.

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The management of superficial TCC of the bladder by flexible cystoscopy and the Ho:YAG laser

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Introduction It is now recognized that check cystoscopy and conventional transurethral resection/ablation of bladder tumours has little influence on outcome. The prognosis is excellent for patients with pTa G1 tumours, whilst pT1 G3 is a potentially aggressive disease [*BJU Int* 1999; 83: 957–63]. Attempts have been made to improve the outcome for pT1 G3 disease with single cytotoxic installation [*Br Med J* 1994; 308: 257–60] but a meta-analysis of EORTC and MRC trials has shown that chemotherapy does not prevent progression to muscle-invasive disease [*Urol Int* 1997; October: 15–17].

Patients and methods We have changed from conventional management to surveillance by flexible cystoscopy, ablating recurrences whenever possible using the Ho:YAG laser, which is safe and virtually painless. All patients with G1 and as many as were judged manageable with G2 and G3 superficial disease were recruited. Patients suspected of having large or multiple higher grade tumours were excluded, as were patients undergoing (at least) their first check after radiotherapy. Using this technique, $> 75\%$ of patients are managed under local anaesthesia and there is the potential to increase this further.
Conclusion Flexible cystoscopy and the Ho:YAG laser are safe and effective in the surveillance of superficial bladder cancer. Frequent checks are logistically possible, optimising management decisions. The cost at £20 per treatment episode is highly economical compared with conventional management, especially if this includes a single cytotoxic instillation.

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Intravesical BCG in patients with carcinoma in situ of the bladder associated with previous muscle-invasive TCC

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Introduction Intravesical BCG is widely used as a bladder-sparing approach for diffuse primary carcinoma *in situ* (CIS) or pTa/pT1-associated CIS. The aims of this study were to assess, in patients with previous muscle-invasive TCC, complete response (CR) rates, 5-year recurrence-free, cancer-specific survival and 'alive with bladder intact' rates after BCG therapy for CIS.
Patients and methods Between 1987 and 1997, 30 patients (median age 69 years) with biopsy-confirmed CIS and previous muscle-invasive TCC (two with T2, three with T3 and one with T4) underwent a standard course of six weekly BCG instillations. Associated tumours were completely resected. At least four random bladder biopsies were taken before and 6 weeks after BCG therapy. A CR was defined as tumour-free biopsies and absence of malignant cells in bladder washings.
Results Of 30 patients, 26 (87%) completely responded to one course of BCG. The median follow-up after BCG was 51 months; there were 18 local recurrences and 10 TCC-related deaths. At 5 years, 21% of patients were recurrence-free, the cancer-specific survival was 56% and 53% were alive with the bladder intact. A CR to BCG was associated with later recurrence ($P = 0.004$) and prolonged cancer-specific survival ($P = 0.004$; Cox regression); all incomplete responders were dead within 5 years. In BCG-treated CIS after radical radiotherapy (seven), 25% were alive with the bladder intact.
Conclusion Intravesical BCG is an acceptable bladder-sparing option for CIS in patients with previous muscle-invasive TCC, provided there is a CR.

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A multicentre prospective, randomized study comparing the effects of different lengths of start and maintenance therapies with intravesical mitomycin C in 3554 patients with superficial bladder cancer

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Introduction Intravesical mitomycin C is an effective chemotherapeutic agent for the treatment of superficial bladder cancer. However, doubts still exist over the optimal initial regimen and the length of maintenance therapy to prevent or delay recurrences.
Patients and methods The effects of four weekly vs eight weekly start therapies were compared in a first study involving male and female patients (aged $\geqslant 18$ years) with primary or recurrent Ta/T1, solitary or multiple, papillary carcinomas of the bladder (except primary solitary Ta tumors) and/or patients with carcinoma *in situ*. In this study, 98 urologists randomized 1163 patients between June 1991 and November 1993. After randomization patient distribution was as follows: 199 patients in Group A, receiving eight weekly instillations of mitomycin C followed by four monthly instillations; 220 patients in Group B, receiving four weekly instillations followed by five monthly instillations; 372 patients in Group C receiving eight weekly instillations followed by ten monthly instillations, and 372 patients in Group D receiving four weekly instillations followed by 11 monthly instillations. The effects of extended maintenance therapy (extra instillations every 3 months after completion of standard therapy: six extra instillations in cases of solitary tumours, eight in cases of multiple tumours) were compared with standard therapy (four weekly instillations followed by five to 11 monthly instillations for solitary and multiple tumours, respectively) in a second study involving patients with identical selection criteria. In this second study 89 urologists recruited 2391 patients between December 1993 and June 1999. After randomization, patient distribution was as follows: 423 patients in Group 1 receiving four weekly followed by five monthly instillations and six 3-monthly instillations; 389 patients in Group 2 (instillations as in Group 1 but without the 3-monthly instillations); 770 patients in Group 3 receiving four weekly instillations followed by 11 monthly instillations and eight 3-monthly instillations, and 792 patients in Group 4 (instillations as in Group 3 but without the 3-monthly instillations). At the time of this evaluation 17 patients could not be allocated to one of these treatment groups. In both studies each instillation consisted of 40 mg mitomycin C dissolved in 50 mL saline, which was kept in the urinary bladder for at least 1 h, but no longer than 2 h. The first instillation was given 1–2 weeks after transurethral resection. The cumulative recurrence rate was evaluated after 36 months.
Results The cumulative recurrence rate in Group A was 19.4%, compared with 21.6% in Group B ($P < 0.05$). In Groups C and D respectively, the cumulative recurrence rates were 34% and 38.2% ($P < 0.05$). Similarly, cumulative recurrence rates were 12.5% and 14.8% in Group 1 and Group 2, respectively ($P < 0.05$), and 16.1% and 21.3% in Groups 3 and 4, respectively ($P < 0.05$). Side-effects among the different treatment groups seem to be similar, but with fewer in the second study.
Conclusion Preliminary results indicate that four weekly start-therapy is as effective as eight weekly start-therapy, and that four weekly start-therapy followed by five monthly instillations (solitary tumours) or by 11 instillations (multiple tumours) is adequate therapy. The side-effect profile in all treatment groups was acceptable.
Funding: Christiaens B.V.

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Dose intensification (q10 v q21/28) of chemotherapy and synchronous chemo/radiation as strategies to improve bladder cancer outcome

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Introduction Conventional bladder cancer cisplatin-based chemotherapy regimens such as CMV and MVAC give treatment every 21 or 28 (q21/28) days. Recently prompted by success in testis cancer we have been able to show that giving methotrexate 60 mg/m^2, Oncovin 2 mg, cisplatin 60 mg/m^2 every 10 days (q10) we achieve results at least as good as those from MVAC, with considerably less

toxicity. Toxicity has been so low that it has been possible to give this regimen synchronously with radiation.

Patients Sequential studies were carried out with MVAC q28 (22 patients), MVP q21 (54 patients), MOP q21 (45 patients) and MOP q10 (53 patients) in those with metastatic disease or failed radiation for local disease who were treated between 1 January 1985 and 1 June 1999. In addition, 17 newly diagnosed T2/3 patients received MOP q10 × 3 synchronously with radiation (5–5500 cGy) in 20 fractions over 4 weeks and 15 received three doses of MOP q10 before elective cystectomy.

Results Twenty-four complete responses (CRs) were observed in 175 patients, in 10 of 80 (13%) patients with locally advanced disease after radiation therapy and in 14 of 95 (15%) patients with systemic metastases; 15 of 122 (12%) receiving q21/28 cisplatin vs nine of 53 (17%) receiving q10 cisplatin had a durable CR. Ten of 24 CRs were durable beyond 12 months, eight are ongoing, the longest at 126 months. Fifteen of the 17 T2/3 patients receiving MOP q10 plus synchronous radiation achieved complete remission at the first check cystoscopy, while seven of 15 undergoing attempted cystectomy after MOP q10 × 3 with no radiation had histologically confirmed complete remission.

Conclusion This low toxicity regimen (MOP q10) shows potential both in combination with cystectomy and radiation and needs testing in prospective randomized trials.

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Bladder cancer registration – a national confusion

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Introduction Cancer registration is important for the planning of care and distribution of resources. Standardization of registration allows regional and national comparisons. This review highlights the regional variation in the registration of bladder cancer and the inconsistency of the system. Bladder cancer is registered by the ICD-9 code: 188, *in situ* carcinoma of the bladder; 233.7, histology by morphology code; TCC (not otherwise specified) 8120; papillary TCC 8130; and suffixed for invasive disease (0.3) or in situ disease (0.2).

Method and results We present the most recent (1992) England and Wales and Northern and Yorkshire Cancer Registry data to highlight regional variation in registration method (1992 populations England & Wales, 51 million; Yorkshire, 3.75 million).

Code	*England & Wales*	*Yorkshire*
'Bladder cancer' ICD 188	12 006	739
Bladder TCC (pT1+)		
M8120.3	5229	356
M8130.3	4013	291
Proportion of TCC in bladder cancer records n (%)	9242 (77)	647 (88)
in situ carcinoma, ICD 233.7	648	347
M8120.2 CIS	146	58
M8130.2 pTa	398	282

Nine of 10 regional cancer registries in England and Wales responded to a national survey on their registration of noninvasive urothelial carcinoma (Ta) and flat tumour (Tis). There was only 50% agreement on morphological codes used. Comparative figures for Yorkshire and England & Wales highlight this inconsistency, as Yorkshire cannot account for 70% of all pTa tumours.

Conclusions There are 10 regional cancer registries in England and Wales which appear to interpret the coding method differently, and only half the centres agree on coding for pTa and CIS. Most pTa tumours may not currently be registered nationally. That pTa tumours are not included in bladder cancer (pT1+) registrations may be enlightened regarding tumour biology, but this misrepresents the urologist's new bladder tumour workload. The national incidence of pTa is not clear. Inter-regional variation in registering bladder tumours leads to confusing national data. A simplified system for national registration of bladder tumours is required.

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Mean CT number predicts ESWL stone fragmentation

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Introduction Helical CT is an accepted diagnostic tool in the management of acute loin pain. CT has the additional value of providing information about stone composition. We evaluated the use of mean CT Hounsfield units (CT HU) of upper tract calculi as a predictor of ESWL stone fragmentation *in vitro* using the Technomed Sonolith 4000 plus lithotripter.
Method Thirty-two consecutive radio-opaque calculi and four (chalk) artificial calculi were scanned *ex vivo* at 120 kV,1 mm collimation (GE CT Prospeed) and subjected to ESWL (2 Hz, 18 kV). The number of shock waves and energy required for fragmentation to < 2 mm was the end-point. A mean CT HU was derived for each stone from the CT HU of each stone section. Mean CT HU and stone volume were correlated with the number of shock waves and energy required to achieve the end-point.
Results There was a significant correlation between mean radiological density (CT HU) for both the number of shock waves and the energy required (correlation coefficient -0.55, $P < 0.05$, and 0.58, $P < 0.05$ respectively). There was a significant correlation between stone volume (mm^3) and both the number of shock waves and energy required (correlation coefficients -0.55, $P < 0.05$ and 0.52, $P < 0.05$ respectively). The correlation of both mean CT HU and volume with number of shock waves and energy required was improved if the stone volume was $> 50\,mm^3$.
Conclusion Mean CT HU and stone volume predict the number of shock waves or energy required for fragmentation with ESWL *in vitro*. Caution should be used in the prediction of ESWL fragility based upon both mean CT HU and stone volume in stones of $< 50\,mm^3$ because of the partial volume effects.

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A comparison of lithotripters using a robust electromagnetic probe

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Introduction Shock wave lithotripsy (SWL) is an established procedure for treating most urinary calculi. Present practice is based largely on experience from the Dornier HM-3, the original lithotripter; however, this machine has been largely replaced and may no longer be in use in the UK. Over 30 lithotripsy machines are presently on the market, with a variety of claimed success rates. A robust electromagnetic probe has been developed to measure the output from lithotripters while withstanding the forces of repeated shock waves. This probe measures the forces generated by cavitation bubbles in the focal zone.
Methods The probe was placed in the focal zones of four separate lithotripters: the Dornier MPL-9000X (green and blue electrodes); the Wolf 2300 piezoelectric; the Dornier Delta; and the Dornier Lithotriptor S. The output was repeatedly measured at every setting, in degassed water.
Results The Dornier Lithotriptor S had the greatest cavitational energy at full power, which we arbitrarily defined as 1.00. By comparison, the Dornier MPL 9000X (green) was 0.44, the Dornier MPL 9000X (blue) 0.38, the Dornier Delta 0.31, and the Wolf 2300 0.22. Thus, the Dornier Lithotriptor S can generate cavitational bubbles with more than twice the energy of any of the other lithotripters assessed. Although fragmentation may not be dramatically different among these lithotripters, because of the short-term stresses produced by the incident shock wave, cavitation is generally believed to be responsible for tissue damage during lithotripsy. As a result there are substantial differences between different lithotripters which are not highlighted by the manufacturers' technical specifications.
Conclusions The cavitational energy associated with shock waves generated by a variety of lithotripters varies considerably. These differences may be associated with differences in fragmentation; more likely is the possibility that they may be associated with an increased risk of tissue damage during lithotripsy.

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To stent or not to stent: that is still the question!

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Introduction Most patients are routinely stented after having undergone ureteroscopy for stone extraction. This necessitates a second procedure to remove the stent, with its inherent morbidity. The aim of our study was to determine whether routine stenting of the ureter after ureteroscopy is necessary.
Patients and methods Sixty patients were evaluated in this prospective study (36 males and 24 females). All were admitted for elective distal ureteric stone fragmentation and had stones of 0.6–1 cm. Sixteen patients (10 male) had been stented before ureteroscopy. A 9 F semi-rigid ureteroscope was used in 43 patients and a 7.5 F semi-rigid ureteroscope was used in the other 17; there was no need for ureteric orifice dilatation with either ureteroscope. Ballistic intracorporeal lithotripsy was performed in all cases with the Swiss Lithoclast; all visible stone fragments were retrieved with a 3 F helical basket. Thirty-three patients underwent day-case ureteroscopy; seven were followed-up as inpatients for up to 24 h, and all were reviewed in the clinic one week later with a request to report if they felt significant discomfort, loin pain or became pyrexial.
Results Only one patient (male) had to be readmitted with loin pain. Two others (both females) complained of having had dull lower abdominal pain and some frequency when they attended for follow-up.
Conclusions The low incidence of complications in this preliminary study suggests that routine stenting is not necessary after ureteroscopic stone fragmentation in the lower third of the ureter; the major caveat to this statement is that difficult and prolonged stone fragmentation is an indication for stenting.

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Retroperitoneal laparoscopic pyelolithotomy: 9-year experience and its comparison with percutaneous nephrolithotripsy for larger stones

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Introduction We report a 9-year experience of retroperitoneal laparoscopic pyelolithotomy, an infrequent minimally invasive operative procedure. The results were compared with our experience of percutaneous nephrolithotripsy for larger renal stones to determine if, in a selected group of patients, the role of retroperitoneal laparoscopic pyelolithotomy can be extended beyond its contemporary role of a salvage procedure. Methods to make the laparoscopic procedure more effective and to minimize the leakage of urine are emphasized.
Patients and methods Thirty-eight patients (mean age 38.2 years) underwent 39 retroperitoneal laparoscopic pyelolithotomies

using Gaur's balloon technique. There were 48 stones (10 at the PUJ, 18 in the extrarenal pelvis, 11 in the intrarenal pelvis and nine in the calyces), with a mean (range) size of 19.5 (10–48) mm. Only one patient was in chronic renal failure because of bilateral impacted renal calculi and required previous bilateral percutaneous nephrostomy. Forty-eight percutaneous nephrolithotripsies performed in the same unit during the last 2 years in patients with calculi > 2 cm (not staghorn) were included for comparison, as presently the smaller stones are better removed by percutaneous nephrolithotomy.
Results There were seven failures in the laparoscopic group, mostly during the initial stages, caused by peri-pelvic fibrosis, peritoneal tear, stone impaction and stone migration. The mean operative duration was 116.9 min, the mean blood loss 37.9 mL and the mean analgesic intake 2.8 days. No blood transfusion was needed in any case and the mean hospital stay and return to work were 3.6 and 16.7 days, respectively. However, the efficacy of the laparoscopic procedure in the last quarter of the series, with cumulative experience and proper case selection, was increased to 100% and the leakage of urine decreased from a mean of 6.6 days to a mean of 3 days by stenting and suturing. Compared with percutaneous nephrolithotripsy, while the open conversion rate and the drainage period were higher for retroperitoneal laparoscopic pyelolithotomy, the operative duration, blood loss, analgesic intake, hospital stay, residual stone rate, re-treatment rate and major complication rates were lower.
Conclusions Retroperitoneal laparoscopic pyelolithotomy is a safe, viable minimally invasive salvage procedure for treating renal calculus disease. Nevertheless, an experienced laparoscopic surgeon might consider it as the primary procedure of choice in a selected group of patients with large renal calculi (not staghorn).

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Flexible ureterorenoscopy for upper urinary tract stones: a retrospective analysis

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Introduction Renal stones with diameters of < 1.5 cm not amenable to ESWL have traditionally posed a management problem for the urologist. However, in recent years the advent of flexible ureterorenoscopy used in conjunction with either electrohydraulic lithotripsy (EHL) or a laser has revolutionized the management of these stones. We analysed the results in our patients undergoing this therapy to assess its effectiveness.
Patients and methods The notes of 81 consecutive patients who underwent ureterorenoscopy for upper renal tract stones in our department were analysed.
Results Twenty-four patients underwent EHL and 57 were treated with the holmium laser; in all patients an Olympus PF2 flexible ureteroscope was used. The table summarizes the outcome for both treatments:

Site of stone	*No.*	*Outcome**
EHL:		
PUJ	1	Complete clearance
Middle or upper calyx	13	10 cleared, 3 obscured vision from bleeding
Lower calyx	8	6 failed access, 1 cleared, 1 IC
Diverticular	2	2 IC
Laser:		
Lower calyx	30	8 failed access, 18/22 GF
After lithoclasty	20	20 GF
Diverticular	7	2 failed access, 3/5 GF

*IC, incompletely cleared; GF, good fragmentation

No significant damage was caused to the anatomical structures containing the stones. The ureteroscope was damaged during a procedure at the end of this series of patients when using EHL
Conclusions Using flexible ureterorenoscopy, 80% of the stones in this series were accessible, with most of those that were inaccessible being in the lower calyx. Both EHL and the laser were safe and effective lithotripters, although EHL was less easy to use.

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Stone management in children

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Introduction The minimally invasive management of stones in children has developed more slowly than in adults, primarily because of technical limitations associated with smaller patients. With constant improvements in technology the benefits of a minimally invasive approach can be offered to most children with urinary tract stones.
Patients and methods Between January 1997 and September 1999, 71 procedures were performed in 53 children; 21 children underwent ESWL, 23 percutaneous nephrolithotomy (PCNL), six ureteroscopy and three open nephrolithotomy. Investigations of these children included radiological imaging, metabolic screening and DMSA renography.
Result Thirty-nine patients were evaluated metabolically: 61% had a UTI, 13% had hyperoxaluria, 5% had cystinuria, and 2.5% had hypercalciuria, and no identifiable cause was found in 18.5%. The stone-free rate was 95.2% for ESWL and 89% for PCNL, which improved to 100% after ESWL. Ureteroscopy cleared the stones in all children. In open nephrolithotomy, one in three children had a residual stone that was successfully treated with ESWL. In total, the stone-free rate after treatment by a single modality was 89%, and when different modalities were combined 98% of children were cleared of their stones. Complications were few and consisted mainly of pyrexia ($> 38^{\circ}$C), and were treated conservatively with intravenous antimicrobial agents.
Conclusion Technological advances in ESWL, ureteroscopy and PCNL have made a significant impact on the management of urolithiasis in children, which can now be performed safely and with a good outcome.

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The changing pattern of urinary stone disease in the UK and its causes

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Introduction The age at onset of stone formation has been decreasing in both sexes in the UK since 1975; this has been particularly noticeable in females. This study examines various possible reasons for this change.
Methods Within a period of 21 months, over 600 patients who had formed urinary stones were screened at Stone Clinics in a major referral centre in the UK. Demographic, epidemiological, biochemical and dietary data were collected from each patient. Data on the age of onset of stones were compared with previous observations in the UK in 1975 and 1985.
Results Comparisons show that within the past 25 years there has been a progressive decrease in the age of onset of stone formation in both males and females. Within the group of stone-formers as a whole, the male/female ratio among patients who formed their first

stone before the age of 20 years is now 1.5 : 1. In the group of stone-formers currently aged < 20 years the male/female ratio is now 1 : 1, and 10.6% of male and 18.4% of female stone-formers now form their first stone before the age of 20 years. Analysis of the data indicates that changes in lifestyle and diet within the past 25 years, particularly among girls and young women, may be the main causes of this phenomenon.

Conclusions The changing pattern of stone disease in the UK over the past 25 years may be explained by changes in diet and lifestyle.

Prostate Cancer I (Paper session)

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Tumours of the prostate: analysis of the 1999 Section of Oncology registry

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Introduction A register of all new urological cancers has been organised through the BAUS Section of Oncology, commencing on 1 January 1999. The first 6 months of data are available for this abstract, but the 12-month figures will be presented.
Methods Data were submitted by 287 urology consultants from 138 hospitals; 8164 urological tumours were registered, of which 3792 were prostate carcinoma. The mean (range) age of the patients was 73.2 (21–100) years; 10 patients were aged < 50 years. The diagnosis was confirmed by histology in 3766 (94.8%), the remainder being diagnosed by: radiology in 40 (1%); PSA level in 159 (4%); or clinical features in 119 (3%). Age was the commonest reason for an absent biopsy.
Results Of these patients, 1731 had G2 tumours (52%), 688 had G1 (20.7%) and 910 had G3 (27.3%); 155 (4.8%) were stage 1, 1523 (47%) were stage 2, 887 (27.4%) stage 3 and 672 (20.8%) stage 4 tumours. The initial treatment intention was cure in 951 patients (27.7%). In 39 (4.6%) of these, the PSA level was > 50 ng/mL. Radical prostatectomy was the preferred option in 188 (4.9%) and direct radiotherapy in 223 (5.9%). Surveillance was intended in 550 (16%) and palliative treatment predominantly by hormone manipulation in 1931 (56.3%). The median (range) time from referral to diagnosis was 59 days (0 days to 7 years 2 months), with 137 patients taking > 1 year.
Conclusions This database will be a valuable resource for comparing trends in staging and treatment over subsequent years. It will also be useful for planning future trials in the management of this disease.

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Why is prostate cancer mortality declining? Comparing trends in England and Wales with the USA

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Introduction After the widespread introduction of PSA testing in the USA death rates from prostate cancer have declined. In contrast, PSA screening has been discouraged in the UK.
Methods Secular trends in prostate cancer mortality and incidence in England and Wales (E&W) and the USA were compared using directly age-standardised rates, to assess whether differences in screening practice are reflected in different disease patterns.
Results From 1970 to 1983 mortality rates rose by 1–2% per year in E&W. Age-standardized mortality in E&W peaked in 1992 at 27/100 000, then decreased to 25/100 000 by 1997. This pattern is strikingly similar to that in the USA, in both timing and scale. In the USA, death rates rose to 27/100 000 in 1991, falling to 24/100 000 by 1996. During the 1980s the incidence in E&W rose by 3% per year, increasing more rapidly in the early 1990s; there is evidence to suggest that this rise may have halted in 1994. In contrast, the incidence in the USA increased by $> 20\%$ per year from 1989 to 1992 and then decreased by $\approx 10\%$ per year.
Conclusions Although trends in prostate cancer screening and disease incidence differ markedly between the USA and E&W, trends in mortality are very similar. The use of radical therapies in E&W is insufficient to explain the decline in mortality in E&W. Changes in palliative management could extend disease survival sufficiently for a competing cause of death to intervene. Whilst the similar reversal of prostate cancer mortality trends in the USA and E&W does not necessarily imply similar causation, it confirms that it is too soon to claim success for screening in the USA on the basis of observational data alone.

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Psychosocial morbidity in patients with prostate cancer and their partners

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Introduction We compared the nature and severity of psychosocial morbidity in patients with prostate cancer and in their partners, using a novel psychometrically tested questionnaire.
Patients and methods A questionnaire was systematically constructed to measure aspects of psychosocial morbidity related to prostate cancer in patients and their partners. There were two subscales, one assessing general cancer-related distress and one measuring social morbidity. There were five further questions to measure psychological morbidity caused by pain, urinary symptoms, treatment, physical limitation and sexual dysfunction. The questionnaire was administered to 135 patients with prostate cancer and their partners in their homes, as part of a semi-structured interview. The disease characteristics of the group were typical of patients attending a general urology clinic in a district general hospital.
Results Some general cancer-related distress was shown by 47% of patients and 76% of partners; severe distress was found in 11% and 30%, respectively. Social morbidity was of limited severity, with no inter-group difference. Treatment-related worries and concerns about pain and physical limitation were more common among partners than patients, whereas there was no difference for worries about urinary symptoms. Sexual concerns were the least prevalent and were more of a problem for patients than partners.
Conclusions Psychosocial morbidity is highly prevalent in both patients with prostate cancer and their partners. Much of the morbidity relates to the diagnosis of cancer itself, rather than aspects specific to prostate cancer. Clinically significant psychological problems may be identified using a simple questionnaire. Mild degrees of morbidity may be addressed by provision of basic informational and emotional support. Severe morbidity may require the involvement of other disciplines, such as palliative care or psychiatry.

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The impact of patient position on the detection of prostate cancer by DRE

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Introduction The DRE continues to play an important role in evaluating the prostate gland. The detection rate for prostatic carcinoma is optimised by combining DRE and PSA findings [*J Urol* 1993; 149: 798A]. The patient can be positioned in several ways for a DRE, including knee-elbow, standing and the lithotomy position. That most commonly used in the UK is the left lateral position, which offers maximum patient comfort, but its critics suggest that palpation of the left lobe is more awkward, thus compromising the detection of cancer within it. The alternative positions provide a central prostate location with equal access to both lobes, at the expense of patient comfort. We determined whether the left lateral

position compromises the detection of cancer within the left lobe of the prostate gland.
Methods One hundred radical prostatectomy specimens containing histological stage T2 tumours were analysed. A preoperative DRE was carried out on each patient by a consultant urologist and the results for each lobe were compared with the respective histological findings.
Results The data were analysed using chi-squared tables.

Variable (%)	*Right lobe*	*Left lobe*
Negative predictive value	24	20
Positive predictive value	95	89
Specificity	87	76
Sensitivity	51	40

Conclusion Although a DRE of the right lobe carried out by a consultant urologist showed better predictive values for detecting prostate cancer than the left, none of the differences were statistically significant. This suggests that the left lateral position for DRE does not compromise the detection of prostate cancer enough to warrant the use of a less comfortable position.

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Molecular prediction of prostate cancer progression in patients managed with watchful waiting

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Introduction Older patients with localised and low-grade prostate cancer are often managed conservatively. Recent evidence suggests a high progression rate and considerable morbidity in some of these patients. RT-PCR is a molecular technique that can detect circulating prostate cells in peripheral blood. Our aim was to investigate whether RT-PCR could be used to predict which of these patients are likely to progress.
Patients and methods Blood samples (5 mL) were taken from patients with hormone-escaped prostate cancer, hormone-controlled cancer (PSA < 10 ng/mL), conservatively managed cancer (PSA < 50 ng/mL) and female volunteers. Samples were then analysed by RT-PCR assay using primers for PSA and prostate specific membrane antigen. PSA doubling times were calculated using the serum PSA value at the time of the RT-PCR sample and the change in PSA level over 2 years.
Results The assay reliably detected 20 LNCaP cells added to 5 mL of blood. None of the 10 female volunteers, 18 of 24 (75%) patients with advanced prostate cancer, two of 34 (6%) stable hormone-treated patients and 14 of the 51 (27%) conservatively treated patients were RT-PCR positive. The conservatively managed RT-PCR-positive patients had a lower median PSA doubling time than the RT-PCR-negative patients (7.2 vs 20 years, $P = 0.02$) although there was no significant difference in serum PSA level or histological grade.
Conclusions The RT-PCR assay is specific for prostate cells but only 75% sensitive in patients hormone-escaped disease. A significant minority of conservatively managed patients with localised disease had circulating prostate cells. RT-PCR results in this group correlated with PSA doubling time but not static PSA values. RT-PCR positivity may suggest a rapid PSA doubling time and could potentially be used to predict disease progression even at initially low serum PSA levels.

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The use of bisphosphonates for osteoporosis in prostate cancer

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Introduction Hormonal therapy in prostate cancer is a recognised risk factor in the development of osteoporosis.
Patients and methods A cross-sectional study of 48 patients with prostate cancer was undertaken and measurements taken for bone densitometry, urine NTX (urine assay for the excretion of N-linked telopeptides as a marker for bone resorption), serum PSA and serum bone alkaline phosphatase (as a marker of bone formation). The study patients were being treated with LHRH agonists, anti-androgens or had undergone orchidectomy. Eight patients were identified with very low bone density (> 2.5 SD from the reference mean) and high markers of bone resorption. Under WHO criteria these patients have at least six times more risk of osteoporotic fracture. Conventional therapeutic options include hormone replacement or an oral bisphosphonate and the patients were offered treatment with alendronate at a dose of 10 mg. Serum and urine markers were monitored.
Results Six of the eight patients had a decline in urine NTX to $< 50\%$ of the upper range of normal by 6 months. This is regarded as a excellent response by WHO criteria and significantly reduces the risk of fracture. The treatment was well tolerated with no side-effects reported.
Conclusion The trend towards the use of hormonal therapy in younger patients for longer periods has important implications for quality of life. Bisphosphonates may be therapeutically useful in minimising potential osteoporotic complications in these patients.

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ATP-mediated cavernosal smooth muscle relaxation via stimulation of P2Y1-like purinoceptors and its impairment in the rabbit diabetic model

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Introduction ATP potently relaxes both human and rabbit cavernosal smooth muscle (CSM) via P2Y purinoceptor stimulation. We investigated, in a rabbit model, the subset of P2Y purinoceptors that may be associated with CSM relaxations and assessed ATP-mediated CSM relaxation in a rabbit model of diabetes mellitus (DM).
Materials and methods CSM strips from New Zealand White rabbits were mounted in organ baths and pre-contracted with phenylephrine (100 μmol/L). These were then relaxed with ATP alone (0.1 μmol/L − 5 mmol/L), or in the presence of 8-phenyltheophylline (10 μmol/L, an adenosine receptor antagonist) or PPADS (100 μmol/L) of reactive blue (500 μmol/L; the latter two are P2 receptor antagonists). The effect of ATP on tissues that were not pre-contracted and the potency of ADP were also investigated. After inducing DM for 6 months, ATP-mediated CSM relaxation was also determined.
Results ATP produced a concentration-dependent relaxation of pre-contracted CSM strips, but had no effect strips that were not pre-contracted, indicating that the CSM has no P2X1 or P2X2 receptors. 8-phenyltheophylline did not reduce ATP-mediated relaxation, suggesting that it is not caused by breakdown to adenosine and action via P1 purinoceptors. PPADS had no effect on ATP-mediated CSM relaxation. Reactive blue significantly reduced ($P < 0.05$) ATP-mediated relaxation (IC_{50} 340 μmol/L for ATP alone vs 640 μmol/L with reactive blue). ADP (IC_{50} 140 μmol/L) was significantly ($P < 0.05$) more potent than ATP. ATP-mediated diabetic CSM relaxation was significantly ($P < 0.05$) impaired (IC_{50} 1.1 mmol/L).
Conclusions ATP appears to mediate rabbit CSM relaxation via P2Y1-like purinoceptors; evidence suggests that this is endothelium-dependent. In diabetes, this pathway is impaired and may contribute to the pathogenesis of erectile dysfunction associated with DM.
Funding: Charles Wolfson Charitable Trust

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Advanced glycation end products are responsible for the impairment of corpus cavernosal smooth muscle relaxation seen in diabetes

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Introduction We have previously shown that neuronal and endothelial-derived NO-mediated relaxation of corpus cavernosum is impaired in tissue from diabetic animals compared with controls. We conducted experiments to determine if advanced glycation end products (AGEs) may be responsible for this effect.
Methods Diabetes was induced in male Wistar rats by an intraperitoneal injection with streptozotocin (65 mg/kg). One group of diabetic rats was given water and a standard diet. A second group was given a standard diet and aminoguanidine (AG) with their water (50 mg/100 mL) from the time of commencement of diabetes. Two groups of non-diabetic animals acted as age-matched controls. After 8 weeks animals were killed by cervical dislocation, and corpus cavernosal tissue strips harvested and mounted in an organ bath for measurement of isometric tension. After 90 min of equilibration at optimal resting tension and contraction with 1 μmol/L noradrenaline the response to either acetylcholine or electrical field stimulation (EFS) after the addition of guanethidine (5 μmol/L) and atropine (1 μmol/L) was determined for each experimental group. of Tissue from control and diabetic animals was examined immunohistochemically using 6D12, an antibody specific for AGEs.
Results There was no difference between the baseline characteristics of all experimental groups. After 8 weeks the mean body mass and HbA1c were significantly greater in the diabetic than in control animals. AG had no effect on the recorded body mass or HbA1c. There was more deposition of AGEs in the intima of cavernosal blood vessels and the trabeculae of the cavernosum in tissue from diabetic animals than in control animals. The *in vitro* relaxation response to the application of acetylcholine or EFS of tissue strips from age-matched control animals fed a standard diet and those supplemented with AG were the same. The administration of AG to diabetic animals for 8 weeks reversed the expected impaired relaxation response to acetylcholine. The response to EFS was similar.
Conclusion AGEs are more prevalent in erectile tissue from diabetic rather than non-diabetic animals. AG reversed the impairment in neuronal and endothelial NO-mediated penile smooth muscle relaxation seen in diabetes. As AG prevented AGE formation we believe that erectile dysfunction in diabetes is caused partly by the generation of AGEs.
Funding: BUF/Wyeth Research Scholarship

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A possible cellular mechanism for atropine resistance in human detrusor

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Introduction Atropine-resistant contractions mediated by ATP neurotransmission are present in detrusor samples from abnormal human bladders [*J Urol* 1999; 162: 1840–7, *J Urol* 1993; 150: 2007–12]. This study compared the sensitivity of detrusor specimens from normal and unstable bladders to ATP.
Methods Bladder biopsies were obtained with approved consent. Detrusor strips (1–1.5 mm diameter) tied to an isometric force transducer were superfused with Tyrode's solution at 5–10 mL/min and αβ-methylene-ATP (ABMA) was added from 10 mmol/L stock or ATP added as a powder. Results are expressed as the median (interquartile range). The null hypothesis was tested using the Mann–Whitney *U*-test.
Result Dose–response curves were constructed for ATP and its undegradable analogue ABMA. The pEC_{50} (–log EC_{50}) for ATP was 3.18 (0.39–0.5) in control detrusor (13 samples). Obstructed (10 samples) and unstable bladder tissue (10 samples) gave a pEC_{50} of 3.89 (1.04–0.76) and 4.03 (0.13–0.23) (both $P < 0.05$), respectively. The mean (SD) pEC_{50} with ABMA (six samples) was 5.44 (0.16) and less than that for ATP ($P < 0.001$). The variances of the pEC_{50} values were different between groups ($P < 0.01$, F-test). The mean (SD) response to 100 μmol/L ATP was 26 (11)% of that to 10 μmol/L ABMA in a combined unstable and obstructed group (five samples) but in the control group it was significantly less at 8.9 (5.3)% ($P < 0.05$).
Conclusions The low potency and greater variability of the response to ATP compared with ABMA suggests the presence of an ecto-ATPase in detrusor. The larger ratio of the ATP:ABMA

response and lower pEC_{50} in the unstable group suggests that ecto-ATPase activity is less than in control specimens.

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M2 and M3 muscarinic receptors of detrusor muscle

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Introduction The M2:M3 muscarinic receptor ratio is about 9:1 and 3:1 in the rat and human urinary bladder, respectively. Several studies have identified the M3 receptor as the sole muscarinic receptor subtype responsible for bladder contraction. This study examines whether there is a role for M2 receptors in pig bladder.
Methods Displacement experiments were carried out using the receptor ligand [^{3}H]1-quinuclidinyl[phenyl-4-3H]benzilate (QNB), 4-diphenylacetoxy N-methylpiperidine (4-DAMP), darifenacin (M3-selective antagonist) and methoctramine (M2-selective antagonist) to determine the M2:M2 receptor ratio in pig bladder membranes. The affinity of these antagonists against carbachol-induced contractions of pig detrusor were also calculated in normal tissues and after selective M3 inactivation (incubation with 40 µmol/L 4-DAMP in the presence of 1 µmol/L methoctramine to 'protect' M2 receptors), pre-contraction with 50 mmol/L KCI and relaxation with isoprenaline (30 µmol/L).
Results Displacement of [^{3}H]QNB binding with the antagonists indicated an M2:M3 ratio of 3:1. In normal detrusor muscle, 4-DAMP and darifenacin had a high mean (SD) affinity (pKB value) of 9.4 (0.07) and 8.6 (0.10), respectively, while methoctramine had a relatively low affinity of 6.1 (0.05). In tissues where the M3 receptors had been inactivated, the affinity of 4-DAMP, at 8.7 (0.1), and darifenacin, at 6.74 (0.07) was significantly reduced ($P < 0.01$), whilst that of methoctramine, at 7.0 (0.01) was significantly increased ($P < 0.001$) compared with control tissues.
Conclusions These data suggest that in the pig bladder, where the muscarinic receptor population appears to be similar to that of human, the M3 receptor subtype mediates contraction of the normal detrusor muscle. However, an involvement of M2 receptors in contraction may occur after pharmacological manipulation of the receptor population.

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Depolarization-induced Ca^{2+} rise under voltage-clamp in human detrusor myocytes

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Introduction After the detection of the L-type Ca^{2+} current in human detrusor myocytes [*J Urol* 1992; 147: 176–84] no studies have been carried out showing directly its role in determining the rise of intracellular Ca^{2+}, $[Ca^{2+}]_i$, associated with the action potential. This study examined if Ca^{2+} influx through this channel is sufficient to contribute to the transient rise of $[Ca^{2+}]_i$ responsible for the detrusor contraction.
Methods Isolated cells were obtained from human detrusor samples by enzymatic dissociation. Membrane ionic currents were recorded under voltage-clamp using patch-type electrodes filled with a high-K solution. Ca^{2+} was measured simultaneously using the fluorescent Ca^{2+} indicator, fura-2.
Results Cells were clamped at voltages of −60 to +40 mV, in 10 mV increments. An inward current, followed by a Ca-transient, were generated. The rise of $[Ca^{2+}]_i$ mirrored the Ca^{2+} current, with a threshold at −40 mV and a peak at +10 mV. $[Ca^{2+}]_i$ remained elevated during depolarization and returned to normal upon repolarization. The mean (SD) resting $[Ca^{2+}]_i$ was 105 (5) nmol/L, rising to a transient peak of 326 (93) nmol/L ($n = 9$). The magnitude of the Ca-transient was 54 (5)% of the maximum carbachol transient in the same cells.
Conclusion Ca^{2+} entry induced by membrane depolarization can cause a substantial rise of $[Ca^{2+}]_i$ in human detrusor smooth muscle. This suggests that it could play an important role in regulating intracellular Ca^{2+} and hence detrusor contractility.
Funding: St Peter's Trust for Kidney, Bladder and Prostate Research

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Identification of the β-adrenoceptors in pig urinary bladder

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Introduction β-adrenoceptors mediate relaxation of detrusor muscle in several species. This relaxation may be mediated via β_1, β_2, or β_3-receptors, or a mixture of these subtypes [*Br J Pharmacol* 1997; 122: 1720–4]. The pig is often used to study the physiology and pathophysiology of the bladder because many *in vitro* and *in vivo* responses in pig have shown a similarity to findings in human. The purpose of this study is to identify the functional β-adrenoceptor subtypes in pig urinary bladder.
Materials and methods Pig detrusor strips (dome region) were set up in gassed Krebs solution and pre-contracted with 50 mmol/L KCl. Concentration-relaxation curves to β-agonists (isoprenaline, salbutamol and BRL37344) were obtained in the absence and presence of antagonists.
Results Salbutamol (a β_2-selective agonist) had a high potency, and 3–30 nmol/L ICI11851 (a β_2-selective antagonist) antagonised responses with high affinity. Isoprenaline (a nonselective β-agonist) also had high potency, and was antagonised by propranolol (β_1,β_2-selective antagonist) competitively, but 0.3–3 µmol/L CGP20712A (a β_1-selective antagonist) failed to antagonize these responses. ICI11851 (3–30 nmol/L) antagonized responses to isoprenaline with high affinity, but analysis of the antagonism by a Schild plot suggested that the responses were mediated by more than one β-receptor. BRL37344 (a β_3-selective agonist) had a low potency on the bladder and the concentration–response curve was very shallow.
Conclusion β_3-mediated responses of the pig bladder are predominantly mediated via the β_2-subtype but the data also suggest a contribution from adrenoceptors other than β_1 and β_2.

P64

Influence of genitofemoral nerve laser neurostimulation on experimentally cryptorchid rat model

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Introduction The aim of this study was to investigate the influence of genitofemoral nerve laser neurostimulation (LNS) on spinal cord and testicular histology in a unilateral cryptorchid rat model.
Methods An rat model of unilateral cryptorchidism was created by surgically displacing a testicle into the abdomen for 14 days in 32 immature Wistar rats. After this period the testis was replaced into the scrotum and 20 days after displacement the spinal cord was opened at L3–L4 and neural filaments of the dorsal roots isolated. The spinal cord and neural filaments at the site of the electrodes were irradiated by a low-power helium-neon laser at a power density of 12.7 mW/cm^2 and 8.5 J/cm$^{2.}$ LNS was then applied for 7 days using a 320 µm diameter optical fibre, with the tip of the fibre in gentle contact with the surface of the nerve. The compound action potential was monitored from the genitofemoral nerve. Ten

animals were killed after 1 and 10 after 30 days of LNS. In a control group of six rats with cryptorchidism, the contralateral part of the spinal cord was irradiated.
Results After 1 day of LNS the spinal nucleus of the genitofemoral nerve showed active nucleoplasmatic exchange, with nuclear synthesis in neurones and moderate numbers of synaptic vesicles (3900–5100), and movement of the vesicles to the active zone of synapsis. The nucleo-cytoplasmic coefficient which characterized cell metabolism increased by 47%. Physiological investigation showed an increase in intensity of mediator mobilization (from 1721 to 3125) and a compound action potential; the amplitude was increased. Histology of the testicle after 30 days of LNS showed complete restoration of testicular structure and an increase in the main steroidogenic enzyme activity. Regeneration was more intense than in the control group, which showed damaged spermatogenesis.
Conclusions: Neuronal transmission might have a role in the damage sustained by the undescended testicle. LNS of the spinal nucleus of the genitofemoral nerve leads to an improvement in neuronal transmission and activates the regenerative processes in this cryptorchid animal model.

P65

Physiological studies of the vas deferens: towards a treatment for testicular pain?

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Introduction Clinical observations in individuals with chronic testicular pain suggest that stress can cause a sympathetically driven contraction of the smooth muscle in the vas deferens and epididymis. Increased understanding of human vas deferens pathophysiology will help to elucidate this mechanism.
Methods The different components of the contractile responses to the electrical field stimulation (EFS) of human vas, obtained from vasectomy or at retroperitoneal resection of metastatic testicular teratoma, were assessed. Receptor subtypes along the vas deferens were classified using: prazosin hydrochloride, WB4101, α,β−methylene ATP, suramin and neuropeptide-Y (NPY) 13-36.
Results There appear to be three major components of the contractile response to EFS in both scrotal and pelvic portions of the human vas; an adrenergic (prazosin and WB4101 sensitive) component, a purinergic (suramin and α,β−methylene ATP sensitive) component, and a nonadrenergic nonpurinergic compound, perhaps mediated by NPY. Preliminary results using NPY 13-36 suggest there might be pre- and postjunctional effects of NPY. The combination of prazosin and WB4101 produced equivalent inhibition of the EFS response in both pelvic and scrotal ends, in contrast to rodent vas deferens in which the purinergic component is dominant in the prostatic end.
Conclusions These observations might lead to the identification of appropriate blocking agents for use in the management of testicular pain and related disorders. Vas deferens may also provide a more convenient source of tissue than prostate to study adrenergic receptors in the male lower genital tract.

P66

Measuring the ultrastructure of extracellular collagen in prostate tissue by scanning electron microscopy

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Introduction The three-dimensional structure of extracellular collagen reflects its role in providing a skeletal framework and in maintaining a microenvironment suitable for cell function. The fibrillary pattern is specific to individual organs and tissues. The aims of this study were to determine the patterns in prostatic disease states and to develop a means of measuring these features.
Methods Prostate tissue was obtained during radical prostatectomy and TURP. Cellular elements were digested with NaOH and prepared specimens examined by scanning electron microscopy. Fibrillary patterns were measured using latex microspheres as standards.
Results Acini were surrounding by parallel unbranched collagen fibres. In BPH the mean (SD) fibre diameter was 1.1 (0.1) μm, whereas in carcinoma of the prostate it was 2.4 (0.5) μm. These fibres were tightly packed into a stratified layer that was 9 (3) μm thick surrounding BPH acini and 18 (7) μm in prostate cancer.
Conclusion There is a clear difference between the patterns of the extracellular collagen matrix in BPH and prostate cancer. These can be quantified by objective measurements. Knowledge of these differences provides a useful model for the study of trophic mechanisms in benign and malignant growth of the prostate.

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Role of intraprostatic pressure on apoptotic resistance in a model of BPH

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Introduction The underlying process in BPH is likely to be a disturbance in the normal balance between programmed cell death (apoptosis) and cell proliferation. This results in an overall increase in cell number and an enlargement of the prostate. Elevated tissue pressure has been measured in BPH. We hypothesise that elevated intraprostatic pressure contributes to the development and maintenance of BPH. The aims of this study were to determine the effect of pressure on prostate epithelial and stromal cell apoptosis and proliferation.
Methods Benign stromal cells from patients with BPH and LNCaP epithelial cells were cultured under stretch-induced pressure for 48 h. Apoptotic resistance was measured by assessing the effects of etoposide (60 μmol/L) on apoptotic induction. Apoptosis and cell division were measured by propidium iodide DNA staining, using flow cytometry.
Results

Mean (SD) % apoptosis	*Pressure (cmH_2O)* 0	40	80	120
Stroma				
control	11.9 (3.1)	16.8 (2.0)	12.5 (1.6)	17.1 (3.4)
etoposide	22.2 (6.3)*	38.3 (7.2)	11.2 (1.5)†	18.1 (0.8)
LNCaP				
control	12.3 (6.4)	7.9 (2.8)	11.1 (2.8)	13.7 (4.1)
etoposide	23.9 (5.2)*	15.4 (3.0)†	15.7 (2.6)†	13.6 (2.6)†

*$P < 0.01$ vs control at 0 pressure; †$P < 0.01$ vs etoposide at 0 pressure; both Student's *t*-test

Conclusion Stromal and epithelial cells grown under pressure develop resistance to etoposide-induced apoptosis. There was no change in the number of dividing cells. Altered apoptotic rates may result in increased cell numbers. This study shows for the first time a direct role for pressure in prostate cell life-span and may represent an additional component in the pathogenesis of BPH.

P68

Diversion colitis in children with colovaginoplasty

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Introduction Congenital anomalies of the genitalia remain a major ethical and technical challenge. Recently colovaginoplasty has been used successfully for children with congenital adrenal hyperplasia (CAH), androgen-insensitivity syndrome and vaginal agenesis. However, we describe three cases of diversion colitis in children with colovaginoplasty. Diversion colitis is a nonspecific inflammatory process that occurs in segments of colorectum surgically diverted from the faecal stream.
Patients and methods Eighteen children underwent colovaginoplasty, of whom nine had androgen-insensitivity syndrome, three had CAH, three had vaginal agenesis and the remaining three had Meyer-Rokitansky syndrome. A segment of sigmoid colon was isolated on its vascular pedicle and brought to the perineum in a plane between the urethra and rectum.
Results There were no major complications in the early follow-up; however, three children developed severe vaginal discharge with bleeding 2–7 years after colovaginoplasty. Examination showed erythema, oedema, ulceration and bleeding. Biopsy of the diverted segment in two cases confirmed diversion colitis, typical features of which are acute and chronic nonspecific inflammation, crypt abscesses and lymphoid hyperplasia. One patients responded to butyric acid and in the other two cases the colitis was treated with steroid enemas and mesalazine after having a poor response to short-chain fatty acids.
Conclusion Since the original description of diversion colitis by Glotzer in 1980, numerous case reports have been described but we are the first to describe its occurrence in children with colovaginoplasty. A multicentre study to assess the true incidence and natural course of diversion colitis in these children is needed.

P69

How effective is bladder augmentation alone in the treatment of urinary incontinence secondary to neuropathic bladder?

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Introduction Patients with neuropathic bladder may have reduced bladder compliance/capacity and/or inadequate outlet resistance. We investigated which of these factors predicted the response to bladder augmentation alone.
Methods Between 1983 and 1997 we retrospectively reviewed 30 patients who underwent bladder augmentation alone for their incontinence. The patients' incontinence history, urodynamics and radiological investigations before and after surgery were assessed.
Results Eighteen patients (mean age 9 years) had complete records and urodynamic evaluations; the follow-up was 3–10 years. After augmentation, 14 patients were dry and four wet. Comparing these two groups there was no difference in capacity before (160 vs 138 mL) and after surgery (385 vs 387 mL), or for end-fill pressure (36 vs 35 cmH_2O and 16.5 vs 12.5 cmH_2O), respectively. Detrusor sphincter dyssynergia was present before surgery in three of four patients in the wet group, but in only two of 14 in the dry group. After surgery the leak-point pressure increased from 9 to 41 cmH_2O in the dry group and from only 21 to 23 cmH_2O in the wet group.
Conclusion In these patients urinary incontinence was controlled in 14 of 18 by augmentation alone. Detrusor sphincter dyssynergia was an indicator of postoperative incontinence but capacity, compliance and leak-point pressure were not prognostic. In patients incontinent after surgery the leak-point pressure was lower than in the dry group. In patients with no detrusor sphincter dyssynergia bladder augmentation alone may be sufficient to treat urinary incontinence.

P70

The buried penis – an anatomical approach

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Introduction Surgical correction of the buried penis continues to present a challenge. Re-evaluation of the anatomy suggests a failure of developmental separation of the scrotal and penile tissues and tethering of the penile corpora to the deep fascia. We describe a new approach based on these anatomical principles.
Method We report on 16 boys (aged 11 months to 4 years) whose presenting symptoms included ballooning of the foreskin, dysuria and balanitis. An incision is made between the scrotal and penile shaft skin. Dissection is carried down to the deep fascia, allowing the scrotum to assume a more caudal position. The penile shaft is dissected to the level of Buck's fascia, freeing all its deep attachments. The redundant inner preputial skin is excised, leaving a cuff of mucosa. The remaining skin is wrapped around the shaft and anastomosed to the mucosal cuff, leaving the final circumcised appearance.
Results At a mean 9-month follow-up the cosmetic and functional results were excellent, with good penile protrusion. In one patient the penis became reburied and this required revision.
Conclusion Correcting the buried penis along these anatomical lines appears to represent an important advance in the management of this condition.

P71

Hypospadias repair: surgeons, techniques and results

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Objective To compare hypospadias repairs (mainly single-stage) performed by a urologist and those (mainly Bracka procedures) by a plastic surgeon in one institution between August 1996 and 1999.
Patients and methods There were 48 consecutive repairs, 36 by the urologist (group 1) and 12 by the plastic surgeon (group 2). Patients were reviewed by a member of each service at least 3 months after repair.
Results The mean age at initial surgery was 21 months for group 1 and 35.75 months for group 2. In group 1, 22 (62%) patients had anterior hypospadias, 10 (27%) mid-shaft, and four (11%) posterior hypospadias. Fourteen (38%) of these had a MAGPI repair, five (14%) a transverse island onlay, six (16%) a Snodgrass, three (8%) a Mathieu, three (8%) a two-staged Bracka repair, one a transverse island tube, one a pyramid repair for MIP hypospadias, one a vertical island onlay, and two were salvage repairs using buccal mucosa. All MAGPI repair patients were day-cases and the mean hospital stay for all patients in group 1 was 1 day. Six patients (16%, two transverse island, two buccal mucosal, one Mathieu and one Snodgrass) developed a fistula, four a meatal stenosis and two a more major breakdown. In group 2, three of 12 patients had anterior and nine mid-shaft hypospadias. One patient had a MAGPI repair and the remaining two a staged Bracka repair. The mean

hospital stay for stage 1 was 7 days and for stage 2, 7.5 days. The only complication was a fistula after a Bracka repair. The aesthetic appearance in all was good but the meatus was better after the Bracka repair.
Conclusion The better meatal appearance and complication rates for patients in group 2 were impressive but must be viewed against the expense and trauma of more prolonged hospitalization.

P72

Onlay island flap – a review of 100 cases

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Introduction The onlay island flap urethral reconstruction is an accepted hypospadias repair with the theoretical advantage of avoiding circumferential anastomoses and hence risk of stricture proximally or meatal stenosis distally. Our objective is to report its results in 100 patients.
Patients and methods One hundred patients (mean age 29 months, range 14–144) with hypospadias consecutively underwent repair between 1989 and 1997; the repair was performed as described by its originator. The meatal site was 1–20 mm below the corona and the flap was 15–40 mm long. Particular attention was given to the severity of hypospadias and the correction of chordee.
Results The functional and cosmetic results were excellent and satisfying in all 100 patients. The urethral plate was mobilized on 12 occasions and 10 had plication sutures to correct chordee. Nineteen patients developed urethral fistulae after surgery, typically subcoronally; there were no strictures, meatal stenoses or breakdown of the glans wrap. Excess penile skin was excised in 12 patients, six simultaneously with a fistula repair.
Conclusions The onlay island flap repair is a simple and versatile technique producing good cosmetic and functional appearance of the glans, and offers more predictable viability and neat ventral skin cover. On this basis we recommend it and have extended it successfully to include patients with more severe degrees of chordee and more proximal hypospadias. The complications were a little less than those encountered with tubed flaps; urethral fistulae were less troublesome than stricture from the patient's perspective and more readily amenable to surgical correction.

P73

When should a gynaecologist be involved in the management of children with complex urogenital abnormalities?

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Introduction Developmental disorders of the cloaca and complex anorectal anomalies are often associated with Müllerian abnormalities. In childhood, the gynaecological aspects of these conditions are irrelevant and surgery concentrates on urinary and gastrointestinal aspects. because surgery has improved, more girls are surviving into adolescence and the problems of menstruation, sexual activity and fertility become important. We present three cases of adolescent girls presenting with haematometra caused by obstructed outflow tracts.
Patients and results All three girls had complex cloacal or anorectal anomalies and had undergone extensive surgery as children. In two, a laparotomy in infancy had described the uterus as absent or vestigial. All presented with primary amenorrhoea, cyclical pelvic pain and a pelvic mass of haematometra. Ultrasonography and MRI confirmed a haematometra in all. All underwent abdomino-perineal vaginoplasty. One had large haematosalpinges and extensive endometriosis caused by the outlet obstruction. Both Fallopian tubes had to be removed.
Conclusion Gynaecologists should be involved in the care of these patients in childhood. Even if a uterus is thought to be vestigial it may develop enough to produce menstruation at puberty. Monitoring the uterus by ultrasonography or MRI should allow uterine obstruction to be identified at an early stage. In the short-term the symptoms of pain should have been prevented. In the long-term, prompt surgery may prevent some of the extreme sequelae. These girls already have limited chances for fertility, and damage to the Fallopian tubes or the development of significant endometriosis can only compromise this further.

P74

The modified Breteville technique for hypospadias repair

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Introduction Many operations have been described this century for hypospadias repair, but few have proved successful for all levels of hypospadias and for all surgeons. We present a reliable two-stage repair using a vascularized preputial flap, which has been further modified to allow the second stage to be routinely carried out as a day-case procedure.
Methods The first stage consists of a radical chordee release and the formation of a neourethra from an axial pattern preputial flap which is tubed to the glans penis. At the second stage the flap is divided and inset, and the foreskin trimmed. Routinely performed at 18 months of age, with the second stage at an interval of 6 months, this procedure has been successfully used on adults presenting late. All patients were prospectively assessed and followed.
Results Since 1992, over 90 patients have been treated with this technique. The major complication rate (fistula and stenosis) was $< 5\%$ within the first year (three stenoses and one fistula). With growth, four patients have required meatotomy and four patients have developed a minor fistula > 1 year from surgery.
Conclusion This technique offers a reliable and versatile vascularized flap for reconstructing all levels of hypospadias and reduces the second stage to a day-case procedure.

P75

The objective assessment of hypospadias repair

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Introduction The success of hypospadias repair is routinely assessed by the complication rate of fistula, stenosis or recurrence of chordee. Although undoubtedly important they shed little light on the outcome of social function, i.e. the ability to stand up and pass urine into a receptacle with a well-controlled coherent stream.
Patients and methods Thirty patients of school age and above were recalled from our hypospadias database and assessed objectively using uroflowmetry and a novel technique of digitally imaging the scatter of an incoherent urinary stream.
Results Analysis of uroflowmetry showed that 18 of 28 (65%) children were below the 10th centile of the Miskolc nomogram; two previously unsuspected stenoses were identified and corrected. Two adults treated late were above the 50th centile. Digital imaging to measure the direction and quantity of spillage/spray identified three patients with loss of coherent stream and directional aim, resulting in a socially unacceptable outcome.
Conclusion This study analyses for the first time the results of hypospadias repair objectively, studying both flow and spray

characteristics, and can identify strictures and socially unacceptable outcomes.

P76

PUV with persistent high serum creatinine levels: does supravesical diversion have a role?

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Introduction In patients with PUV and persistent high serum creatinine levels irrespective of vesical drainage, proximal urinary diversion would be indicated for the management of presumed concomitant vesico-ureteric junction (VUJ) obstruction. To evaluate the justification and value of proximal diversion in such cases, a retrospective study was conducted.
Patients and methods Between 1982 and 1995 all patients with PUV and persistent high serum creatinine levels (> 15 mg/L) irrespective of adequate vesical drainage were reviewed. Patient characteristics, methods of treatment and eventual outcome were determined. Radiological and pressure studies to exclude obstruction at the VUJ were also reviewed.
Results Of 48 patients evaluated, 28 underwent primary valve ablation, 16 high-loop ureterostomy and four vesicostomy. After a mean (range) of 78 (23–147) months, chronic renal failure developed in five of the patients who had high-loop ureterostomy and in 25% of the patients who had not. However, patients who underwent initial ureterostomy had significantly higher rates of reduced bladder capacity and incontinence of urine. Augmentation cystoplasty was required only for those patients with a history of loop ureterostomy. Twenty-two percutaneous nephrostomies were performed in 14 patients, during which seven of 22 had radiological evidence of obstruction at the VUJ. After a mean 2 weeks of diversion, both radiological and pressure evidence of obstruction were found in only one of 22 units. After a mean 18 months of urinary diversion via a ureterostomy, radiological evidence of obstruction was found in two of 27 (7%) vesico-ureteric units. Early in the series 15 of 34 (44%) patients had a ureterostomy. Later, following an algorithm including percutaneous nephrostomy before formal diversion, only one of 14 boys had a high-loop ureterostomy.
Conclusions From these findings, high-loop ureterostomy does not prevent progression to renal insufficiency and is associated with more complications than primary valve ablation or vesicostomy. Unresolved VUJ obstruction is rare. Thus proximal urinary diversion is rarely justified and percutaneous nephrostomy drainage for a short period helps to identify those who would require formal diversion.

P77

Combined buccal mucosal grafting and Snodgrass technique for salvage hypospadias repairs: a promising alternative

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Introduction Buccal mucosal grafting (BMG) is widely practised for salvage hypospadias repair. Significant complication rates are reported, many of which may be related to graft failure. The commonest technique used is an onlay patch of BMG, which is dependent on penile skin for its neovascular supply. In these cases the penile skin is frequently deficient and this could contribute to graft failure. The Snodgrass procedure provides an alternative approach to BMG.
Methods BMG is harvested in the standard way; the residual urethral plate is dissected and a dorsal longitudinal Snodgrass urethrotomy performed down to the corpora. The gap provides a fixed, vascular bed onto which the BMG is laid. The composite urethra is tubularized in the standard way.
Results Thirteen grafts have been used in 11 patients (mean age 9 years), with a mean follow-up of 12 months; on average the patients had undergone three previous hypospadias operations. Twelve grafts currently remain patent, with a good cosmetic result. One graft failed in a patient with mixed gonadal dysgenesis who underwent two simultaneous grafts for a long narrow segment. There were no fistulae.
Conclusion These early results are encouraging and suggest that this approach may cause less graft failure and have a lower complication rate. This could be explained by the presence of a fixed graft bed with a better blood supply that is not dependent on deficient and scarred penile skin. We would recommend its use.

P78

Paediatric lower urinary tract rhabdomyosarcoma: a single-centre experience of 30 cases

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Objective To retrospectively analyse the long-term outcome of children with bladder and/or prostate rhabdomyosarcoma who were diagnosed in our centre over the last 17 years.
Patients and methods The study comprised 30 children (26 boys and four girls, mean age 5 years); 23 had stage III and seven had stage II disease. The initial biopsy showed an embryonal variant in 27 and round cell sarcoma in three. All patients received eight weekly doses of vincristine, actinomycin D and cyclophosphamide (VAC). Subsequent treatment relied on the response to chemotherapy.
Results Fourteen patients had a complete (CR) or partial response (PR) to chemotherapy (> 50% reduction in size). They were maintained on VAC chemotherapy for 2 years. Twelve patients survived with no evidence of disease for 7 months to 10 years. Additional therapies were used in three patients, i.e. radical cystectomy in one and external irradiation in two. Sixteen patients had a minimal response (MR) to chemotherapy; in six, radical cystectomy was feasible. All patients were free of disease for 4–11 years. Radiotherapy was given to the remaining 10 patients. Thereafter radical cystectomy became feasible in five while partial cystectomy was possible in three. Only three of these 10 patients survived for 4–9 years.
Conclusion The tumour response to the initial chemotherapy serves as a mean of stratifying patients into two risk groups, i.e. low-risk patients, with CR and PR, in whom the bladder could be salvaged, and high-risk patients with MR, in whom intensive treatment should be followed with no attempt at bladder salvage.

P79

Shock wave lithotripsy in children – the Edinburgh experience

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Introduction Shock wave lithotripsy (SWL) is the least invasive and most preferred treatment modality for urinary calculi in adult populations, but its acceptance in paediatric practice has been slow. The aim of this study was to determine the efficacy of SWL in children and to record its associated complications.
Methods Ninety-five children with urinary calculi who were treated with SWL at the Scottish Lithotriptor Centre between 1987 and 1998 were analysed retrospectively. Treatment was delivered using a Wolf Piezolith 2300 lithotripter.

Results Follow-up was unavailable for 28 of these children and they were omitted. Of the remaining 67 children, 22 (33%) had abnormalities of the genitourinary system and 12 (18%) had congenital abnormalities affecting other organ systems; one child had cystinuria. The mean (range) age was 10.5 (2–16) years and the mean stone size 18.8 (3–110) mm. Six children (9%) had auxiliary measures undertaken before SWL, i.e. a JJ stent in four, ureteroscopy (URS) in one and URS with electrohydraulic lithotripsy (EHL) in one. In all, 78 kidneys and ureters underwent a total of 135 treatment sessions (mean 1.7) carried out with the patients under sedation (55%) or general anaesthesia (45%). Of these, 60 (77%) were rendered stone-free and asymptomatic fragments of < 4 mm were found in a further 13 patients (17%). Complications occurred in 12 (15%) patients; two required percutaneous nephrolithotomy (one with cystinuria), one underwent a meatotomy for a large urethral fragment, eight had ureteric colic (four steinstrasse and four solitary fragments). These were managed conservatively in five cases, by URS + EHL in three and by *in situ* lithotripsy in one.
Conclusion SWL is a safe and effective therapy for urinary calculi in children and should be considered as first-line therapy in such cases.

P80

Magnetic resonance urography in the management of complicated duplex kidneys

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Introduction In a young girl who is always dribbling urine, a nonfunctioning upper moiety of a duplex kidney should always be suspected. In most patients standard imaging is sufficient to detect this but in a few the cryptic duplex can be extremely difficult to diagnose. We describe our experience with magnetic resonance urography (MRU) in diagnosing a duplex kidney.
Methods Children under 8 years undergoing MRU require general anaesthesia. The protocol adopted uses heavily T2-weighted images and the maximal intensity projection method (MIP). In addition, gadolinium intravenous contrast medium is used. MRU was used in five patients with suspected duplex kidneys that caused symptoms. A nonfunctioning upper moiety was diagnosed in two and in one a nonfunctioning lower-pole moiety was found. In these patients standard imaging had failed to diagnose these entities. They underwent heminephrectomy, with resolution of their symptoms.
Conclusion The diagnosis of a cryptic duplex system may be one of the most challenging in paediatric urology. In most such patients, ultrasonography, IVU and renal scintigraphy are sufficient. When standard techniques fail to diagnose a duplex in a patient with strong clinical indications, we recommend MRU.

P81

Intraoperative autotransfusion in major urological surgery

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Introduction The 1998 Edinburgh Consensus Conference concluded that intraoperative autotransfusion (IAT) was safer than homologous transfusion. The NHSE has recommended that all Trusts should have assessed the feasibility of implementing autologous blood transfusion by March 2000. The aim of this study was to review the use of IAT in urology.
Methods IAT has been used in 109 open urological procedures, including 46 cystectomies, 39 nephrectomies, seven radical prostatectomies, 10 prostatectomies and seven other operations. Data were collected prospectively on a computerized database and verified by an independent IAT coordinator.
Results Overall, 243 units (range 0–25, mean 2.4) of autologous blood were salvaged and re-transfused; 193 units (range 0–20, mean 2.1) of bank blood were given peri-during and 136 units (range 0–17, mean 1.3) after surgery. In the cystectomy group, 91 % received IAT, of whom 86% had two units or more; 24% received no bank blood. In the nephrectomy group, 41% received IAT, of whom 21% had two units or more and 49% received no bank blood. There were no complications associated with use of IAT. No cases of coagulopathy were seen. The clinical follow-up will be presented.
Conclusion IAT has been used safely for 5 years with no significant side-effects. The recent increased cost (from £32 to £78 per unit) and perceived risks of homologous transfusion reinforce the utility of the technique in major urological operations.

P82

An investigation into serum PSA levels after aorto-iliac surgery. How common is prostatic infarction?

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Introduction Postoperative acute urinary retention is a well recognised complication of aorto-iliac surgery (AIS). Risk factors for its development include pre-existing BOO, opiates, intravenous fluid loads and recumbency. This study investigated the frequency of a further putative factor, i.e. prostatic infarction.
Method Serum PSA level is elevated in prostatic infarction. After obtaining ethical committee approval the PSA levels before and after surgery (24 h) were assessed in 15 patients undergoing AIS and compared with a group of 15 controls undergoing femero-distal bypass and bowel surgery. Both groups were matched for age, preoperative PSA level and IPSS; all were free of urinary sepsis. Data were not normally distributed so summary statistics are presented as the median (interquartile range) and nonparametric methods of analysis used.
Results The PSA level before surgery in the control group was 2.7 (0.9–6.6) ng/mL, and similar to that in the AIS group of 1.1 (0.7-5.2) ng/mL; it remained unchanged at 24 h in the control group, at 3 (0.9–4.8) ng/mL. After surgery the levels in the AIS group were significantly higher, at 5.1 (0.8–10.7) ng/mL, than before and than in the control group ($P < 0.005$). In addition, 10 of the AIS patients had a $> 50\%$ increase in baseline PSA level, compared with one of the controls. Although there was no difference in the length of procedure (AIS vs controls) there was an association between the increase in PSA level and the duration of cross-clamping in the AIS group ($P < 0.05$).
Conclusion In the absence of UTI, the acute rise in PSA level observed here was probably caused by prostatic infarction. This event will be followed by oedema and this may be a factor in postoperative voiding dysfunction. In addition, it is likely that, because of the similar blood supply, the detrusor is also rendered ischaemic, with subsequent loss of function. The correlation with the duration of cross-clamping suggests that the prostatic infarction is not simply related to clamp manipulation (and resulting atheroembolism) but to prolonged ischaemia. We have identified the existence of a further reversible factor in the development of postoperative retention in vascular patients. These findings support the trend towards conservative management of this complication.

P83

Long-term outcome of microscopic haematuria

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Introduction A full urological investigation of patients with microhaematuria is required, although for most no serious cause is found. The concern is that significant pathology may be missed or not manifest during the investigation. Thus a long-term 5-year follow-up study was conducted.
Method At BAUS 1994 we presented a prospective audit of 292 consecutive patients referred with asymptomatic occult haematuria. They underwent urine testing, upper tract imaging and cystoscopy. Urinary tract malignancy was found in 16 patients and benign urological/renal pathology in 148 (51 %); 128 (44%) had no obvious cause for their occult haematuria at the initial evaluation. All have now been reviewed.
Results Of the 16 patients, eight with urinary tract malignancy are alive; 10 patients developed new nonurological malignancies, six have been followed by the renal physicians and two others have rheumatoid disease. Of the remaining 258 patients, 168 had subsequent negative urine analysis, 27 have persistent occult haematuria and 11 had confirmed UTI. The remaining 51 patients died from benign causes such as heart disease, or have moved away from the region, or were lost to follow-up. Only one patient developed a new bladder tumour 3 years after a negative initial investigation of microhaematuria. He re-presented with frank haematuria after 3 years, and re-evaluation revealed a G2pTa transitional cell tumour of the bladder.
Conclusion This study has shown that after an initial full investigation of patients with microscopic haematuria, it is unnecessary to re-investigate patients unless they become symptomatic or develop frank haematuria.

P84

The urological complications of renal transplantation: a series of 1535 cases

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Objective To evaluate the incidence of urological complications in renal transplantation.
Methods The case notes were reviewed of all 1535 cases of renal transplantation between 1975 and 1998; 1292 patients underwent

1386 cadaveric and 149 living-related donor transplants. A stent-less Leadbetter-Politano vesico-ureteric anastomosis was used routinely.
Results Forty-five cases of urinary leak occurred; 38 were from the ureter, 19 with ureteric necrosis, 14 anastomotic or lower ureteric leakage and five upper ureteric leakage. These were management by observation (one), nephrostomy (one), retrograde stenting (one), re-exploration with defect oversewn (one), open drainage (one), open stent insertion (four), ureteric reimplantation (eight), native ureteropyelostomy (15), native ureteroureterostomy (four) or Boari flap (two). The anterior cystotomy leaked in six cases, two requiring open repair. In one case the source of urinary leakage could not be ascertained. Ureteric obstruction was seen in 46 cases, presenting early if caused by technical factors (14) or late if caused by ureteric ischaemia (32). Seven further cases were caused by extrinsic compression. Management was with nephrostomy (two), stenting (14), endoscopic balloon dilatation (three), endoscopic ureteric resection (one), open stenting (one), re-exploration and ureterolysis (two), pyeloplasty (one), native ureteropyelostomy (seven), native ureteroureterostomy (two) or ureteric reimplantation (20). Six cases of obstructing transplant calculi were managed by nephrostomy and lithotripsy (one), ureteroscopic retrieval (two), percutaneous nephrolithotomy (one), open nephrolithotomy (one) and graft nephrectomy (one). Nineteen cases of BOO were managed with bladder neck incisions (five), urethrotomy (two), urethral dilatation (two) or TURP (five). Three deaths were attributed to urological complications, with one further graft loss. There was no significant association between donor age, cadaveric vs living-related donors, cold ischaemic time or organ origin (locally retrieved vs via the national sharing scheme) and the incidence of complications.
Conclusions The 1535 renal transplants were complicated by urinary leak (2.93%), primary ureteric obstruction (3.52%), BOO (1.2%) and obstructing transplant calculi (0.4%).

P85

LETs save money!

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Introduction About 4% of the entire NHS budget (£1 billion) is spent on diagnostic tests. Most patients attending a urology outpatient clinic will have a urine sample analysed by microscopy and culture, the results of most being unremarkable. The ability and cost-effectiveness of the leukocyte esterase test (LET; Multistix 85G, Ames) as a screening test for abnormal samples was evaluated.
Patients and methods Two hundred consecutive MSU samples destined for laboratory analysis were first tested with the Multistix 85G dipstick, evaluating the LET, nitrite and blood. Various positive criteria were assigned to each of three laboratory results, i.e. red blood cells (RBC), white blood cells (WBC) and pure growth of organisms. Sensitivity, specificity and negative predictive values (NPV) were calculated by comparing the dipstick results with the laboratory results.
Results

Dipstick test	*Laboratory +ve criteria*	*Sensitivity %*	*Specificity %*	*NPV %*
LET	> 9 WBC/mm^3	75	85.5	84.8
Nitrite	$> 10^5$ pure growth/mL	43.5	98.3	93.0
LET	$> 10^5$ pure growth/mL	95.7	70.1	99.2
LET	$> 10^4$ pure growth/mL	86.7	71.2	96.8
Blood	> 3 RBC/mm^3	87.5	61.3	96.3

Conclusion The Multistix 85G is an excellent screening test for UTI and haematuria. Nitrite estimation is a poor screening test. A protocol using LET and blood dipstick tests will detect 91% of pure growths of $>10^4$ organisms/mL and/or > 3 RBC/mm^3. If this protocol were used, there would be a saving of 39% of urine samples sent for laboratory analysis. In a typical urology unit, there would be a saving of $\approx$ £2500 per 1000 MSU samples tested.

P86

Mortality and morbidity after high-risk procedures in urology is not related to surgeon grade

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Introduction Comparing crude mortality and morbidity (M&M) rates by operating surgeon is unreliable and misleading. A risk-adjusted comparison of M&M is more likely to reflect the true M&M rates for urological operations. Thus we assessed whether the M&M rates for operations performed by junior surgeons differed from those for senior surgeons.
Methods Data were collected retrospectively on 200 patients who underwent major, major plus or complex major urological operations. The risks of M&M were estimated using the Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity (POSSUM) system. The M&M for procedures carried out by junior and senior surgeons were compared both with and with no adjustment for risk.
Results The observed M&M did not differ significantly from the expected M&M calculated using the POSSUM scoring system ($P = 0.20$ and 0.35, respectively). No evidence was found to suggest that there was an association between grade of surgeon and unadjusted M&M, with an odds ratio (OR, 95% CI) for senior and junior of 0.98 (0.52–1.85) and 0.88 (0.31–2.23), respectively, or between grade of surgeon and POSSUM-adjusted M&M of 1.11 (0.54–2.22) and 0.94 (0.36–2.51), respectively.
Conclusion The POSSUM equations provide adequate estimates of M&M for high-risk urological operations. From this study there is no evidence to suggest that the incidence of M&M after high-risk operations in urology is related to surgeon grade.

P87

Vasectomy consent and follow-up: current practice of urologists in England and Wales – a questionnaire survey

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Introduction Vasectomy heads the list of procedures for negligence claims for damages in urology. The follow-up of patients undergoing vasectomy and details of consent are not clearly defined. We aimed to study the existing practices among urologists.
Method A detailed questionnaire was sent to all consultant urologists in the UK and the replies analysed.
Results Of 435 questionnaires sent, 293 (67%) replies were received. Of these, 266 (91%) consultants reported performing vasectomies; 85% of consultants perform < 200 vasectomies per year and 92% of the consultants rely on two consecutive negative samples as the criteria for sterility, with 40% performing the first test at 12 weeks, although there was wide variation in this interval, ranging from 4 to 24 weeks. Fresh samples were analysed by 80% of consultants and if persistent non-motile sperms appeared, an equal number of consultants (44% and 47%) decided for and against repeating the operation; 7% would declare special clearance or act on their patient's decision. For the details mentioned in the consent, 85% include the number of tests required, 88% explain the failure rate, 88% mention re-canalisation, 73% mention the risk of late pregnancy, 74% discuss the risk of chronic testicular pain, 90% mention irreversibility and 32% discuss cancer of the prostate.
Conclusion This survey suggests that there is no standard method among urologists of following up vasectomy. To avoid litigation, a

universal consent form, including all the complications of vasectomy, needs to be devised. A follow-up protocol needs to be standardized based on prospective studies. BAUS should take a lead role in achieving standardization.

P88

Informed consent: friend or foe!

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Introduction Recent guidelines on informed consent have required that consent is obtained by the operating surgeon. In the present climate of litigation it is of paramount importance that urologists are seen to comply with this.
Method In a telephone poll, we asked 100 urology departments about their consent policy. We then audited consent obtained in our department over 1 month of urology operating and the time spent by one individual consultant gaining preoperative consent.
Results Most urology departments are not conforming to national guidelines. In 19% of departments, consultants mostly obtain consent, in 11% specialist registrars and in 70% it is left to senior house officers or housemen. In our department audit showed that in 91% of procedures (214 of 235) consent was obtained by the operating surgeon. The time spent by one consultant alone obtaining consent on the ward in that month was 4.5 h (excluding time spent in outpatients in discussion).
Conclusions This study suggests that most urology departments are not complying with the suggested guidelines, and that the time required to do so represents a significant burden to consultants.

P89

Prioritization of urological waiting lists by patients

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Introduction The management of waiting lists is a controversial area of healthcare. Prioritizing non-malignant conditions is difficult, takes doctors' time and may show poor agreement between patients and clinicians. Our aim was to examine this relationship.
Method The Somerset score is a six-question pro-forma (maximum score 24) used to assess the impact on quality of life (QoL) of disease processes; it is currently used by GPs and consultants in Somerset. It grades factors such as progression, pain, disability, dependence on others and ability to pursue normal activities/occupation. One hundred consecutive patients placed on the urological waiting list also completed the pro-forma, allowing a comparison with their clinicians' assessment.
Result There was a significant correlation in overall score between patients' and doctors' scores ($P < 0.001$). On average, consultants scored 8% higher than the individual male patients and 10% lower than their female patients. The poorest correlation was with the enquiry 'How do you rate the progress of your condition?' Patients reported a more rapid deterioration in their condition. Being in employment did not affect patients' perception of seriousness, but there was an association with their overall score.
Conclusion This study shows significant agreement between patients and clinicians for the impact of patients' diseases on QoL. It seems appropriate that patients should be encouraged to complete prioritization forms before placement on the waiting list. Further validation of the questionnaire is underway in a parallel study, but it appears that patients rank themselves fairly compared with their fellow patients.

P90

The application of bar-coding to clinical data collection

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Introduction In recent years, increasing emphasis has been placed on data capture in medicine. These data are collected for a variety of purposes, from clinical audit to the generation of log-books by trainees. This study evaluates whether using a palmtop computer equipped with a bar-code reader could provide a feasible option for collecting such data.
Method Data were collected on patients referred to one hospital with calculous disease. Data were obtained on the initial management decision, treatment and follow-up, and compared with the hand-written records normally produced. A Workabout MX™ palmtop computer with integral bar-code reader (Psion Industries plc, UK) was used for data collection. Bar codes were generated for data of interest using the 'BC 3 of 9' HR bar-code font, on a standard desktop computer. Questionnaires to collect the data were developed using Questor™ software (Paradigm Technologies Ltd, UK). Data were subsequently transferred electronically to a Microsoft Access™ database.
Results The scanner proved easy to use and required only a brief period of familiarisation. To date, the records of 125 patients have been evaluated. Accuracy of the data collection, compared with the hand-written record, was $> 90\%$. With adjustments to the questionnaire to allow for ease of correction if the wrong bar code is scanned, complete accuracy should be achievable.
Conclusion The Workabout MX™ is a simple and versatile data collection tool. A minimum of computing skills are required to set it up. Data can be collected quickly and unobtrusively in a form compatible with common spreadsheet and database programs, which are already in use in many hospitals. The high degree of accuracy of data collection will be invaluable in generating the sophisticated clinical databases and patient records expected of a modern health service.

P91

A cancer database for urology

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Introduction With the advent of clinical governance, audit and data collection have become increasingly important for clinicians. Existing hospital data collection is often inaccurate and incomplete, and the BAUS Oncology group has recently implemented a registry of new urological tumours. For these reasons, the accurate collection of data on patients with urological tumours is critical.
Patients and methods An Access™ (Microsoft, USA) application has been developed and piloted in our institution.
Results The database allows detailed data collection for patients with all urological tumours. It also allows tracking of patients and enables recall lists, such as those for check cystoscopy, to be generated. Searching and network environments are supported. The BAUS new tumour minimum dataset can be automatically generated, and the database can be customised to allow data collection for clinical trials.
Conclusions This database is user-friendly and robust, yet easily customised. It has helped to simplify the follow-up of patients with bladder cancer and reduces the risk of patients being lost from surveillance programmes. Data entry is quick and a minimum of computer literacy is required. Similar databases are being developed for other aspects of urological practice.

BPH I (Poster session)

P92

How are men with LUTS managed in the primary care setting?

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Introduction The advent of primary-care groups may lead to a shift in the management of patients from secondary to primary care settings. Locally developed guidelines (Camden and Islington) have revealed a high degree of variation in thresholds of referral of patients with LUTS. The aim of our study was to quantify inconsistencies in the management of men with LUTS in the primary care setting.
Methods An anonymous questionnaire consisting of four case scenarios of men with LUTS, followed by 60 'Yes/No' type questions, was distributed to 200 randomly selected GPs in the London area. Consensus for a given question was deemed to have occurred when 70% of respondents were in agreement.
Results There were 129 (64.5%) completed replies. Consensus between GPs was thought to exist for 26 (43%) of the questions posed. There was consensus on 75% of the questions on the investigation of men with LUTS and 50% of the questions on thresholds of symptoms initiating referral to a secondary-care setting. There was least consensus for questions on the management of UTI, irritative voiding syndrome and the use of urological drugs. Of the respondents, 17% would not refer an elderly man with microscopic haematuria and 74% of respondents would not refer a man with symptoms suggestive of chronic urinary retention, unless basic investigations were abnormal.
Conclusions In a representative sample of London GPs there was much agreement in the choice of tests used to evaluate LUTS. However, thresholds of symptoms initiating referral to a secondary care setting differ between GPs. Whether this disagreement represents an appropriate response to a different case mix or reflects professional uncertainty should be the focus of further study.

P93

A care pathway to reduce admission rates for men in urinary retention

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Introduction High-quality care, cost containment and risk management are key issues in the NHS; care pathways can help to achieve these goals. The aim of the pathway was to enable accident and emergency (A&E) staff (SHOs or Nurse Practitioners) to correctly identify those patients in retention who required admission, and those who could be safely discharged with a catheter *in situ*.
Methods The pathway was drawn up jointly by the urology and A&E staff. The guidance and decision points in the pathway were designed to identify those patients with possible chronic retention (who might have major diuresis after catheterization), those with UTI or haematuria, and those who would not be able to manage their catheter at home. The pathway was used for a 6-month pilot phase and minor adjustments made; the results presented are those from using the pathway over a year.
Results The hospital serves a population of 190 000; 70 patients (mean age 74 years) attended A&E in retention during this period. GPs referred 29 and 41 were self referred; 42 (60%) were admitted and 28 (40%) were discharged with a catheter *in situ*. The latter group were also given information sheets on urinary retention and catheter care. Twenty-seven patients were referred to the urology department for a trial without catheter (TWOC); the remaining patient rang the number on his information sheet and no patient was lost to follow-up. The mean time to a TWOC was 12 days; 10 (36%) were successful. All of these patients subsequently had a full urological assessment. Five were suitable for watchful waiting, one commenced α-blocker treatment and four were put on the waiting list for TURP. For 18 patients (64%) the TWOC was unsuccessful; of these, 15 underwent TURP (eight within a month and five within 2 months of the TWOC). Three patients required antibiotics while waiting for surgery. One patient had a prostatic stent and two had a long-term catheter inserted. Two patients who failed TWOC were found to have prostate cancer. Patients who were discharged home, knowing that they would be seen and assessed promptly in the day-care unit, were especially pleased to have avoided a hospital admission.
Conclusions The use of a care pathway enables casualty staff to correctly identify those patients who require admission. Costs are saved, as an admission can be avoided in a significant number of patients.

P94

Predicting prostate volume from serum PSA levels

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Introduction It has been suggested that prostate volume can be predicted from serum PSA levels. We prospectively studied the accuracy of prediction in a well-defined population.
Methods The study included 304 men presenting with high serum PSA levels (as measured using the Elecsys immunoassay) or LUTS. Total prostate volume (TV) was measured by TRUS using a 7.5 MHz transducer in a standardized protocol. Patients with prostate cancer were excluded. A linear regression model was constructed to predict logTV from the serum PSA level. A scatter plot was constructed, and the mean regression line, 95% CI of the mean regression and 95% prediction interval calculated. Spearman's correlation coefficient was calculated for age, PSA and TV.
Results The mean (range) values for age, PSA, TV and logTV were 66.87 (43.0–87.0) years, 5.89 (0.1–19.2) ng/mL, 56.82 (9.3–224) mL and 3.89 (2.23–5.41) respectively. There was small positive correlation between age and TV ($r = 0.23$, $P < 0.01$) and a strong positive correlation between TV and PSA ($r = 0.56$, $P < 0.01$). Using PSA alone as a predictor, r was 0.52 ($r^2 = 0.27$) and if PSA and age were used as predictors, r was 0.54 ($r^2 = 0.29$).
Conclusion Although the 95% prediction interval was wide it is possible to predict prostate volume from serum PSA levels.

P95

Nitric oxide-based influence of nitrates on micturition in patients with BPH

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Introduction Nitric oxide (NO) is involved in the physiological regulation of smooth muscle relaxation in the prostate; organic

nitrates act as NO donors. In this study we determined the influence of oral organic nitrates on micturition.
Methods Thirty-two patients were evaluated urologically before starting nitrate medication for cardiovascular disease, examining peak flow rates, residual urinary volume, IPSS, PSA levels and prostate volume. Specific inclusion and exclusion criteria were defined. Fifteen patients had obstructive symptoms and 17 reported no subjective voiding problems. They were re-evaluated 2 weeks and 3 months after nitrate medication.
Result There was a significant improvement in peak urinary flow rate (+3.5 mLs; $P < 0.05$), and a significant decrease in residual urine volume (−20 mL, $P < 0.05$) and IPSS in symptomatic patients. There were no significant changes in asymptomatic patients. PSA levels and prostate volumes did not change in either group.
Conclusion Organic nitrates influence the voiding variables in patients with obstructive BPH. This might be explained by the mechanisms of NO donation (smooth muscle relaxation) from nitrates. More control studies are necessary to describe the degree of influence of nitrates on the prostate. Orally concomitant medication with nitrates must be considered as a relevant biasing factor in BPH in future clinical studies.

P96

Correlation between the pattern of enlargement of benign prostates and lower urinary tract variables

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Introduction We prospectively studied the correlation between the pattern of enlargement of benign prostates and lower urinary tract variables.
Methods The study comprised 140 men (mean age 66.8 years, 95% CI 6.1–68.4) attending Prostate Assessment Clinics; malignancy was excluded by TRUS and biopsy. The maximum urinary flow rate (Q_{max}) described as typical by the patients with > 150 mL voided volume was used in this study. The anteroposterior diameter (APD), transverse diameter (TD), length (L) and total prostate volume (TV) were measured on TRUS using a 7.5 MHz transducer (Bruel & Kjaer Leopard 2001) in a standardized protocol which has been shown to be reproducible. The residual urine volume (RV) was also measured. The roundness of the prostate was calculated as the ratio of APD and TD. Pearson's correlation coefficient was calculated for the variables.
Results There were negative correlations between Q_{max} and age (r = 0.15, $P > 0.01$), APD ($r = 0.26$, $P < 0.01$), TD ($r = -0.24$, $P < 0.01$), L ($r = -0.37$, $P < 0.01$), APD/TD ($r = -0.097$, $P > 0.01$) and TV ($r = -0.31$, $P < 0.01$). There was a mild negative correlation between Q_{max} and RV ($r = -0.173$, $P < 0.01$) and minor correlations between RV and APD ($r = 0.02$), TD ($r = 0.04$), L ($r = 0.01$) and APD/TD ($r = 0.1$), none of which was statistically significant.
Conclusion The length of a benign prostate gland had the highest negative correlation with Q_{max}, in keeping with the principles of Poiseuille-Hagen, which states that flow in a tube is inversely related to the length.

P97

Is the ultrasonographically estimated bladder weight measurement sufficiently reliable for clinical use?

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Introduction Detrusor hypertrophy is a well-recognized consequence of BOO with potentially important functional implications, yet there is no established technique to assess it quantitatively. Bladder wall thickness (BWT) is easily measured ultrasonographically but depends on the degree of bladder filling. Ultrasonographically estimated bladder weight (UEBW) has recently been proposed as an alternative and shows promise as a predictor of BOO [*J Urol* 1997; 157: 476–9] but the reliability of this test remains to be determined when used by others. The aim of this study was to assess the intra- and interobserver variability of UEBW in men presenting with LUTS.
Methods Fifty-nine paired UEBW measurements were made by one observer on 10 catheterized and nine voiding men (mean age 68 years, SD 8). Six patients with stable symptoms also underwent repeat scanning on another occasion within a 2-week period. A second observer made 31 UEBW measurements on 11 patients (mean age 73 years, SD 7). An unlabelled copy of this ultrasonogram was digitally scanned and enlarged (× 5), and additional UEBW calculations made by the main researcher based on BWT measurements from the enlargements, while unaware of the estimates of the second observer or the patient.
Results For intra-observer variability, the median (range) initial UEBW was 101 (29–446) g and was 109 (34–511) g for the second measurements. The mean (SD) of the paired differences was 7 (54) g, which was not significantly different from zero (95% CI, −7 to 21), despite the observers being unaware of the other estimates. The limits of agreement (mean ± 2 SD) over which 95% of paired differences would be expected to lie were wide, at −101 to 115 g, although the intraclass correlation coefficient was relatively high, at 0.836 (95% CI 0.739–0.899). No further increase in the limits of agreement was seen when scanning on different occasions (−58 to 42 g). For interobserver variability, the mean (SD) difference between paired BWT measurements for the two observers was 0.3 (1.0) mm and again this was not significantly different from zero (95% CI −0.1 to 0.7 mm), indicating no systematic bias. The corresponding value for UEBW was 5.8 (19) g. The limits of agreement were closer, at −1.7 to 2 mm and −32.2 to 43.8 g for paired BWT measurements and UEBW, respectively, and the intraclass correlation coefficient for UEBW was 0.779 (95% CI 0.590–0.887).
Conclusion UEBW measurements in men with LUTS are wide ranging and show unacceptable variability when repeated by the same or different observers. The marked reduction in variability in this study with two observers reflects the limitation of inherent biological variation when using one scan and suggests that operator characteristics alone are insufficient to account for the poor results. Improvement of the technique is necessary before it can be considered for routine clinical use.

P98

Does a change in patient selection affect the outcome after prostatectomy for BPH?

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Introduction In the era of medical treatment for BPH the selection criteria for TURP seem to have changed. Thus we evaluated a change in patient selection pattern and assessed whether this affected outcome.
Methods Ninety-one consecutive patients undergoing prostatectomy were divided into three groups with symptoms of BOO and a postvoid residual volume (PVR) of < 150 mL, symptomatic and/or significant PVR (150–500 mL) and chronic retention (PVR > 500 mL). Frequency-volume charts and the peak urinary flow rate (Q_{max}) were assessed before and 6 months after TURP.
Results The indications for treatment were symptoms of BOO (31%), significant PVR (48%) and chronic retention (22%). The mean (SD) PVR for all patients before and after TURP were 318 (264) and 39.5 (96) mL, respectively. The three groups did not differ significantly in the weight of resected tissue ($P = 0.4$) or age

($P = 0.1$). There was a comparable and significant improvement in PVR and maximal functional capacity, with no difference among the three groups. The Q_{max} improved equally in all groups ($P = 0.1$); 62% of patients in the BOO and elevated PVR group reported that day-time frequency and nocturia had improved, compared with only half of those with chronic retention. Only 80% of those with chronic retention, but 92% in the BOO and high PVR groups, were satisfied with the outcome of TURP.
Conclusion The indications for TURP have shifted towards patients with high preoperative PVRs. This procedure continues to give good symptomatic relief and is well accepted among patients.

P99

The effect of low-dose aspirin on blood loss and complications after TURP

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Introduction The role of low-dose aspirin in haemorrhagic complications after TURP has been studied in retrospective series, with conflicting results. We report the first prospective study to consider the effect of aspirin on bleeding during TURP.
Patients and methods An observational study was conducted on 242 patients undergoing TURP. Aspirin usage was recorded before TURP and blood loss calculated from the haemoglobin concentration in the irrigant, using a photometric technique. The Detsky score was used to measure cardiac risk. Cardiac stress was detected using serum cardiac troponin I.
Results The 66 patients who were prescribed low-dose aspirin were compared with 176 controls. The aspirin group was significantly older (75.6 vs 70.8 years) and had a significantly higher ASA and Detsky score than controls. The mean (SD) operative blood loss was 358 (416) mL in the aspirin group and 320 (342) mL in the controls (not significant). This remained insignificant when adjusted for operative duration and weight of prostate resected. The mean blood transfusion was 0.98 units in the aspirin group and 0.34 units in controls ($P = 0.003$). The mean perioperative change in haemoglobin (adjusted for units transfused) was 26.2 g/L in the aspirin group and 20.2 g/L in controls ($P = 0.04$). After TURP six (9%) of the aspirin group and five controls (3%) had raised serum cardiac troponin I ($P = 0.04$).
Conclusion Patients taking aspirin have increased transfusion requirements after TURP, probably because of the anti-aggregation effect of aspirin on platelets. These patients have increased cardiac risk factors and an increased risk of cardiac stress after surgery. Further studies should establish whether the cardioprotective effect of aspirin overrides the risks of bleeding before aspirin is withdrawn in patients with cardiac disease undergoing TURP.

P100

A bladder infusion trial of voiding after TURP

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Introduction Patients undergoing TURP are normally hospitalized for at least 5 days. With a view to the potential earlier discharge of patients, we examined the effect of bladder infusion before catheter removal on the patients' readiness for discharge and day of discharge after TURP.
Patients and methods Seventy-five consecutive patients undergoing TURP were randomized to either removal of their catheter in the standard way or to bladder infusion before the trial of voiding on the second day after TURP.
Results In the bladder infusion group, 19% of patients were discharged on the same day as their voiding trial, compared with 13% in the standard group; 68% of patients were discharged by the second day after TURP whether or not the bladder had been filled. In the infusion group, 62% were ready for discharge on the same day as their voiding trial, compared with only 37% in the standard group ($P < 0.05$).
Conclusion Bladder infusion before a trial of voiding after TURP significantly increased the rate of readiness for discharge, allowing an early decision to discharge on the second day after TURP in many patients.

P101

TRUS and biopsy: the use of local anaesthetic in the prophylaxis of pain at biopsy

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Introduction The increasing incidence and public awareness of prostate cancer will inevitably translate into more men undergoing transrectal biopsy and re-biopsy. Although generally well tolerated, some men experience significant pain during and after biopsy. We assessed the use of a periprostatic local anaesthetic injection before biopsy.
Methods Sixty men undergoing TRUS and prostatic biopsy were randomized into those receiving no anaesthetic and those receiving a local anaesthetic injection with 10 mL lignocaine into the neurovascular bundles bilaterally under TRUS guidance before biopsy. Pain scores were measured at the time of biopsy and over the following week. Other features (temperature and bleeding) were also assessed.
Results Pain scores were significantly lower in the group treated with local anaesthetic, but only at the time of biopsy; there was no difference at any other time. There was no difference in the rate of infection or rectal or urethral bleeding.
Conclusions Local anaesthetic injected into the prostate before TRUS-guided biopsy was well received, giving lower pain scores and no significant side-effects.

P102

Experience with mobile Storz SLX lithotripter for treating renal and ureteric stones

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Introduction Between November 1996 and January 1999, 120 patients underwent 171 treatments on a mobile Storz SLX lithotripter; 16 sessions were held, with a mean of 10 patients per session, at a cost of £2500 per session.
Patients and methods Of the 120 patients, 65% were male and 35% female, with an age range of 10–79 years. Fifteen patients had more than one stone, including three staghorn stones. There were 72 renal calyceal, 24 renal pelvic and 39 ureteric stones. Five patients required nephrostomy tubes and seven JJ stents before treatment. The procedure was carried out as a day-case procedure, using rectal diclofenac as a routine analgesic with intravenous pethidine given if required. Dual-image control was used and the procedure took 30–40 min.
Results Twenty-four patients with renal pelvic stones (15–20 mm) had a 90% clearance rate. Upper and middle pole calyceal stones were also cleared well but the rate in the 22 patients with lower pole stones was only 30%; 25 of the 39 ureteric stones were treated successfully but 14 patients needed further intervention. Fewer than 10% of the patients required admission after the treatment. Complications included severe colic, UTI and in one patient pleural effusion.
Conclusion The results of this treatment were mixed and were particularly disappointing for lower calyceal stones. The infrequent visits of the mobile machine led to occasional organizational problems, particularly in the timing of patients with obstructed kidneys.

P103

The efficiency of different coupling media in the transmission of extracorporeal shock waves

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Introduction A new generation of lithotripters for the treatment of urinary calculi have excluded water as a coupling medium between the patient and the energy source. Recent work has suggested that the nature of the inert coupling agent may affect pain control during ESWL. We devised a series of experiments to determine the relative efficiency of different coupling agents in current routine use.
Methods Standard 10 mm diameter ceramic 'phantom' stones were used in all experiments. A 2 mm wire mesh basket was mounted in a jig so that the centre of a 10 mm stone placed in the basket was at the F-point of an electromagnetic lithotripter (Dornier Compact, Dornier MediTech, Germering, Germany). A thin layer of either petroleum jelly (Vaseline®), ultrasonic jelly (Aquagel 100®), EMLA® cream, Instillagel® or water-soluble lubricating jelly (K-Y jelly®) was placed between the lithotripter shockwave delivery head and the latex membrane of the jig. The jig was filled with de-gassed water and shockwaves delivered at 100/min at constant power until all fragments had fallen through the basket. A minimum of eight stones was used for each coupling agent. The viscosity of coupling agents was also compared. Student's *t*-test was used to compare the mean number of shockwaves required to fragment each stone, and a significance level of $P < 0.05$ applied.
Results The mean (SEM) number of shock waves required to fragment phantom stones for differing coupling media were: Vaseline, 796 (68); Aquagel 100, 340 (5.8); EMLA cream, 269 (21); Instillagel, 200 (6.5); and K-Y jelly, 222 (4.7). A thin layer of Vaseline was significantly less efficient at transmitting shock waves than all the other coupling agents investigated. K-Y jelly and Instillagel were the most efficient coupling agents tested ($P < 0.05$), and were also the most fluid.
Conclusion Vaseline is unsuitable as a coupling agent for ESWL, as it absorbs shockwave energy and is $> 200\%$ less efficient at transmitting shock waves than other agents commonly in use. Although Instillagel and K-Y jelly are the most efficient transmitters, they are too fluid for practical use. Standard ultrasonic jelly is the optimal ESWL coupling agent in water-free lithotripsy.

P104

Should a routine nephrostogram be taken after percutaneous nephrolithotomy?

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Introduction After percutaneous nephrolithotomy (PCNL), urologists traditionally clamp the draining nephrostomy tube for 24 h and take a plain X-ray of the kidney, ureters and bladder. The nephrostomy is then removed if the patient is pain-free, apyrexic, there is no leakage around the nephrostomy tube and the plain film is satisfactory. We propose that this system of management does not reveal all cases of obstruction and gives no accurate assessment of the position of residual fragments.
Methods From October 1998, the role of a routine nephrostogram taken after PCNL was assessed prospectively. In addition to routine postoperative management, a nephrostogram was taken just before clamping the nephrostomy. Before clamping the nephrostomy an assessment was made as to whether residual fragments, obstruction and extravasation were expected. After clamping the decision of whether to remove the nephrostomy or not was recorded without previously knowing the nephrostogram result. A final decision was taken after reviewing the nephrostogram.
Results Twenty routine nephrostograms were taken; six showed unexpected residual fragments (one), extravasation (two), obstruction (two) and incorrect placement of the tube (one). Four patients had no pain on clamping when the nephrostogram showed it to be unwise to remove the tube (obstruction and extravasation in two each).
Conclusion The absence of pain on clamping the nephrostomy does not reliably exclude obstruction or significant extravasation. Currently, we take a routine nephrostogram at 48 h after PCNL and remove the nephrostomy on the basis of this investigation. Initial evaluation has shown a reduction in hospital stay and the finding of unexpected obstruction in two patients.

P105

An acute infundibulopelvic angle predicts failure of flexible ureterorenoscopy for lower calyceal stones

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Introduction The objective was to determine if the infundibulopelvic angle (IPA) and other factors had any significance for the stone-free rate after flexible ureterorenoscopy (FURS) for lower calyceal stones.
Methods Thirty patients underwent FURS for lower-pole stones

over a 2-year period at Southmead Hospital. Twenty-seven had the results of IVU available. The stone size, number of fragments, IPA, infundibular width and length were measured.
Results The mean (range) stone size, infundibular width and length were 53 (9–208) mm^2, 5.8 (1–19) mm and 3.1 (2.1–4.4) cm, respectively. The stone-bearing lower calyx was accessible in 20 (74%) of the patients; in the units where the access was good the mean IPA was 53 (33–85)° and 70% of these were rendered stone-free. The overall stone-free rate was 52% (14 patients); seven (26%) showed no change and six (22%) had persisting fragments. Patients with failed access and no change in their stone burden had a mean IPA of 16 (8–25)°. In the renal units with good access, 93% of patients with solitary stones were rendered stone-free vs 17% with multiple stones. The IPA ($P < 0.001$) and the multiplicity of the fragments ($P < 0.003$) were statistically significant in predicting the stone-free rate.
Conclusions Access to the lower pole calyces is poor in patients with an IPA of $< 25°$ and undergoing FURS with currently available equipment. We recommend that the IPA is measured in all the patients with lower calyceal stones before FURS and that alternative modalities of treatment should be considered for patients with an IPA of $< 25°$ and/or multiple fragments.

P106

The natural history and management of urinary calculi in patients with spina bifida

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Introduction In patients with spina bifida the associated spinal deformity, abnormal upper tract anatomy and function can interfere with imaging, making percutaneous access difficult and preventing satisfactory stone clearance. We reviewed the natural history and management of a series of such patients.
Patients and methods The records of patients with spina bifida presenting to a regional stone unit over a 15-year period were examined retrospectively. Five patients were identified.
Results The mean follow-up was 8 years; the commonest presenting complaint was recurrent UTI. Stone recurrence was ipsilateral in all but one instance. The split renal function of the affected kidney was 27–43%. Obstruction, as assessed by isotope renography, was detected in only one renal unit. In all, 31 procedures were carried out, comprising 24 percutaneous nephrolithotomy, four ESWL, one rendezvous procedure, one open nephrolithotomy and one nephrectomy. Three patients accounted for 27 (90%) of these procedures and all three still have residual calculi. During the 24 percutaneous procedures, 31 punctures were made (1–3 per patient). Three supracostal punctures were necessary and two of these resulted in complications (one hydrothorax and one haemorrhage).
Conclusion Stone recurrence in patients with spina bifida is usually ipsilateral despite objective evidence of satisfactory differential function and the absence of obstruction. Multiple procedures may be required, making a minimally invasive percutaneous approach desirable. Despite the associated spinal deformity, percutaneous access is usually possible, although a supracostal puncture should be avoided.

P107

Protocol-guided investigation of new and recurrent stone formers

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Introduction Stone formers are frequently under-investigated once their acute problem has been dealt with, particularly as the more specialized tests require collaboration with biochemistry departments. The identification of stone-forming tendencies can lead to prophylaxis to reduce future stone formation.
Methods A protocol for investigating new and recurrent stone formers was jointly developed between the Biochemistry arid Urology departments. The protocol is available as a small reference poster throughout the Urology department. All new stone formers have a urine sample dip-stick tested and cultured, and a full blood count, blood sodium, potassium, chloride, urea, creatinine, calcium, bicarbonate, urate, alkaline phosphatase and phosphate are evaluated. Recurrent stone formers also have two 24-h urine collections and spot urine samples analysed, providing the 24-h volume, calcium, cystine, oxalate, urate and pH values. Stones are sent for analysis where recovered. The biochemistry department undertake more complex tests, e.g. ammonium chloride loading, where required. Patient advice sheets and prophylactic treatment protocols have been produced for all the common conditions.
Results One hundred patients have been investigated so far and preliminary analysis suggests that 40% have a stone-forming tendency revealed by these simple tests, including hyperparathyroidism, hypercalcaemia, hypercalciuria, hyperoxaluria and particularly hyperuricosuria.
Conclusions It is worthwhile investigating stone formers, as a high proportion will have pathology where treatment and diet can prevent future stone formation. Collaboration between departments is productive and protocols aid consistency in diagnosis.

P108

Managing renal colic in the community

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Introduction Renal colic is the severe symptom heralding the presence of a ureteric stone. The diagnosis can only be confirmed by radiological investigations, with IVU being the gold standard. IVU confirms or refutes the diagnosis and provides information on stone site, size, number and degree of renal obstruction, all factors critical to the urologist in deciding subsequent management of the patient and his/her stone. Patients with renal colic in the community are not managed in a standardized way; some are managed at home, some referred electively and some as emergencies to hospital. Perhaps all patients with renal colic should be referred or even admitted for an urgent IVU. To investigate this hypothesis further, all patients admitted to our unit with suspected renal colic were assessed.
Methods All patients admitted to the urology unit with a suspected diagnosis of renal colic over an 18-month period were recruited to a prospective study. The outcome of the radiological assessment and the effect that this had on subsequent management was determined.
Results The study included 156 patients (115 male and 41 female, mean age 45 years, range 20–82) who were admitted with suspected renal colic over this period; 127 (81%) underwent IVU on admission and the remaining 29 underwent plain X-ray with or without ultrasonography of the renal tract, or none of the above. Eighty-six patients (55%) were diagnosed as having ureteric calculi as a result of their initial investigation; 17 of these with evidence of renal obstruction required intervention either by ureteric stent or nephrostomy insertion to preserve renal function. Three patients were referred directly for lithotripsy. Amongst the 70 patients where no stone was detected on IVU, there were 10 with evidence of other pathology including a bladder tumour, ureteric and renal tumour and evidence of recent stone passage.
Conclusion Of patients referred as an emergency with renal colic, 55% had evidence of a ureteric stone; 20% of these patients required emergency surgical intervention to preserve renal function and the decision to intervene was made on the basis of the findings on IVU. Because the management of patients with ureteric colic depends on

stone site, size, number and degree of renal obstruction, all factors determined by IVU, we believe that all patients with renal colic deserve access to urgent IVU even if this means having the patients admitted as an emergency.

P109

Influence of oral citrate and alkali supplementation on urinary citrate excretion and net gastrointestinal alkali absorption

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Introduction Hypocitraturia is an important inhibitor of stone formation. The influence of acid-base balance on renal excretion of citrate has been well established [*Mineral Elec Metab* 1994; 20: 371–7]. Sakahee *et al.* [*J Bone Min Res* 1993; 8: 789–94] reported a significant positive correlation between citrate excretion and net alkali absorption (NAA) in normal subjects on a random diet. Our earlier data suggested no such correlation in both stone formers (38 men and 23 women, $r = 0.194$, $P = 0.134$) and controls (19 men and three women, $r = 0.209$, $P = 0.33$).

Patients and methods Urinary citrate, creatinine and NAA were determined by measuring urinary electrolytes and calculating net gastrointestinal alkali absorption as [(urinary Na + K + Ca + Mg) − (urinary Cl + 1.8 P)]. All electrolytes excretion values are in mmol/L per day. Each patient had a baseline estimate followed by 60 mmol/L/day of either oral potassium citrate or $NaHCO_3$ for 4 days, followed by another estimate. A second baseline urine sample was collected after 2 weeks before the alternative drug. The mean urinary citrate and NAA levels before and after each drug intervention were calculated. Differences were assessed using Student's *t*-test. A group of 26 patients with stones were assessed (18 males and eight females).

Results The results of supplementation with oral citrate or bicarbonate were:

	Mean (SD) level		
Treatment	*Before*	*After*	*P*
Citrate			
Urinary citrate (mg/24 h)	293.2 (159.5)	433.4 (225.2)	0.008
NAA	19.2 (152)	51.0 (531.9)	< 0.001
$NaHCO_3$			
Urinary citrate (mg/24 h)	308.9 (165.5)	355.9 (162.1)	0.258
NAA	28.7 (19.7)	63.2 (29.5)	< 0.001

Conclusion These results show that there is a significant increase in NAA after both oral potassium citrate and $NaHCO_3$ supplementation. The rise in urinary citrate was not significant after an alkali load, further supporting the view that net alkali absorption is not a major determinant of urinary citrate.

P110

Could recurrent oxalate stone disease be timed? The role of *Oxalobacter formigenes*

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Introduction In India, 80% of urinary stones are calcium oxalate and 85% of these recur within 9 years of complete clearance. Although newer modalities to treat urinary stones have greatly simplified complete clearance methods to prevent recurrence are still awaited. *Oxalobacter* (e.g. *O. formigenes*) is an oxalate-degrading anaerobe recently isolated from the gastrointestinal tracts of vertebrates, including humans. This bacterium is known to have a symbiotic relationship with its host by regulating oxalic acid absorption in the intestine, and oxalate levels in plasma and urine. Preliminary studies in calcium oxalate stone formers showed complete absence of this bacterium in the faecal samples of half of stone formers and 80% of recurrent stone formers, as tested by a specific and sensitive PCR-based tst for detecting *O. formigenes*.

Patients and methods Sixty-one patients calcium oxalate stone disease confirmed by X-ray diffraction and who were treated by several methods during 1989–1993 were followed. Besides reviewing hospital records, all possible stone recurrences were recorded. Fresh stool samples were inoculated into special culture vials and *O. formigenes* detected using a PCR-based assay. Whole DNA was isolated and used as template in PCR with 5' and 3' primers specific for the *oxc* gene of *O. formigenes*. Southern blot analysis and hybridization confirmed PCR amplification products with *Oxalobacter* genus-specific internal probes. Urine samples (24 h) were collected in special jars and preserved at −20°C after adjusting the pH to acidic levels; subsequently, oxalate levels were measured using an enzymatic method. Twenty-two age- and sex-matched controls were also assessed using the same protocol.

Results Of 61 patients, 28 (46%) had one, 26 (43%) had two and seven (11%) had three or more recurrent stone episodes. The PCR results were negative (confirming that there were no bacteria) in eight of the 28 patients with one, in 14 of the 26 with two and in six of the seven with three or more episodes of recurrence. There was a statistically significant direct correlation between the number of stone episodes and absence of *O. formigenes* from the intestine. Nine of the 22 controls were also PCR-negative. Of the 61 oxalate stone formers, 31 had hyperoxaluria (> 0.5 mmol/24 h); of these 31, those with no detectable *O. formigenes* had higher urinary oxalate levels than those patients with the bacterium.

Conclusion This study indicates that the absence of *O. formigenes* may predispose an individual to a higher risk of hyperoxaluria, leading to higher stone recurrence rates. The detection of *O. formigenes* has the potential to identify patients who are at high risk of abnormal oxalate metabolism and hyperabsorption from the diet resulting from a diminished bacterial population. Why 40% of the controls had no detectable bacteria needs further investigation.

P111

'Haematuria or not haematuria?' is not the question in the diagnosis of renal colic

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Introduction Haematuria has previously been reported to have a sensitivity of 84–100% in diagnosing urolithiasis, as measured by IVU in the presence of characteristic flank pain. We have revisited this subject since adopting CT in the investigation of acute flank pain to determine whether we could reduce the number of negative investigations.

Methods During a 12-month period, 173 patients with acute loin pain underwent unenhanced helical CT. Dipstick urine analysis data were obtained in 133 patients. The diagnoses were determined by the initial CT scan, additional imaging, medical records and patient interview.

Results Of the 173 patients, 95 (55%) had stones and 78 (45%) did not; in 6% of patients a significant alternative diagnosis was made. Of patients with stones and documented information on dipstick haematuria, 89% had a positive urine dipstick test, and of patients with no stones, 68% had a positive dipstick test. Haematuria testing

had an 89% sensitivity and 32% specificity for detecting upper tract stones.

Conclusion Of patients with urinary tract stones, 11% were dipstick-negative for haematuria. Evidence of haematuria should not preclude diagnostic imaging for suspected renal colic. Likewise, 68% of patients with no stones were dipstick-positive, emphasizing the importance of good clinical skills to avoid a misdiagnosis.

P112

Advanced transurethral thermotherapy for symptomatic BPH: 5-year follow-up data

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Objectives To evaluate the long-term results of treatment with focused high-energy Urologix T3 microwave thermotherapy in symptomatic BPH.
Patients and methods Fifty men with symptomatic BPH were selected by a predetermined protocol and treated as outpatients with the Urologix T3. The men were assessed before treatment, at 3 and 6 months, and annually thereafter for 5 years. Video pressure-flow analyses were conducted before and 3 months after treatment. Patients were graded as obstructed, equivocally obstructed or unobstructed using a simplified adaptation of the linear PURR Shafer's pressure-flow equation. A successful outcome was defined as a reduction in the AUA score by $> 50\%$, accompanied by an increase in the corrected peak flow rate of > 3 mL/s. If patients failed to meet these criteria the treatment was deemed to have failed. Patients with an unsuccessful outcome were recommended an alternative treatment option and were excluded.
Results

Year	*N*	*Successful*	*Failed*	*Unavailable for assessment*
1	50	44	1	5
2	44	21	20	3
3	21	15	5	1
4	15	6	9	1
5	6	4	1	(not yet assessed)

The 15 successful patients at 3 years had a mean prostatic volume of 32.9 mL, compared with 43.5 mL for the 28 in whom the treatment had failed ($P < 0.05$). Most of the successful patients at 3 and 5 years had equivocal obstruction, whereas the treatment had failed in most obstructed patients by 3 years.
Conclusion Urodynamic analysis and prostate size can be used to predict the long-term treatment outcome of high-energy microwave thermotherapy (T3). There is evidence of the diminishing efficacy of T3 over time, but a beneficial effect is more likely to be maintained in patients with equivocal obstruction.

P113

Thick vs thin loop resection of the prostate: a randomized blinded trial

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Introduction Resection of the prostate using a modified thick loop may combine the reduced blood loss of vaporization with the benefit of resection. In a prospective blinded study we compared blood loss, irrigation requirements and hospital stay for patients undergoing thick-loop resection and standard TURP.
Patients and methods Patients were randomly assigned to TURP with a standard resection loop (thin) at 120 W or resection with a Storz roller-cutting electrode (thick) with cutting at 220 W. Haemoglobin and serum sodium were measured at 30 min and 24 h after completing TURP. The postoperative management was by the registrar and nursing staff who were unaware of the resection technique used.
Results Sixty-four patients were randomized to the trial (35 thin and 29 thick loop resection). There was no significant difference in peri-operative variables between the groups, including the number of patients with catheters or taking aspirin. After surgery there was no difference between the groups for the decrease in haemoglobin, decrease in serum sodium, glycine used, or postoperative irrigation. There was a greater tendency for patients in the thick-loop arm to be re-catheterized (11 vs five, Fisher's exact test, $P = 0.43$), but this did not affect the total duration of catheterization or hospital stay.
Conclusion There appeared to be no advantage from altering the resection loop to incorporate vaporization; in particular, there was no evidence of decreased bleeding when using thick-loop resection.

P114

Holmium laser resection of the prostate vs TURP: results of a randomized trial with a 2-year follow-up

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Introduction The holmium laser has been used since 1994 to incise, ablate, resect and recently enucleate the adenomatous prostate. The results of a randomized trial with a 2-year follow-up comparing holmium laser resection of the prostate (HoLRP) and TURP are presented.
Methods Of 120 urodynamically obstructed men randomized to TURP or HoLRP, 90 were available for review at 2 years. Patients were assessed at 1, 3, 6, 12, 18 and 24 months after treatment, and underwent TRUS and urodynamics before and 6 months after treatment. At all other assessments the patient had their peak urinary flow rate (Q_{max}) and AUA symptom score measured, continence and potency assessed and adverse events reviewed.
Results At 2 years the mean Q_{max} was 25.1 mL/s in the HoLRP group (45 men) and 20.0 mL/s in the TURP group (45 men; not significant). The mean AUA symptom score was 3.4 in the HoLRP group and 3.7 in the TURP group (not significant). There were six strictures after TURP, six after HoLRP, seven re-operations after TURP and five after HoLRP, and one patient in each group required pads for ongoing stress incontinence.
Conclusions HoLRP and TURP are equivalent at 2 years, with fewer adverse events in the HoLRP arm to date.

P115

Holmium laser enucleation of the prostate with tissue morcellation

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Introduction: Holmium laser enucleation of the prostate (HoLEP) combined with tissue morcellation efficiently removes large volumes of prostatic tissue in patients with BOO caused by BPH. The advantages of laser surgery with reduced blood loss and low morbidity are important, especially in this group of elderly men. The objective results are better than TURP and it is more cost effective.
Methods We have analysed the results from 110 patients treated with the holmium laser (Versapulse, Coherent 80 W) to enucleate prostatic tissue and compared these with a similar TURP group. The prostate was anatomically enucleated using a bare fibre down a specially adapted resectoscope. The enucleated lobes were removed from the bladder using a tissue morcellator with reciprocating blades. The AUA score and peak flow rate (Q_{max}) were assessed before and after treatment. The prostate volume and morcellation

weight, and the duration of surgery, catheterization and hospital stay were recorded.
Results Initially, only smaller prostates were treated with HoLEP (mean 36.8 mL, first 20 patients) but the mean (range) resection weight of this group with morcellation of the larger glands was 24.6 (2–130) g. Vaporization of the tissue by the laser results in a 50% reduction in weight removed compared to TURP. The efficiency of tissue removal improved, particularly with morcellation, giving a mean operative duration of 36 min for the first 50 patients, decreasing to a mean of 28 min subsequently. The mean overall duration of catheterization for this group was 36 h, with 91% of patients being discharged catheter-free the day after surgery. No patients required a blood transfusion and there were no serious adverse events. The objective variables compared favourably with TURP, with a reduction in the AUA score by 62% at 6 months (61% for the TURP group) and a mean Q_{max} of 23.3 mL/s (22.7 for TURP).
Conclusions These results show that the outcome can be good for patients treated with HoLEP for large prostates, using a technique which is the endourological equivalent of open prostatectomy. The improved results are testimony to this and urologists should have no problems in mastering this technique. Patients return to normal activity more rapidly and the cost benefits with reduced hospital stay and nursing time easily outweigh the cost of using the holmium laser.

P116

A prospective randomized controlled trial of TURP vs retropubic prostatectomy for medium-sized prostates

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Introduction Retropubic prostatectomy (RPP) and TURP are recognised treatments for BPH. High complication rates have been reported for both procedures in large prostates. Most urologists would use TURP for prostates of < 80 mL and RPP for prostates of > 120 mL. We explored the use of these techniques in the intervening overlapping 'grey' area.
Methods In a randomized controlled trial of 36 patients, the PSA level, flow rate, postvoid residual volume (PVR), IPSS, and prostate volume (estimated by TRUS) were measured. Patients were randomized to RPP or TURP; after surgery the mean blood loss was calculated, the resected prostatic weight measured and the resected weight to TRUS volume ratio derived. Patients were followed up with the IPSS, TRUS volume, flow rates and PVR at 3 and 6 months.
Results The mean TRUS volume at TURP was 99.6 mL and at RPP was 106 mL. The resected weight to TRUS ratio was consistently higher in the RPP group; patients in this group also lost more blood. The TURP group were catheterized for a mean of 3 days and the RPP group for 5 days. Half the patients in the TURP group were re-catheterized but no RPP patients were re-catheterized. All patients had good flow rates and a reduction in their symptoms at the 3- and 6-month follow-up.
Conclusion In the short-term, the outcome from TURP was as satisfactory as that from RPP. Blood loss could be significant in both groups. Patients undergoing TURP were re-catheterized more often and thus had a longer mean duration of catheterization. A long-term follow-up may show differences in re-operation rate and haematuria caused by the less complete removal of tissue during TURP.

P117

Effect of split-beam high-intensity focused ultrasound on the canine prostate: an acute study

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Introduction The aim of this study was to define the accuracy and safety of transrectal split-beam high-intensity focused ultrasound (HIFU) therapy to ablate a pre-defined zone of canine prostatic tissue.
Materials and methods The Sonablate-200™ (Focus Surgery Inc.) ultrasound transducer was modified to produce simultaneously within the focal zone a single central main beam surrounded by four ultrasound beams. The object was to ablate prostatic tissue locally more effectively and more quickly than with the earlier single-beam method. The rectal wall temperature was maintained at 22–24°C throughout by an automated cooling system. Five dogs were treated with transrectal HIFU, the energy being delivered to a predetermined peri-urethral therapy zone extending from the bladder neck to the apex in the anterior part of the prostate. The total acoustic power delivered was 34-36 W; this is $\approx 25\%$ greater than that normally used to ablate BPE in humans. The temperature at various sites within the prostate and rectal wall were continuously monitored using 50 μm thermocouples. Dogs were killed after therapy and the bladder, prostate, proximal urethra and adjacent rectum extirpated en bloc for macroscopic and full organ mount histological studies.
Results During therapy there was no significant rise in rectal wall temperature and no concomitant significant rise in the temperature of surrounding prostate tissue. In the focal zone the temperature increased to 80–90°C. The overall improvement in treatment efficiency was 35%. Cut sections of the prostate showed well-defined areas of tissue damage with a normal surrounding prostate and rectal wall.
Conclusions Split-beam HIFU therapy is accurate, reduces the treatment time and is safe for the surrounding normal tissue.

P118

Interstitial laser ablation (Indigo™) of the prostate: a randomized prospective study with a 2-year follow-up

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Introduction A prospective study was conducted to evaluate the efficacy and safety of interstitial laser therapy (diode laser, 830 nm) to produce coagulation necrosis of prostatic adenoma of < 60 g against standard TURP.
Methods From January 1997 to June 1999, 100 patients with BPH entered the study (mean age 68.2 years, range 52–84). Their mean (range) prostatic weight was 35.5 (17–60) g and they were randomized 2 : 1, such that 65 patients were treated by interstitial laser coagulation (ILC) using the Indigo™ 830 laser optic system and 35 underwent standard TURP using a continuous-irrigation resectoscope. The variables assessed were the IPSS (and QoL question), urinary flow rate, postvoid residual volume (PVR) and TRUS findings.
Results The results during follow-up were:

Mean (SD) variable	*Before*	*6 weeks*	*1 years*	*2 years*
ILC (65)				
IPSS	21.0 (7)	11.0 (5)	6.4 (3)	7.4 (3)*
QoL	4.2 (1)	2.8 (1)	1.7 (1)	1.6 (1)*
Q_{max} (mL/s)	8.5 (3)	16.6 (4)	18.4 (4)	22.0 (3)*
TURP (35)				
IPSS	21.0 (5)	8.6 (4)	6.0 (3)	7.7 (3)*
QoL	4.5 (1)	1.7 (1)	1.6 (1)	1.3 (1)*
Q_{max} (mL/s)	8.8 (3)	20.6 (5)	20.4 (4)	19.3 (4)*

*$P < 0.001$

Retrograde ejaculation was recorded in 45% of patients after ILC, compared with 68% after TURP. No blood transfusion was needed during ILC, compared with 9% during TURP. In 11% of patients irritative symptoms occurred after ILC and lasted 6 weeks. Of the ILC group, 3% later required TURP. The mean hospital stay was 1.5 days after ILC and 3.5 days after TURP.
Conclusions At the 2-year follow-up both ILC and TURP produced equal improvements in IPSS, QoL, flow rate and PVR. ILC caused irritative symptoms in 11% and failed in 3% of patients; TURP required a longer hospital stay but did not fail.

P119

Transurethral electrovaporization of the prostate: has it run out of steam by 2 years?

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Introduction Transurethral electrovaporization of the prostate (TUVP) has been shown to be effective for the treatment of symptomatic BPE. However, there have been few published multicentre studies and little information on the outcome beyond 1 year. We report the results of the largest multicentre randomized controlled trial of TUVP and TURP performed in the UK.
Patients and methods Between March 1996 and August 1999, 239 patients were randomized to TUVP (115) or TURP (123). Patients were assessed by the IPSS, uroflowmetry, residual urine measurement, TRUS and pressure-flow urodynamics, according to the study protocol. The IPSS and overall patient satisfaction were assessed at 2 years.
Results There was no significant difference between the groups at baseline. The mean inpatient stay was 4.4 days for TUVP and 4.7 days for TURP. The mean values for IPSS, Q_{max} and residual urine volume at 6 months were 8.4, 20.0 mL/s and 66 mL for TUVP, and 6.6, 22.6 mL/s and 70 mL for TURP. At 2 years, the mean IPSS was 8.0 and 7.7 in the TUVP and TURP groups, respectively. The number of patients requiring further surgery was two after TUVP and five after TURP.
Conclusion TUVP is an effective treatment for symptomatic BPE. The results at 2 years are equivalent to TURP.

P120

A prospective randomized study between transurethral vaporization using Plasmakinetic™ energy and TURP

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Introduction A prospective study was conducted to evaluate the efficacy and safety of the Plasmakinetic™ energy system (Gyrus Electrosurgical) which vaporizes tissue immersed in isotonic saline, against standard TURP.
Methods Randomization to the study began in October 1998 with a ratio of 2:1 for Plasmakinetic to TURP; 45 patients (20 with retention of urine) have so far been enrolled (mean age 69.2 years, SD 8, range 55–82; mean prostatic weight 47.9 g, SD 22, range 27–105). No postoperative irrigation was used and the catheter was removed at 36 h. The patients were assessed before and at 6 weeks and 6 months after treatment using the IPSS, QoL score and maximum urinary flow rate (Q_{max}).
Results

Mean (SD) variable	*Before*	*6 weeks*	*6 months*
Plasmakinetic (30 patients)			
IPSS	18.3 (3)	7.5 (6)	5.7 (7)
QoL	4.3 (1)	2.1 (2)	1.7 (2)
Q_{max} (mL/s)	7.7 (2)	20.6 (6)	23.9 (6)
TURP (15 patients)			
IPSS	18.2 (7)	6.4 (4)	4.5 (3)
QoL	4.2 (1)	1.0 (1)	0.5 (1)
Q_{max} (mL/s)	10.4 (3)	21.3 (12)	26.2 (15)

There were no significant differences in creatinine and sodium levels before and after surgery. The mean (range) blood loss in the Plasmakinetic group was 194 (49–660) mL and in the TURP group was 504 (50–1750) mL ($P < 0.001$). Fluid absorption in the TURP group was $\leqslant$ 500 mL. One patient in the Plasmakinetic group was catheterized for 5 days and three patient had mild stress incontinence lasting 3 months. No complications were recorded in the TURP group. The hospital stay was similar in both groups (mean 3.1 days).
Conclusions The Plasmakinetic method caused less intraoperative bleeding and no risk of TUR syndrome because it uses saline irrigant. This technique is simple to learn and offers safety with no increased morbidity

P121

The 2-year results of a prospective trial of interstitial radiofrequency therapy in the management of acute urinary retention

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Introduction The clinical benefits of all new therapies must stand the test of time. We previously described a method for delivering interstitial radiofrequency therapy (IRFT) with a simple needle electrode for patients after acute urinary retention (AUR) [*Br J Urol* 1998; 81: 726–9]. We now report the 2-year results of this prospective trial.
Patients and methods Twenty-six patients were evaluated in a trial of IRFT after AUR. All had previously failed a trial of voiding one week after initial catheterization. Six failed a trial of voiding after IRFT and subsequently underwent TURP; 20 patients were reassessed at 6, 12 and 24 months with the IPSS, quality-of-life score (QoL), maximum urinary flow rate (Q_{max}), postvoid residual volume (PVR) and serum creatinine level.
Results The values of the variables are shown in the table; one patient was lost to follow-up before the review at 3 months and another died from an unrelated cause before review at 24 months.

Variable	*Before treatment*	*6 months*	*24 months*
Patients	20	19	18
IPSS*	16	9	10
QoL*	2	1	1
Q_{max}†	-	10.5	9.2
PVR†	950	136	147
Creatinine†	99.7	102.6	103

* median, †mean

Conclusions For those who received initial benefit from IRFT (20 of 26, 77%) the symptomatic and physiological benefits seen at 6 months were maintained at 2 years in the treatment of AUR.

Prostate Cancer II (Paper session)

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Radical radiotherapy for early prostate cancer: a study of the incidence of gut complications

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Introduction The morbidity of treating localised prostate cancer is particularly important in the older patient, in whom radical radiotherapy is often chosen. We assessed the frequency and impact of gut complications in our patients undergoing radiotherapy.
Patients and methods Over a 7-year period, 111 men (aged 54–82 years) with early prostate cancer were given conventional radical radiotherapy. All patients were sent a questionnaire about their bowel symptoms before and at intervals after radiotherapy; 82 men responded, 20 had died and nine failed to respond.
Results A bowel-related symptom score showed a substantial deterioration after radiotherapy that persisted until the fifth year; 78% of patients reported loose or frequent stools, 77% ascribed bother to their symptoms and 43% reported rectal bleeding. As a result of these symptoms, 34% of patients were investigated using lower gastrointestinal endoscopy (primarily for rectal bleeding) and 40% were prescribed medication.
Conclusion The higher incidence of lower gastrointestinal side-effects, particularly proctitis and rectal bleeding, in our study compared with previous reports may reflect under-reporting of this problem. These side-effects have an impact on quality of life, require resources for lower gastrointestinal endoscopy and increase health care costs.

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Salvage radiotherapy for biochemical relapse after radical retropubic prostatectomy for prostate cancer

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Introduction The efficacy of salvage radiotherapy (SRT) for local recurrence after radical retropubic prostatectomy (RRP) is controversial. There is limited information on the success of SRT initiated for biochemical failure diagnosed using a 'supersensitive' PSA assay.
Patients and methods Between 1992 and 1999, 219 consecutive patients underwent RRP. Patients with biochemical relapse were offered SRT. After the introduction of a supersensitive PSA assay the policy was to offer SRT to patients with three consecutive increases in PSA level above the nadir. Radiotherapy was delivered to the tumour bed using a three-field 10 MV photon isocentrically planned technique with a mean target volume of 540 cm^3. The doses delivered ranged from 60 to 64 Gy in 30–32 fractions, respectively.
Results Fifty patients (mean age 60 years, range 45–73) underwent SRT. In this cohort the median (range) preoperative PSA level was 13.1 (4–59) ng/mL, the specimen Gleason score was $\geqslant 7$ in 44%, extracapsular spread was present in 67%, seminal vesical invasion in 34% and the surgical margins were positive in 76%. Only 12% of patients had a postoperative PSA nadir of < 0.01 ng/mL. The median (range) postoperative nadir was 0.21 (0.01–6.8) ng/mL. All patients had an initial reduction in their PSA level after radiotherapy and the PSA level declined by $\geqslant 50\%$ in 82% of patients. The median (range) PSA level was 0.28 (0.02–2.8) ng/mL at 3 months and 0.43 (0.01–7.2) ng/mL at 6 months after radiotherapy. Grade 1–2 dysuria was observed in seven patients during irradiation. The treatment was generally well tolerated.
Conclusion Most patients had a PSA response of $> 50\%$ after salvage radiotherapy. Patients treated early reached a lower nadir after SRT. The supersensitive PSA assay allows an early assessment of the durability of this response.

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A pretreatment predictive model for PSA control after neoadjuvant androgen deprivation and radical radiotherapy for clinically localized prostate cancer

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Introduction Phase III studies have shown the clinical benefit of combining short-course neoadjuvant androgen deprivation (NAD) with radical radiotherapy (RT) for clinically localized prostate cancer. We have developed a nomogram to predict the likelihood of PSA control.
Patients and methods The study included 527 men with histologically confirmed cancer of the prostate who were treated with 3–6 months of NAD (LHRH antagonist and 3 weeks of CPA) and radical prostate radiotherapy (64 Gy in 6.5 weeks) between 1989 and 1997. The median PSA level at presentation was 20 ng/mL and 56% of patients had T3/T4 disease. Pretreatment factors were assessed using univariate/multivariate (MV) analyses and a nomogram constructed to predict the probability of PSA failure-free survival.
Results After a median follow-up of 35 months, 224 men had developed PSA failure. Clinical T stage, presenting PSA level and histological grade were all highly predictive of PSA failure on MV analysis. The nomogram gave the maximum coefficient (PSA > 50 ng/mL) the value of 100. The score for an individual patient is given by the summation of T stage (T1/2 = 0, T3,4 = 29), PSA level ($< 10 = 0$, 10–19 = 12, 20–49 = 37, $> 50 = 100$) and histology (Gleason 2–4 = 0, 5–7 = 42, 8–10 = 79) values.

Patient score	*2/5 year PSA failure-free survival (%)*
0	9/74
50	83/55
100	69/31
150	50/11
200	20/6

Conclusion These results are at least equivalent to those reported using surgery or higher doses of radiotherapy alone. Simple graphical display of the nomogram can inform both clinician and patient of the likely outcome of treatment.

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Improvement in urinary symptoms after radical retropubic prostatectomy: a prospective evaluation of flow rates and IPSS

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Introduction Of men with prostate cancer undergoing radical retropubic prostatectomy (RRP), 44% have moderate or severe urinary symptoms. This study followed patients by assessing urinary

flow rates (Q_{max}) and urinary symptoms (with the IPSS) before and after RRP.
Patients and methods Between 1994 and 1998 one surgeon performed 125 RRPs (median age of the patients 63 years). Urinary flow rates, the IPSS and strictures or bladder neck stenoses were recorded before RRP and at each follow-up visit.
Results Before RRP 38% of men had a flow rate of < 10 mL/s, suggesting obstruction. At the first review (median 2 months) there was an increase in Q_{max} (median 16.8 vs 11.6 mL/s, $P < 0.001$). At 6, 14 and 20 months, the Q_{max} improved further to 20, 21 and 24 mL/s, respectively. Before RRP, 44% of men had an IPSS of > 10; at 2, 6, 14 and 20 months the percentage of men with an IPSS of > 10 decreased to 18%, 11%, 11% and 15%, respectively ($P < 0.001$). Stricture or stenosis developed in 20% of the men; initially, these men had a decrease in Q_{max} and a higher IPSS. Their symptoms improved with treatment of the stricture.
Conclusions Two-fifths of men with prostate cancer undergoing RRP have BOO and bothersome symptoms. This study shows that there is a highly significant increase in flow and decrease in symptoms after surgery. RRP offers improvement in voiding function and urinary symptoms, and the possibility of a cure for cancer.

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The outcome of extraprostatic (pT3) adenocarcinoma of the prostate treated by radical retropubic prostatectomy

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Introduction An increasing PSA level after radical retropubic prostatectomy (RRP) is more likely with extraprostatic (pT3) prostate cancer. Probability nomograms based on preoperative PSA level and biopsy Gleason score ('Partin's Tables') can be used to reduce the number of patients with pT3 disease selected for RRP. We propose that many patients with pT3 disease treated with RRP actually have a good outcome and this study aimed to show this using clinical and biochemical follow-up data.
Patients and methods Two hundred consecutive patients treated with RRP were reviewed; 82 (41%) had pT3 disease despite being considered clinically organ-confined (mean age 61.3 years). The median Gleason score was 7 (range 3–9) and 63% had a Gleason score of > 7. The median (range) preoperative serum PSA level was 13 (1.5–59) ng/mL and the median follow-up was 1.4 years (maximum 5.8).
Results Fifty-five patients were followed using a supersensitive PSA assay and 20 (36%) achieved an undetectable nadir (PSA < 0.01 ng/mL). Two patients have died, one from metastatic prostate cancer. The overall survival at 3 years was 98.6% (95% CI 95.8–100). The biochemical disease-free survival at 3 years was 31.8% (95% CI 18–46). Compared with the 118 patients with pT1/2 disease, patients with pT3 disease were less likely to achieve an undetectable PSA nadir ($P < 0.001$) and had a shorter biochemical disease-free survival (log-rank $P < 0.001$).
Conclusion Despite the worse outcome after RRP in patients with pT3 disease, a third remain free of biochemical relapse at 3 years and salvage radiotherapy at biochemical relapse has been successful for many other patients. RRP offers potential therapeutic benefit for many patients with pT3 disease.

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Intraoperative isovolaemic haemodilution for radical retropubic prostatectomy to avoid donor transfusion: a practical solution

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Introduction We investigated prospectively the impact of intraoperative haemodilution on homologous blood transfusion rate during radical prostatectomy.
Patients and methods One hundred and five patients (mean age 59.2 years, range 48–69) underwent radical retropubic prostatectomy carried out by one surgeon using combined general and epidural anaesthesia; 98 patients (93%) underwent haemodilution. The first three patients were not offered haemodilution and four (3.8%) were considered unsuitable. Two units of blood (0.9–1.0 L) were taken if the patient weighed ≈ 70 kg and three units (1.3–1.5 L) if 90 kg, the volume being replaced with starch solution (Haestrell) to maintain baseline central venous and arterial pressure. The haemoglobin level was monitored and blood was re-infused towards the end of surgery when haemostasis was complete. Postoperative transfusion was considered if the haemoglobin level was < 80 g/L.
Results The mean (range) estimated intraoperative blood loss was 1.49 (0.4–4.6) L and the mean operative duration 3.3 (2.2–5.6) h. Homologous transfusion was required in 12 patients (12%) with a mean of 2.8 (1–6) units. One patient developed impaired renal function on the first day after surgery which returned to normal by the fourth day. The mean haemoglobin concentration and haematocrit values were:

	Mean (range)	
Sample time	*haemoglobin (g/L)*	*haematocrit*
Before surgery	143 (129–170)	0.425 (0.380–0.490)
After 1 day	976 (63–135)	0.277 (0.190–0.406)
After 3 months	139 (103–165)	0.417 (0.320–0.480)

Conclusion In this series, the homologous transfusion rate was 12% with no significant morbidity, using an aggressive haemodilution protocol, a procedure which is safe, simple and effective.

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Learning curve and change in patient selection of a UK radical prostatectomy series

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Objectives To assess the effect of training, experience and the selection of patients on the complication rate and outcome after anatomical radical retropubic prostatectomy (RRP).
Methods From 1987 to 1999, 259 patients underwent RRP for localized prostate cancer. The mean (range) age of the 217 patients with complete records was 63.7 (47–76) years and the mean follow-up 5.2 (0.5–12.2) years. Records of operative variables and complications were kept throughout the series and procedures carried out before 1995 were compared with procedures from 1996 onwards.
Results Comparison of the two groups showed a significant decrease in operative duration (mean 153 vs 130 min), blood loss (mean 1.549 vs 1.29 L), transfusion rate (mean 2.6 vs 1.2 units) and hospital stay (mean 7.8 vs 6.1 days). The mean preoperative PSA level changed only marginally, from 16 to 13 ng/mL. Only 16% of later patients were diagnosed by a DRE, compared with 29% in the early years. The proportion of clinical T1 tumours increased from 32% to 50%. This did not lead to a reduction in organ-confined tumours on pathological staging. However, the incidence of a postoperative PSA nadir of 0.2 ng/mL increased significantly (70% vs 85%). The thrombo-embolic complications, bladder neck stenosis rate and incontinence rates also decreased significantly.
Conclusion This single-centre study showed that the effect of experience and training is unavoidable when surgery is as radical as possible to keep the positive margin rate low. Tighter selection

criteria translate into a higher rate of undetectable PSA after surgery.

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Radical prostatectomy – current practice in Britain and Ireland

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Introduction Despite an undoubted increase in recent years it is still unclear who is performing radical prostatectomy in Britain and Ireland. We have therefore conducted a survey to provide a 'snapshot' of attitudes, current practice and referral patterns for radical prostatectomy at the millennium.
Methods A simple questionnaire was sent to BAUS members in Britain and Ireland and compared with a similar survey conducted in 1995.
Results Of 487 questionnaires, 342 (70%) were returned; 333 returns were from practising urologists, of whom 146 (44%) do and 187 (56%) do not perform radical prostatectomy. Of the 141 using radical prostatectomy only 29 (20%) carry out > 20 per year, whilst 73 (53%) carry out $\leqslant 10$. Only seven (5%) surgeons use both the retropubic and perineal approaches, five (3%) the perineal alone, and the vast majority (134, 92%) exclusively use the retropubic route. Of 187 urologists not performing radical prostatectomy, 97 (52%) refer to others within their department, 72 (38%) refer to regional centres, nine (5%) refer to both, and nine (5%) do not believe that radical prostatectomy should be used. A geographical analysis has been completed, highlighting centres performing > 20 operations each year and a further survey of the original 30% not responding continues, to complete the picture.
Conclusion In 1995, $\approx 30\%$ of British urologists had performed a radical prostatectomy and 30% intended to start, compared with 44% now and only 8.6% still intending to start. This suggests that the number carrying out this surgery has stabilised. The survey shows that there are now sufficient surgeons treating sufficient patients to allow a meaningful audit of outcomes, essential if the concepts of the cancer centre are to be confirmed and comparisons with other treatments are to be made.

P122

Expression of the hypoxia-inducible factors 1α and 2α in human renal cancer: relationship to the von Hippel–Lindau mutation and to the angiogenic factor vascular endothelial growth factor

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Introduction The hypoxia-inducible factors HIF-lα and HIF-2α control the expression of many genes involved in the cellular response to hypoxia, including vascular endothelial growth factor (VEGF). In this way, hypoxia may control the 'switch' to an angiogenic phenotype. In cultured von Hippel-Lindau (VHL) mutant cells, HIFs are constitutively over-expressed and VEGF is upregulated. We have investigated the expression of HIFs and VEGF in human renal cancers and relate this expression to the presence of VHL mutations.
Materials and methods HIF-1α/2α expression was assessed in a panel of 46 human renal cancers, most with paired normal controls. In a subset of tumours the expression was evaluated by immunohistochemistry and *in situ* hybridization. VEGF expression was determined by ELISA. The presence of VHL mutations was determined by HPLC and by DNA sequencing.
Results Of 35 sporadic clear cell tumours 25 (70%) strongly expressed HIF-1α/2α; neither factor was detected in paired normal tissue. Both factors were expressed in tumour cell nuclei on IHC; HIF-2α was also expressed strongly in macrophages. HIF-2α mRNA was expressed in tumour-associated vascular endothelium. The expression of HIF-1α/2α was associated significantly ($P = 0.03$) with elevated expression of VEGF and 10 of 11 tumours mutant for VHL expressed HIF-1α/2α.
Conclusion HIFs are expressed in tumours but not in normal tissue. These results strongly support the hypothesis that VHL mutations are associated with the expression of HIFs and elevated expression of VEGF.

P123

Bcl-2 antisense therapy sensitizes human RCC cells to interferon

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Introduction The *bcl-2* proto-oncogene encodes a mitochondrial membrane protein that inhibits apoptosis, promoting resistance to cytotoxic therapies. Bcl-2 is over-expressed in a proportion of primary and metastatic RCCs. The objective of this study was to down-regulate Bcl-2 by inhibiting gene expression with an antisense oligonucleotide, and to determine if antisense therapy sensitized a human RCC line (SKRC42) to IFN-α2a.
Methods G3139, an 18mer phosphorothionite oligonucleotide corresponding to the human bcl-2 translation initiation site, a reverse sense oligonucleotide and a two-base mis-match control were obtained from Genta, Inc (USA). IFN-resistant SKRC42 cells were incubated with oligonucleotides in the presence of cationic lipids. Bcl-2 protein expression was determined by western blot analysis. Antisense and control treated cells were incubated with 100, 300 or 1000 IU of IFN and cytotoxicity determined using the MTT assay.
Results G3139 at concentrations of 50 and 25 nmol/L in the presence of cationic lipid caused an 80% reduction in Bcl-2 protein expression. At 25 nmol/L there was no effect of reverse-sense or mismatch controls on Bcl-2 expression. There was a dose response to IFN. SKRC42 cells incubated with 1000 IU IFN showed a 20% reduction in cell viability, but SKRC42 treated with G3139 then incubated with 1000 IU IFN showed a 70% reduction in cell viability.
Conclusion Down-regulation of Bcl-2 in a resistant RCC line by antisense therapy enhances the effect of IFN. Antisense therapy combined with IFN is a potential strategy for the treatment of RCC.

P124

Insulin-like growth factor-1 alters prostate cancer cell apoptotic signalling

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Introduction IGF-1 may represent a novel survival factor in prostate cancer growth. The aim of this study was to determine if IGF-1 alters prostate cancer cell resistance to chemical- and radiation-induced apoptosis, and to examine the intracellular mechanisms involved.
Methods Androgen-independent PC-3 prostate cancer cells were pre-treated (24 h) with and without IGF-1. Cells were then further incubated with and without apoptosis-inducing agents. The percentage of apoptosis was assessed by propidium iodide DNA staining using flow cytometry. Protein was extracted after IGF-1 treatment (24 h) and western blotting carried out to assess $Bcl X_L$, Mcl-1 and caspase-3 expression.
Results

	Mean (SD) % apoptosis	
	IGF-1 (0 ng)	*IGF-1 (100 ng)*
Control	1.9 (1.6)	2.1 (1)
Etoposide (60 μmol/L)	26.8 (6.4)*	10.3 (5.7)†
Cycloheximide (1 μg/mL)	25.6 (5.0)*	6.5 (0.7)†
Radiation (5 Gy)	22.2 (0.9)*	5.5 (1.1)†

ANOVA, $^{*}P < 0.05$ vs control, $^{\dagger}P < 0.05$ vs treatment with 0 ng

Bcl-X_L and Mcl-1 expression were increased, with no change in caspase-3 expression.
Conclusion IGF-1 induces resistance to known apoptotic stimuli in PC-3 cells with increased expression of Bcl-X_L, and Mcl-1 proteins. Altered apoptotic resistance may represent a novel mechanism by which IGF-1 stimulates tumour progression in prostate cancer.

P125

Expression of E-cadherin by *in situ* hybridization in matched primary and metastatic prostate cancer

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Introduction E-cadherin is a cell adhesion molecule involved in the structural and functional organization of epithelia. Decreased E-cadherin expression is associated with an invasive phenotype, and it is proposed that E-cadherin is an important determinant of metastatic potential in prostate cancer. This study sought to test this hypothesis by comparing the expression of E-cadherin in paired primary and metastatic tumour tissue specimens from patients with untreated prostate cancer.
Methods Metastatic prostate tumour was identified in 14 iliac-crest trephine bone biopsies taken from patients in whom primary tumour specimens were available. the tumours were graded histologically by an independent pathologist. *In situ* hybridization was used to detect whether mRNA for E-cadherin was present within the tumour cells. The expression of E-cadherin mRNA was described as uniform, heterogeneous or negative.
Results Thirteen of the 14 primary carcinomas and 11 bone metastases expressed mRNA for E-cadherin. E-cadherin expression was down-regulated in the metastases in nine cases, similar to the primary tumour in two cases and paradoxically three metastatic specimens had higher levels of E-cadherin than their paired primary tumour:

E-cadherin mRNA levels in:

	in corresponding prostatic bone metastases		
primary prostate cancer	*uniform*	*heterogeneous*	*negative*
Uniform	1	6	3
Heterogeneous	2	1	-
Negative	-	1	-

Conclusions E-cadherin is expressed in bone metastases of prostate cancer. Positive expression E-cadherin in the primary tumour did not prevent the formation of bone metastases in these patients. These results suggest that loss of E-cadherin expression in primary prostate tumours may not be critically linked to metastatic potential, and hence prognosis.
Funding: Prostate Research Campaign, UK

P126

AIB1/RAC3 (a steroid hormone receptor co-activator) in prostate cancer

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Introduction AIB1/RAC3 (Amplified In Breast 1) is over-expressed in up to 64% of breast and ovarian cancers. AIB1/RAC 3 is known to enhance transcriptional activity of the oestrogen receptor and is putatively a co-activator of the androgen receptor (AR). We were interested in the expression and role of AIB1/RAC3 in prostate cancer.
Methods The interaction between AR and full-length AIB1/RAC3 were assessed *in vitro* in DU145 prostate cancer cells. A murine-derived monoclonal antibody was used to investigate protein expression in cell lines and 25 clinical prostate cancer biopsies by western blot and immunohistochemistry. *In situ* hybridization (ISH) confirmed expression of the transcript in prostate cancer biopsies.
Results AIB1/RAC3 enhanced the activity of the AR by 10–15-fold in the presence of synthetic androgens. Western blot showed expression of AIB1/RAC3 in LNCaP cells (androgen-dependent) and in DU145 and PC3 cells (androgen-independent). IHC in all 25 clinical cancers confirmed the expression of the protein in the cytoplasm of malignant epithelium, with more intense staining than in adjacent BPH ($P < 0.01$). In BPH the expression was predominantly in the luminal cells whereas in cancer it was more homogeneous. ISH on four prostate biopsies confirmed the expression of AIB1/RAC3 at the mRNA level.
Conclusion We present the first evidence of over-expression of AIB1/RAC3, a steroid hormone co-activator, in prostate cancer cell lines and in clinical cancers.
Funding: Cancer Research Campaign

P127

The development of an osteoblastic model of skeletal prostate cancer growth in nude mice

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Introduction The mechanisms involved in the formation of sclerotic metastases in prostate cancer are still poorly understood. Whilst several factors have been implicated *in vitro*, there has been relatively little work *in vivo*. The available animal models are limited and most do not mimic the human situation, including the difficulty in producing osteoblastic lesions. Using Swiss male nude mice, we have been able to induce osteoblastic tumour growth *in vivo* following direct intra-tibial inoculation of a metastatic variant of the LNCaP prostate cancer cell line (LNCaP-LN3). Within 3 weeks the animals develop gross osteosclerotic intra-osseous tumours. Because the tumours grow rapidly the mice are killed humanely after ≈ 9 weeks.
Conclusion This model represents an invaluable tool in the investigation and modulation of various factors involved in the cascade of events responsible for osteoblastic metastases in prostate cancer. The technique will be discussed in full, including its advantages and limitations.
Funding: BUF

P128

Expression of parathyroid hormone-related peptide and its receptor in primary and metastatic prostate cancer

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Introduction Parathyroid hormone-related peptide (PTHrP) is a regulatory protein associated with cell grow in nonosseous tissues and with osteoclast stimulation in bone. It has been implicated in the pathogenesis of bony metastases, particularly in breast carcinoma. PTHrP is widely expressed in primary prostate cancers, but the are few reports of its expression in prostatic metastases. The aim of this study was to examine the expression PTHrP and its receptor in matched primary and in bone metastatic tissue from patients with untreated adenocarcinoma of the prostate.
Methods Trephine iliac-crest bone biopsies (8 mm) containing metastatic prostate cancer were obtained from patients from whom matched primary tumour tissue was also available. The tumour was

graded histologically by an independent pathologist. The cellular location of mRNA for PTHrP and PTHrP receptor was identified using *in situ* hybridization with ^{35}S-labelled probes. The expression of PTHrP and its receptor was described as uniform, heterogeneous or negative within the tumour cell population.
Results PTHrP expression was positive in 13 of 14 primary tumours and in all 14 metastases. Receptor expression was evident in all 14 primaries and 12 of 14 metastases. Co-expression of PTHrP and PTHrP receptor was common (13 primary tumours, 12 metastases).

Expression of PTHrP or PTHrP receptor	*PTHrP*	*PTHrP receptor*
Primary tumour		
Uniform	9	12
Heterogeneous	4	2
Negative	1	-
Bone metastasis		
Uniform	11	7
Heterogeneous	3	5
Negative	-	2

Conclusions The co-expression of PTHrP and its receptor suggest that autocrine PTHrP mediated stimulation may be a mechanism of escape from normal growth-regulatory pathways. The high frequency of PTHrP expression in metastases is consistent with a role in the pathogenesis of bone metastases.
Funding: Prostate Research Campaign, UK

P129

Loss of heterozygosity analysis of a tumour suppressor gene at chromosome 10q23.3 in paraffin-embedded prostate cancer tissue

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Introduction Loss of heterozygosity (LOH) at chromosome 10q23.3 is a recognized finding in patients with prostate adenocarcinoma. This region of LOH contains the PTEN gene, a tumour suppressor gene which has been implicated in the progression of tumours, including prostate cancer. Correlating the significance of this region of LOH with clinical outcome is important. However, to undertake the study would require the analysis of archival samples. We have established a method which allows a detailed analysis of LOH from paraffin-embedded tissue.
Methods Slides containing paraffin-embedded radical prostatectomy tissue was microdissected to separate cancer tissue, and the DNA extracted from these samples. Microsatellite markers around and within the PTEN gene were amplified in both the blood and the tissue of 32 patients. The 5′ primer was fluorescently labelled to allow LOH studies on the ABI Prism 377 DNA Sequencer.
Results Using four microsatellite markers we have analysed 32 tumour/blood pairs; this showed LOH of 50% in the radical prostatectomy specimens. All archival paraffin-embedded tissue was successfully analysed using our technique.
Conclusion LOH analysis on an ABI 377 sequencer is successful using DNA samples obtained from archival paraffin-embedded radical prostatectomy specimens. Correlating the significance of this region of LOH with clinical outcome would help in the development of a prognostic marker for prostate cancer.

P130

Targeting BPH with gene therapy? Adenoviral transduction with pro-apoptotic vectors in mammalian models

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Introduction We have undertaken a series of studies evaluating gene therapy for the treatment of BPH. Adenoviral vectors have been constructed that induce apoptosis in both epithelial and stromal prostatic cellular components. Transduction was examined using vectors expressing either the reporter genes β-galactosidase (AdZ) or luciferase (AdL), or the pro-apoptotic genes Fas ligand (AdFasL/G) or caspase-8 (AdCaspase-8).
Methods Apoptosis induced by Ad-FasL and Ad-Caspase-8 was evaluated in independent primary cell cultures of human prostatic smooth muscle cells and epithelial cells. Transduction of rat and dog prostate was then examined by detecting expression of reporter genes with AdZ and AdL, and detecting apoptosis induced by Ad-FasL/G and AdCaspase-8 with the TUNEL assay.
Results In cell culture, apoptosis was detected within 6 h of infection. In both rat and dog prostate, transduction with AdL and AdZ induced a 1000- and 100-fold increase in expression of luciferase and β-galactosidase activity, respectively, above background. In the dog, transduction was localized to the site of injection, and multiple injections achieved good intra-glandular distribution. Apoptosis induced by pro-apoptotic vectors was confirmed by TUNEL staining.
Conclusion Rat and dog prostate can be transduced by adenoviral vectors expressing reporter and pro-apoptotic genes. Potentially therapeutic changes in the target tissue are localized at the site of delivery. Gene therapy can be precisely delivered in the prostate and our findings represent an exciting new development for the minimally invasive treatment of BPH.

P131

The effects of TGF-1 and FGF-2 on cultured prostatic stromal cell populations isolated from BPH tissue grown in serum-free media

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Introduction FGF-2 and TGF-β1 are autocrine growth regulators in prostatic stroma and both have been shown to be higher in BPH than in normal prostate. Our previous studies suggested that these two growth factors have opposing effects on growth and differentiation in prostatic stromal cultures. As others have shown that treatment of prostatic stromal cell with TGF-β1 increased the levels of FGF-2 expression it may be that reciprocal, mutual induction of each of these growth factors by the other could be part of a negative-feedback system for the regulation of cell numbers and matrix production in prostatic stroma.
Methods Growth experiments were conducted on five cell lines of stromal origin isolated from patients with BPH. Replicated cultures were challenged with TGF-β1 and FGF-2 using a defined serum-free medium. Cell population growth was followed using growth curves assessed by Coulter Counter analysis. Simultaneously, RNA was harvested 6 and 24 h after adding treatments. RT-PCR analysis was performed using duplex with primers for β-microglobin and TGF-β1. The intensity of signal was analysed using densitometry.
Results Growth experiments showed that cells were dependent on FGF-2 (5 ng/mL) for rapid growth in defined media. The addition of TGF-β1 (5 ng/mL) abolished the growth stimulatory effect of FGF-2. Adding FGF-2 to cultures increased the expression of TGF-β1 mRNA at 24 h after treatment.

Conclusion The effects and expression of TGF-β1 and FGF-2 in prostatic stroma have been shown to be interdependent. This may represent a key regulatory interaction for the modulation of the mass and composition of prostatic stroma, the tissue compartment shown to be primarily involved in BPH.
Funding: RCS and Research into Ageing

P132

Magnetic resonance spectroscopy in the monitoring of suicide gene therapy in the Dunning model of prostate cancer

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Introduction We have previously shown the role of suicide gene therapy in the rat model of prostate cancer. MRI and spectroscopy allows the noninvasive serial analysis of tumours and treatments, and is therefore useful both in research and in the clinic.
Methods MATLyLu rat prostate cancer cells were transfected with the HSVtk gene. Subcutaneous tumours were established in the flanks of Copenhagen rats. The animals were treated with a 5-day course of ganciclovir (GCV, 100 mg/kg) or saline intraperitoneally, and tumour volumes assessed. ^{31}P MR spectroscopy (MRS) with VARPRO analysis was used to assess the response to GCV in these tumours *in vivo*.
Results MRS spectra showed an increase in the β-NTP/Pi ratio in the treated regressing tumours, implying a paradoxical improvement in tumour health. Untreated tumours continued to grow and showed a decrease in β-NTP/Pi, indicating that these tumours were outgrowing their blood supply. The PME/total phosphate ratio remained unchanged.
Conclusions We have shown *in vivo* monitoring of suicide gene therapy with ^{31}P MRS. Untreated tumours showed markedly different behaviour from suicide gene-transfected tumours after treatment with GCV. MRS may be used in further research into these new treatments and developed for monitoring immunotherapy in the clinic.

P133

Ureterosigmoidostomy vs the valved S-shaped rectosigmoid pouch: comparison of long-term complications

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Introduction Various modifications of urinary diversion to the sigmoid colon have been described to reduce the complications associated with ureterosigmoidostomy (USS). The valved S-shaped rectosigmoid pouch (RSP) has been previously reported from this centre. We report a comparison of complications from these procedures.
Patients and methods In this retrospective study the medical records of patients who underwent USS between 1975 and 1985, and RSP between 1989 and 1997, were reviewed. The variables assessed included recurrent pyelonephritis, upper tract dilatation, deterioration of renal function and metabolic acidosis. Fisher's exact test was used for comparative analyses, with $P < 0.05$ considered to indicate significant differences.
Results There were 31 patients in the USS group (mean age 45.3 years, range 10–75) and 37 in the RSP group (mean age 49.5 years, range 11–77). The mean (range) follow-up was 54.6 (3–216) months for the USS and 31 (15–81) months for the RSP group.

Complication n (%)	*Ureterosigmoidostomy*	*Rectosigmoid pouch*
Recurrent pyelonephritis	9 (29)	1 (2.7)†
Upper tract dilatation	18 (58)	4 (11)‡
Renal impairment	13 (42)	3 (8)‡
Metabolic acidosis	22 (77)	6 (16)‡

†$P < 0.01$; < 0.001

There was only one patient in USS group who developed adenocarcinoma of the colon at the uretero-colic anastomotic site.
Conclusion The S-shaped rectosigmoid pouch urinary diversion is associated with significantly fewer complications than ureterosigmoidostomy, possibly because there is low pressure in the pouch and an antireflux nipple valve.

P134

Hemi-Kock pouch for orthotopic substitution: a long-term evaluation

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Objective To evaluate the long-term outcome of the orthotopic hemi-Kock pouch by assessing the functional results and complications.
Methods Between 1986 and 1997, cystectomy and orthotopic ileal bladder replacement were carried out in 747 patients. The hemi-Kock pouch was used in 374, of whom 222 males had undergone surgery > 5 years previously; 131 patients are currently evaluable with no evidence of disease, and with a minimum follow-up of 5 years.
Results The 5-year minimum direct survival was 59%. IVU showed a stable and/or improved upper tract in 225 of 256 renal units (88%); 31 units deteriorated because of reflux (20), uretero-ileal stricture (nine) and pyelonephritis (two). An unstable nipple valve was diagnosed in 28 patients (21%) of whom 19 required open surgical revision. Pouch stones were detected in 43 patients (32.8%). Other complications included urethral stricture in six patients, urethro-ileal stenosis in 10 and mucus retention of urine in five. Urine cultures were obtained in 102 patients and were positive in 47%. Urodynamic studies showed a mean (SD) capacity of 648 (116) mL, a mean maximum pouch pressure of 25.9 (9.9) cmH_2O and a mean maximum urethral pressure at rest of 73.2 (23.85) cmH_2O; 93% of the patients were continent during the day and 65% were completely dry at night.
Conclusions The hemi-Kock orthotopic ileal pouch is associated with satisfactory long-term functional results. Most of the complications were related to the construction of the antireflux nipple valve. This prompted us to find another means of reflux prevention with no valve construction.

P135

The results of total cystectomy and orthotopic bladder substitution in women

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Introduction After total cystectomy most female patients in the UK are offered some form of urinary diversion. The avoidance of a stoma is a priority for female patients but few are offered orthotopic reconstruction after total cystectomy. Lack of experience amongst urologists, a fear of incontinence or the need for CISC are factors that make orthotopic reconstruction less popular. We have evaluated this procedure in a series of women.
Patients and methods A series of 18 women were selected who underwent surgery between 1992 and 1999; the reason for cystectomy was intractable interstitial cystitis in 12, invasive bladder TCC in three, and one each with bladder sarcoma, schistosomiasis and tuberculous cystitis. One patient with TCC had previously undergone radiotherapy. The entire bladder was removed to the bladder neck. Orthotopic reconstruction was performed with ileum as a hemi-Kock pouch (in 16) or Studer pouch (in two). A cystogram was taken after 2 weeks.
Results The patient who had previous radiotherapy had a prolonged urinary leak from the pouch, necessitating catheterization for 8 weeks. All 18 women are continent by day but five leak at night and wear a pad. CISC is necessary in six. Bladder calculi have been removed endoscopically from four. The mean follow-up is now 60 months. One patient has died from metastatic TCC and another from *Pseudomonas* septicaemia.
Conclusions Cystectomy and orthotopic bladder substitution in women is not associated with significant incontinence but CISC is necessary in a third of the patients. It is possible after radiotherapy but delayed healing should be anticipated. The women in this series preferred the avoidance of a stoma.

P136

Short-term complications of cutaneous continent urinary diversion

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Introduction Up to a half of patients undergoing cutaneous continent urinary diversion (CCUD) require re-operation. Complications are usually caused by conduit, stomal and ureteric

anastomotic problems. We reviewed our results in consecutive patients at one centre undergoing CCUD.
Patients and methods Twenty-five patients underwent CCUD (mean age 37.4 years, range 25–59) between 1994 and 1999 (mean follow-up 31 months, range 7–55). Eight had neuropathic bladders, of whom three had incontinent ileal conduits. Eight patients had malignancies (six TCC, one leiomyosarcoma and one cervical carcinoma). Six patients had intractable urinary incontinence and three had interstitial cystitis. Three patients had their native bladders used as the reservoir. In the remaining 22, the reservoir was formed from the ileocolonic segment; of these, detubularized colon was used in three and a Penn pouch was constructed in the other 19. Patients with ileal conduits had the conduit incorporated into the reservoir. An antireflux reimplantation of ureters was performed in all patients who did not have an ileal conduit. The conduit was formed using tapered ileum or appendix. Patients were reviewed with bi-annual electrolyte estimations and annual IVP or ultrasonography.
Results The median hospital stay was 14.7 days; there were no perioperative deaths. Of the 25 patients 21 (84%) were continent after surgery. One patient required augmentation of a detubularized segment and three required re-exploration of a tapered ileal segment. The segment of tapered ileum was taken down, refashioned into an isolated tube and then reimplanted into the reservoir; these patients are currently continent. Three of eight patients with malignant disease died at 4, 9 and 36 months after surgery. One appendix conduit perforated on catheterization and required immediate revision. Stomal stenosis occurred in four patients, two in appendiceal stomas and two in tapered ileum. All patients underwent meatotomy and insertion of a skin flap. All patients use meatal dilators and are catheterizing with no problems. One patient with a severe depressive illness was undiverted into her native bladder and another patient who developed severe bladder pain elected to have an ileal conduit constructed. All patients with CCUD are currently dry. No uretero-anastomotic strictures or serious metabolic disturbances requiring hospital admission have occurred. Overall, complications requiring reoperation occurred in 11 of 25 patients (44%).
Conclusion CCUD carried a 44% complication rate in this series, but complete continence can be achieved. Improvements in surgical technique should eliminate continence problems caused by conduit failure. Stomal stenosis occurs in 15% of patients and can usually be managed with simple revision. CCUD is a safe and reliable method of achieving continence in properly selected, informed and highly motivated patients.

P137

Does enterocystoplasty alter renal function? A 10-year follow-up

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Introduction The metabolic complications after enterocystoplasty have been intensively studied, but seldom with reference to long-term renal function. Our aim was to study the effect of enterocystoplasty on long-term renal function and the cause of deterioration.
Patients and methods Eighty-seven patients (aged 4 to 35 years) with bladder exstrophy who underwent reconstruction of the lower urinary tract using bowel segment were enrolled in a prospective protocol. The GFR was measured before and 1, 2, 5 and 10 years after surgery using ^{51}Cr-EDTA clearance.
Results Of 58 patients with a follow-up of >10 years, 53 were evaluable. The mean (SD) GFR decreased from 97.9 (20.4) to 92.9 (23.6) mL/min ($P = 0.24$). In 10 patients the GFR decreased by $>20\%$ during the 10-year observation period. Causes were inadequate catheterization by poorly compliant patients (five), uretero-ileal stenosis (one), high-pressure reservoir (one) and unknown (three).
Conclusion For 80% of these patients, enterocystoplasty does not seem to alter their long-term renal function. However, in $\approx 20\%$ of the patients renal function deteriorated during the 10-year follow-up, usually from identifiable and remediable causes. Storage of urine in bowel does not appear to be inherently damaging to kidney function. Patients with an enterocystoplasty need regular monitoring of renal function. The urinary tract must be functionally assessed when deterioration is detected.

P138

Antibiotics lower urinary N-nitrosamine levels in enterocystoplasties

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Introduction N-nitrosamines are carcinogens implicated in the development of bladder and enterocystoplasty carcinoma. UTI is associated with elevated urinary N-nitrosamine levels. We assessed the microbiological characteristics of cystoplasty urine and evaluated the effect of bacteria type, prophylactic antibiotic administration and therapeutic antibiotic administration on cystoplasty N-nitrosamine levels.
Patients and methods The study included 39 patients with an enterocystoplasty and six normal controls. Urine samples were collected for the determination of N-nitrosamine level (using a modification of the Pignatelli method) and for microscopy, culture and sensitivity. A subgroup of five cystoplasty patients with a confirmed UTI were further evaluated with measurements of urinary N-nitrosamine levels before, immediately and 1 week after completing a therapeutic course of antibiotics (according to bacterial sensitivity).
Results Twenty-two of the 39 cystoplasty patients and none of the controls had a confirmed UTI; eight were taking prophylactic antibiotics and had control N-nitrosamine levels (1.03 vs 1.0 μmol/L). N-nitrosamine levels were highest in patients with UTI (1.89 μmol/L, $P = 0.05$). *Escherichia coli* was the commonest infecting organism (11 patients) and resulted in the highest urinary N-nitrosamine levels (1.98 μmol/L). N-nitrosamine levels decreased as the UTI was treated, from a mean of 2.26 μmol/L before to 0.44 μmol/L afterward.
Conclusions UTI occurs in about half of patients with an enterocystoplasty and is associated with increased levels of urinary N-nitrosamines. *E. coli* is the causative agent in half of the UTIs. Antibiotic prophylaxis reduces N-nitrosamine levels to that in control subjects. Treatment of the UTI results in a rapid reduction of elevated N-nitrosamine levels to control levels.

P139

Reduction of bone strength after enterocystoplasty in rats

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Introduction As shown previously in a chronic animal model of urinary diversion [*Br J Urol* 1998; 81 (suppl): 28] bone loss occurs through expansion of the marrow cavity area. However, the relevance of such skeletal changes in terms of biomechanical features has not yet been investigated systematically.
Methods Young male Wistar rats (120) were distributed equally among four groups undergoing: ileocystoplasty; ileocystoplasty and resection of the ileocaecal segment; colocystoplasty; and controls. After 8 months the lumbar vertebrae and right tibia were obtained at necropsy. Vertebral body cylinders were compressed in a material testing machine and load deformation curves recorded. The

proximal tibial metaphysis was assessed using static histomorphometry. The bone volume per tissue volume (BV/TV, %), trabecular thickness and trabecular number were determined.
Results Isolated ileocystoplasty resulted in a decreased maximum load value of the vertebral body (−16.4%) and a substantial reduction in tibial BV/TV (−34.7%). Ileocystoplasty combined with resection of the ileocaecal segment led to a significant loss of bone strength (−32.4%; $P < 0.0015$) and a dramatic reduction of tibial BV/TV (−45.9%). Colonic augmentation had no significant effect on bone strength (−10.2%) or histomorphometric values.
Conclusions This is the first experimental study to confirm the relevance of previously reported bone loss after urinary diversion in terms of biomechanical variables. There was a reduction of bone strength in all animals with an enterocystoplasty, being most significant in ileocystoplasty and ileocaecal resection.

P140

Neovaginoplasty using rectosigmoid colon on a superior rectal artery pedicle

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Introduction Many methods have been used to create a vagina when congenitally absent or in male-to-female gender reassignment. Although described previously [*Br J Obstet Gynaecol* 1996; 103: 1148–55] we have devised a technique independently that uses rectosigmoid colon supplied from below by the superior rectal artery.
Patients and methods The procedure has been used in seven patients since 1985, three for congenital absence and four for gender reassignment. An appropriate length (≈ 10 cm) of rectosigmoid is defined. The inferior mesenteric artery is divided, as are the mesocolonic vessels to the site of colonic division. The rectum is then divided, ensuring preservation of the superior rectal artery which supplies the bowel segment. The graft is inverted and tunnelled between the bladder and rectum to the perineum; colonic continuity is then restored.
Results The graft was viable in all patients; four patients with introital stenosis required dilatation or minor revision. Sexual intercourse was established by all patients with congenital absence. Poor patient compliance has not permitted a long-term follow-up, although one patient is known to be functioning normally 12 years later.
Conclusions This useful new graft is available for vaginal replacement or possible small-volume bladder augmentation.

P141

The long-term outcome of artificial urinary sphincters

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Introduction The outcome of a series of AUS inserted > 10 years ago was reviewed in 100 patients.
Methods The notes were reviewed for 100 patients and postal questionnaires were sent to those with no recent follow-up.
Results Overall, 84 patients were continent; of these, 36 had their original AUS *in situ* and were dry with a median follow-up of 11 years. Twenty-seven patients had had their AUS successfully replaced for mechanical failure, having previously been continent at a median of 7 years, and 21 had had their AUS removed for infection or erosion and had subsequently had a successful reimplantation 3–6 months thereafter or remained dry with no further AUS. In the two main subgroups of patients 91% of those with post-prostatectomy incontinence and 86% with neuropathic bladder dysfunction were continent. The survival of the device was 66% at 10 years. Removal for infection or erosion over the 10-year period was 37% overall, with the highest risk in patients with stress incontinence and 'other indications' (56%), and lowest in patients with post-prostatectomy incontinence (17%).
Conclusions The AUS is an effective long-term treatment for post-prostatectomy incontinence or neuropathic bladder dysfunction. In the few patients with stress incontinence and 'other indications' the results were less satisfactory.

P142

The Barbagli procedure gives the best results for patch urethroplasty of the bulbar urethra

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Introduction Over the last 4 years the Barbagli procedure (a dorsal rather than a ventral stricturotomy and patch) has become popular for patch urethroplasty. Theoretically the dorsal siting of the graft gives the graft better support. At the same time the buccal mucosal free graft (BMG) has become popular as an alternative to the rather more complicated pedicled skin flap.
Patients and methods Of the 71 patients who have undergone BMG urethroplasty of the bulbar urethra in the last 6 years, 42 have undergone a Barbagli procedure with the stricturotomy and patch on the dorsal aspect of the bulbar urethra, and 29 have undergone the more traditional or ventral stricturotomy and patch procedure.
Results At 3 years of follow-up 5% of patients who underwent the Barbagli procedure developed recurrent strictures, whereas 14% of patients undergoing a ventral stricturotomy and patch did so. In addition, 17% of patients undergoing a ventral stricturotomy and patch procedure developed complications attributable to out-pouching of the patch, whereas these complications were not seen after the Barbagli procedure. The only complication common to both methods was post-micturition dribbling and pooling of seminal fluid at the site of the urethroplasty after sexual intercourse.
Conclusions The Barbagli procedure has a higher success rate and a lower incidence of complications than the traditional ventral urethroplasty.

P143

The genetic basis of adenocarcinoma of the bladder with special emphasis on those arising in 'clam' bladders

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Introduction Since its introduction in 1982, the clam enterocystoplasty has become widely used for treating detrusor hyper-reflexia and instability. There is thought to be a small risk of malignancy in these bladders and in our unit alone there have been four patients with such tumours. The tumours were all highly aggressive adenocarcinomas entirely in the native bladder segment. Our aim is to identify genetic irregularities peculiar to these tumours, for use as reference points.
Methods DNA was extracted from the slides of these tumours and from biopsy samples taken from the bladder remnant of the patients with a clam enterocystoplasty. The DNA was then subjected to an *in situ* hybridization technique, comparative genomic hybridization, which detects amplifications and/or deletions anywhere in the chromosomal series.
Results Fifteen patients in the 'at risk' latency period were biopsied. DNA analysis of these biopsy samples from the bladder remnant showed no significant DNA changes. The tumour DNA analysis (three clam cancers and three de novo adenocarcinomas) showed several amplifications, especially on chromosome 8p and 21q.
Conclusion The possibility of cancer in clam enterocystoplasties remains. There is a need to be able to predict which patients are most at risk. If a sequence of DNA changes leading to tumour formation can be identified, then such changes can be used as indicators for these patients. If any patients develop similar DNA changes they can be followed more closely.

P144

An organ-culture urothelial tumour cell line model system of superficial bladder cancer

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Introduction The properties of superficial urothelial tumours have traditionally been investigated by culture of immortalized tumour cell lines grown as monolayers. There are no good animal models because of the difficulties of keeping the tumour superficial and consistent. We describe a system in which intrinsically fluorescent urothelial cancer cells are grown on rat bladder organ cultures.
Methods Explants of rat bladder (5 mm square) were cultured in Petri dishes in Waymouth's MB 752/1 Medium (Gibco) supplemented with 10% fetal calf serum, antibiotics and cholera toxin. Parental and resistant MGHU-1 urothelial carcinoma cell lines were transfected with a green fluorescent protein (GFP) vector, and transfected cells purified by a fluorescence-activated cell sorter (FACS) machine. Cells were seeded onto 2–5-day-old explants and viewed by confocal microscopy. The effects of exposure to conventional cytotoxic agents were studied by applying the drug for a fixed period (usually one hour) and subsequent imaging. The novel intravesical agent meglumine γ-linolenic acid was also assessed in the system. Cytotoxicity was quantified either by the change in fluorescence of the colony or more reliably by the change in the area of the colony. 3-D reconstructions were possible using the computer software of the confocal microscope.
Results The explants grew 'skirts' of normal urothelium by 5–7 days and these could be used to study the characteristics of normal urothelium, and to observe their interaction with tumour cells. The surface of the explant was stained with acridine orange to confirm its viability before and after applying cytotoxic agents. Colonies of GFP-MGHU1 cells became established on the explants and their progress was followed by serial imaging. However, once established in a colony at the centre of the explant or at the edge, little further growth took place. Conventional cytotoxic agents such as epirubicin, mitomycin C and estramustine had similar differential toxicities to those seen in monolayer culture, but appeared to need higher concentrations to achieve similar cell kill. Infection was a constant problem with the explants, with an overall rate of 33%, mainly with yeasts and other fungi.
Conclusion This model allows the survival and behaviour of tumour cells within an organ culture system to be followed over time and after applying cytotoxic agents. The different parts of the system mean that both normal monolayer urothelial cells and the more complex urothelial surface may be examined after applying agents. The interaction between tumour cells and this 'skirt' can also be followed. The full urothelial tumour explant system enables the behaviour of tumour cells to be investigated in a more physiological setting, but without the disadvantages of animal models. Selective properties of anti-cancer agents may also be assessed.
Funding: Scotia Pharmaceutical

P145

In vitro detection and potential clinical importance of two distinct pathways regulating vascular endothelial growth factor expression in bladder cancer

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Introduction One of the key regulators of vascular endothelial growth factor (VEGF) expression is hypoxia. We have previously shown that this hypoxic regulation in human bladder cancer cells *in vitro* occurs via the transcription factors, hypoxia-inducible factor-1α and 2α (HIF-1α and HIF-2α) [*BJU Int* 1999; 83 (suppl 4): 12]. We show for the first time the expression of HIF-1α and HIF-2α in human primary bladder tumours. We also identified a second regulatory pathway for VEGF expression.
Methods Using a ribonuclease protection assay and western blotting, VEGF, HIF-1α and HIF-2α mRNA and protein were analysed in 12 tumour and four normal bladder samples. *In vitro*, several signalling pathway inhibitors were examined for effect on VEGF expression by four human bladder cancer cell lines under normoxic and hypoxic (0.1% O_2) conditions.
Results There was up-regulation of both HIF-1α and HIF-2α mRNA and protein in tumours compared with normal bladder, although there was significant inter-tumour variation. There was a significant correlation ($r = 0.68$, $P = 0.02$, Spearman rank) between VEGF and HIF-1α mRNA. Of various signalling inhibitors tested, only the phosphatidyl inositol 3-kinase inhibitor LY294002 was effective. Whilst this reduced total VEGF expression under both basal and hypoxic conditions, it did not affect hypoxic inducibility. This effect was independent of HIF-1α, as shown by western blotting.
Conclusions VEGF is a key component in the biology of bladder

cancer. This first demonstration of HIF-1α and HIF-2α in primary human bladder tumours and the detection of a distinct VEGF regulatory pathway identifies novel therapeutic targets that have clinical potential.
Funding: RCS and BUF

P146

The demonstration of a functional role for the angiogenic factor thymidine phosphorylase in bladder cancer invasion identifies a therapeutic target and potential prodrug activator

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Introduction The expression of thymidine phosphorylase (TP) is upregulated in human primary invasive bladder cancers [*Cancer Res* 1991; 55: 510–3]. To determine the functional relevance of this we induced over-expression of TP in a human superficial bladder cancer cell line (RT112) and tested the effect of this in an *in vitro* rat bladder model. The prodrug furtulon, activated by TP to 5-fluorouracil, was then tested for its ability to inhibit invasion.
Methods An empty vector clone (EV11) and a high TP expressing clone (2T10) were induced from RT112 using retroviral techniques. These three cell lines were seeded onto an *in vitro* model of bladder cancer invasion (developed using de-epithelialized rat bladder stroma) and invasion quantified. Furtulon was added onto this model, akin to intravesical therapy. Experiments were carried out in triplicate and repeated three times. Cell growth as conventional subcutaneous xenografts in 20 nude mice was also tested.
Results Compared with a panel of human primary bladder tumours, clone 2T10 expressed significantly higher levels of TP, comparable with invasive tumours, whereas RT112 and EV11 expressed very little TP, equivalent to or less than superficial tumours. Both RT112 and EV11 formed superficial layers in the *in vitro* model, with no invasion, whereas 2T10 invaded across a broad front. Conversely, there was no difference in xenograft growth. Addition of furtulon to the *in vitro* model abolished the invasion of 2T10.
Conclusions Rather than being an incidental finding, this work suggests a functional role for increased TP in bladder cancer invasion. Direct antagonism of TP may be a potential therapeutic approach. Alternatively, high TP expression in these tumours could be used to specifically activate prodrugs such as furtulon, nullifying the malignant advantage of high TP. The different behaviours in an orthotopic *in vitro* model compared with subcutaneous flank injection confirms the importance of orthotopic models in cancer biology.
Funding: RCS and BUF

P147

Lysosomal-associated membrane proteins in the assessment of basement membrane invasion in superficial TCC of the bladder

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Introduction Lysosomal-associated membrane proteins (LAMP-1 and LAMP-2) are primarily intracellular and localised within lysosomal membranes with minor cell surface expression. In normal cells these proteins have roles in the recognition and transport of molecules, fusion with other cellular components and resistance to lysosomal enzymes. LAMPs have strong similarity to proteins bearing oncodifferentiation antigens and the expression of these molecules has been observed to be increased in some transformed cell lines. It is suggested that LAMP upregulation may affect cell-cell and cell-matrix adhesions, tumour invasiveness and immune recognition. We tested the hypothesis that increased expression of these molecules may be of use in identifying invasive foci in superficial TCC of the bladder.
Methods Formalin-fixed tumour specimens of 45 newly diagnosed superficial TCCs of the bladder (16 Ta and 29 T1) were evaluated for the expression of LAMP-1 and LAMP-2 by immunohistochemistry after microwave antigen retrieval.
Results LAMP-1 was expressed in all tumours studied, and was present in invasive and noninvasive areas in a uniform pattern, with some enhancement in umbrella and basal cells. LAMP-2 showed a similar but low level of expression in noninvasive tumour, although greater staining was prominent in invasive foci, and in high-grade areas and adjacent regions.
Conclusions LAMP-2 expression is increased in the invasive portions of T1 and high-grade tumours, and may be helpful in assessing suspected invasive portions of superficial bladder cancer.

P148

Urinary matrix metalloproteinase-9 and tissue inhibitor of metalloproteinase-1 in bladder cancer: relationship to EGFR status and tumour progression

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Introduction We previously showed that bladder tumour cell lines (RT4, RT112) synthesise matrix metalloproteinases (MMPs) when stimulated with EGF. We also showed that patients with bladder tumours that over-express EGFR have higher urinary levels of MMP-1 than patients with EGFR-negative tumours. We have now extended those studies to measure levels of urinary MMP-9 and tissue inhibitor of MMP-1 (TIMP-1) in patients with bladder cancer, and studied their relationship to tumour EGFR status.
Patients and methods MMP-9 and TIMP-1 were measured by ELISA in voided urine samples from 129 patients with bladder tumours (six CIS, 74 Ta, 29 T1, 20 T2–4, 45 G1, 43 G2 and 35 G3) and 36 healthy volunteers. In a subset of 100 patients, the corresponding bladder tumour sections were stained by immunohistochemistry for EGFR using the monoclonal antibody NCL-EGFR. Clinical follow-up data were available for 80 patients (median duration 25 months, range 4–36).
Results Urinary MMP-9 and TIMP-1 levels were higher in patients with bladder cancer than in healthy volunteers ($P = 0.0072$ and $P = 0.0131$, respectively). Patients with stage T2–4 tumours had higher urinary MMP-9 ($P = 0.0065$) and TIMP-1 ($P = 0.019$) levels than had patients with CIS/Ta/T1 tumours, and levels of both urinary MMP-9 and TIMP-1 strongly correlated with tumour size (both $P < 0.001$). EGFR was over-expressed by 37% of bladder tumours and patients with EGFR-positive bladder tumours had higher urinary TIMP-1 levels than patients with EGFR-negative tumours ($P = 0.0257$). Also, patients with urinary TIMP-1 levels above the median (1.816 ng/mL) were at higher risk of disease progression than were patients with urinary TIMP-1 levels of < 1.816 ng/mL ($P = 0.019$). There was no association between urinary MMP-9 levels and tumour progression or EGFR status.
Conclusions Urinary MMP-9 and TIMP-1 are detectable in urine samples from patients with more aggressive bladder tumours. The association between EGFR over-expression and higher levels of urinary TIMP-1 may contribute to the biological processes underlying tumour progression.
Funding: BUF, RCSI, Research and Development Directorate, CRC

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Target orientated anticancer drug screening: its relevance to bladder cancer and pro-drugs activated by the cytosolic enzyme DT diaphorase

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Introduction We recently showed that a subset of patients with bladder cancer have increased levels of DT diaphorase (DTD) in their bladder tumours, whilst normal bladder mucosa is relatively devoid of activity [*BJU Int* 1999; 83: (suppl 4): 42]. A mitomycin C analogue (EO9) is a pro-drug that is selectively activated by the action of DTD. We aimed to screen six other mitomycin C analogues (termed mitosenes, WV14, WV15, WV16, WV18, WV21 and WV28) for suitability as pro-drugs activated by DTD.
Methods Using recombinant human DTD the substrate specificity was determined. DNA-damaging assays were conducted using supercoiled plasmid DNA. Chemosensitivity was studied at pH 7.2 and pH 6.0 on a cell line devoid of DTD activity (BE) and another cell line with high DTD activity (A549) using the MTT assay.
Results Only WV18 and WV21 were poor substrates for DTD; WV14 and WV21 were toxic to plasmid DNA but not cytotoxic to either cell line. WV15 and WV16 showed cytotoxicity but little selectivity for DTD-rich cells. WV18 and WV28 were both cytotoxic with high selectivity for DTD-rich cell lines (IC_{50} for BE/ IC_{50} for A549 > 85]. This was surprising as WV18 was a poor substrate for DTD. The selectivity of WV28 for DTD-rich cell lines was enhanced 10-fold by reducing the extracellular pH from 7.2 to 6.0.
Conclusion WV28 was identified as a pH-dependent DTD activated pro-drug and a candidate for further evaluation.
Funding: Kyowa-Hakko UK, Ltd

P150

The role of IL-18 in the immune response to bladder cancer

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Introduction IL-18 plays a pivotal role in the development of a cell-mediated immune response. It dramatically enhances the T cell secretion of IFN-γ, and T cell cytotoxicity and natural-killer (NK) cell activity. Melanomas are known to suppress cell-mediated immunity. We investigated whether this was also true for bladder cancer and if so, whether genetically engineering tumour cells to secrete IL-18 (a potent enhancer of cell-mediated immunity) could prevent this.
Methods The expression of IL-18 mRNA and protein was assessed in a panel of bladder cancer cell lines. These were engineered to express IL-18 using retroviral gene transfer. Three bladder cancer lines (RT112, VMCUBIII and 5637), in their parental and IL-18-expressing forms, were co-cultured with peripheral blood mononuclear cells and IL-2. After 7 days, specific cytotoxicity was assayed for against three target cells (parental tumour cells, NK cell-sensitive K562 cells, lymphokine-activated killer cell sensitive Daudi cells).
Results All bladder cancer cell lines examined expressed IL-18 mRNA and precursor IL-18 protein. Two of these (RT4, RT112) also expressed mature IL-18 protein. None of the cell lines in the panel secreted IL-18 unless they were infected with BCG. RT112 and VMCUBIII cells completely suppressed the generation of cytotoxicity *in vitro,* preventing killing of parental tumour, K562 and Daudi cells. However, recombinant bladder cell lines permitted the generation of cytotoxicity. Specific cytotoxicity increased from 0% to 21% against parental cells and from 0% to 53% against K562 cells. Interestingly, Daudi cells were not killed.
Conclusions Bladder cancer cell lines express IL-18 but they do not appear to secrete it. They suppress the generation of cytotoxic lymphocytes, in a manner analogous to melanomas. Retroviral gene transfer of IL-18 to bladder cancer cell lines permitted the generation of cytotoxicity. Infection of bladder cell lines with BCG organisms resulted in the secretion of bioactive IL-18. With further work, this may lead to the production of an IL-18-based tumour cell vaccine for use against bladder cancer.
Funding: ICRF

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Increased urothelial permeability induced by BCG: a window of opportunity ?

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Introduction The intravesical administration of BCG is currently the most effective treatment for carcinoma *in situ* (CIS) of the bladder. In an effort to improve its efficacy it is being combined with other agents, i.e. mitomycin C or IFNα. Apart from a requirement to bind with fibronectin little is known about the direct interaction of BCG with the urothelium. This study aims to evaluate the effect of BCG on normal urothelial permeability.
Methods Anaesthetized female New Zealand white rabbits were catheterised and BCG (8 mg TICE) instilled intravesically for 1 h; control animals were instilled with normal saline. Five groups were studied: (1) five control rabbits; (2) six given 8 mg BCG, assessed at 1 h; (3) four assessed at 6 h; (4) four assessed at 12 h; and (5) three assessed at 24 h. The rabbits were killed with a pentobarbitol overdose, the bladder excised and placed in modified Ringer's buffer solution at 37°C (pH 7.4). The excised bladder was stretched, the muscle dissected free of the urothelium and then mounted on a ring between the halves of an Ussing chamber. The transepithelial resistance (TER), and diffusive urothelial water and urea permeability were measured, with the results given as the mean (SEM).
Results

Group	*Mean (SEM) TER ($k\Omega/cm^2$)*	*Permeability (cm/s) water ($\times 10^{-5}$)*	*urea ($\times 10^{-7}$)*
1	3.56 (0.44)	5.11 (1.11)	6.65 (0.99)
2	4.07 (1.58)	4.07 (1.58)	27.1 (5.04)
3	1.92 (1.09)	1.92 (1.09)	36.78 (13.6)
4	4.17 (4.16)	4.98 (0.76)	5.72 (3.77)
5	4.73 (1.86)	5.55 (1.2)	5.92 (1.39)

There was no significant difference in TER or water permeability. Urea permeability increased significantly ($P < 0.05$, Bonferroni *t*-test) by 6 h but returned to normal by 12 h.
Conclusions BCG instillation resulted in a significantly increased urothelial permeability to urea at 6 h ($P < 0.05$); this increased permeability appeared to return to normal by 12 h. This time-dependent (and limited) increased urothelial permeability has implications in the design of combination therapy regimens allowing the use of a second agent within this window, thus maximizing its potential benefit. Given the short duration of the effect it is unlikely that it is caused by a BCG-mediated immune response.
Funding: AFUD, NIHR37DK48217

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Talin expression in bladder cancer assessed using *in situ* hybridization

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Introduction Altered cellular adhesion and cell motility are among the processes implicated in tumorigenesis. Talin is a cytoskeletal adhesion plaque protein with a 47 kDa N-terminal domain which interacts directly with the cell membrane, and a 190 kDa C-terminal domain which interacts with the intracellular cytoskeletal components actin and vinculin. Talin is usually found at focal cell contacts and is thought to be important in anchorage-dependent and anchorage-independent growth.

Method We examined, using *in situ* hybridization, talin expression in 22 bladder tumours of varying stage and grade.

Results Talin expression was restricted to epithelial cells; no expression was found in cells of stromal components. Talin was variably expressed by both low- and high-stage tumours. Seven tumour specimens showed strong positive staining for talin, with weaker positivity identified in a further 11; four samples showed no evidence of talin staining. T3/T4 tumours appeared to less frequently express high positivity for talin but this relationship was not statistically significant. Metastases occurred in patients with low/zero expression of talin.

Conclusion This preliminary report suggests a role for this cellular adhesion molecule in the mechanisms of aggressive bladder tumour behaviour.

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Urinary leakage during coitus is a sign of instability in women with urinary urgency

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Introduction Coital urinary incontinence (CUI) has been reported to be associated with genuine stress incontinence (GSI) on urodynamic testing and less commonly with detrusor instability (DI). Past studies have relied on static urodynamics, which lack sensitivity in the detection of DI. This study examined the prevalence of CUI in women with urinary urgency using videocystometrography (VCMG) and ambulatory monitoring (AUM).
Methods Ninety-nine women recruited to a prospective study of urodynamics for assessment of urinary urgency completed the Bristol Female Symptoms Questionnaire. VCMG was performed and interpreted according to ICS criteria, with the person reporting the investigation present throughout. AUM was performed using the MMS-UPS2020® according to a standardized protocol. DI was diagnosed in the presence of involuntary detrusor activity associated with urgency and/or urge incontinence.
Results Fifty-eight women (mean age 48 years, 95% CI 2.5) reported being sexually active; 27 of these (47%) reported CUI. The table summarises the detection of GSI and DI by VCMG and AUM. Clinically significant DI was present in 24 (89%) women with CUI and in 19 (61%) with no CUI ($P = 0.01$, chi square). GSI was present in 14 (52%) of women with CUI and seven (24%) with no CUI ($P = 0.01$). Of the 27 women with CUI, 25 (93%) reported the symptom to be a significant problem.

	CUI, n (%)	
Diagnosis/test	*present*	*absent*
Number	27	31
GSI		
on VCMG	11 (41)	6 (19)
on AUM	7 (26)	5 (16)
on either	14 (52)	7 (23)
DI		
on VCMG	11 (41)	7 (23)
on AUM	22 (81)	19 (61)
on either	24 (89)	19 (61)

Conclusions CUI was a common distressing symptom in this population and was rarely volunteered as a presenting feature. In a sexually active woman with incontinence, the presence of this symptom should be actively sought as its presence correlates highly with the presence of DI (89%). AUM and VCMG appear to be complementary in the objective assessment of lower tract function in women with urinary urgency.

P154

Inter-observer agreement in interpreting ambulatory urodynamics in women with urgency

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Introduction Ambulatory urodynamic monitoring (AUM) is being evaluated as a clinical tool. Little has been published on the reliability of the data generated during AUM. This prospective study assessed the level of agreement between independent observers using a standardised protocol for the conduct and interpretation of AUM in women presenting with urinary urgency.
Methods One hundred and eleven women underwent both AUM and videocystometrography (VCMG) in random order. VCMG was performed and interpreted according to ICS criteria. AUM was carried out using the MMS-UPS2020® according to a standardized protocol. Two investigators (OBS1 and OBS2), unaware of the other's findings and those on VCMG, independently interpreted the traces along with the subject's urinary diary. Detrusor instability (DI) was diagnosed in the presence of involuntary detrusor activity with urgency and /or urge incontinence.
Results The diagnoses recorded in 100 women completing the study are listed in Table 1; Table 2 shows the agreement for DI and GSI between the observers on AUM and between AUM and VCMG. The inter-observer agreement on AUM for DI and GSI was 87% and 83%, respectively.

Table 1 Overall diagnosis

Diagnosis	*OBS1*	*OBS2*	*VCMG*
Pure DI	53	47	21
Pure GSI	11	12	30
Mixed DI + GSI	20	20	9
Normal	10	15	39
Uninterpretable	6	6	1
Total	100	100	100

Table 2 Agreement for DI and GSI

Agreement	*OBS1 with OBS2*	*OBS1 with VCMG*	*OBS2 with VCMG*
For DI			
with DI	65	28	25
no DI	18	20	24
Unsure*	4	0	0
Percentage	87	48	49
For GSI			
with GSI	24	22	25
no GSI	55	49	51
Unsure*	4	0	0
Percentage	83	71	76

* uninterpretable traces

Conclusions This is the first study of inter-observer agreement on AUM. Interpreting AUM according to a standardised protocol results in a high sensitivity for DI with consistency between observers. The findings lend further support for AUM as an objective clinical tool in the investigation of LUTS.

P155

The effects of pudendal afferent nerve electrical stimulation on detrusor instability secondary to obstructive BPH

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Introduction Brief sacral magnetic stimulation suppresses both idiopathic detrusor instability (DI) and detrusor hyper-reflexia (DH) but fails to suppress unstable contractions in obstructed patients with either detrusor sphincter dyssynergia (DSD) or BPH. However, prolonged electrical stimulation (ES) of the dorsal penile nerve has now been shown to suppress DH in patients with obstructive DSD [*Eur Urol* 1998; 33: 60]. The aim of this study was to assess the effects of prolonged ES in patients with DI secondary to obstructive BPH.
Patients and methods Nine patients with urodynamically confirmed DI secondary to BPH were investigated. During standard-fill cystometry, ES (200 μs pulses at 15 Hz, at the highest tolerable intensity for each patient up to twice the pudendo-anal threshold) was given for 60 s when an unstable contraction occurred. Unstimulated contractions were used as controls. The effects of ES were analysed by measuring the mean (SD) area under the unstable pressure curves with ES ($MAUC_{ES}$) and with no ES ($MAUC_{con}$) and expressed as the percentage suppression.
Results Prolonged ES produced only a transient decrease in the unstable pressure curves. Overall, the $MAUC_{con}$ was 5421 (3452) and the $MAUC_{ES}$ was 3579 (2280). The change in the MAUC was $< 10\%$. There was no statistically significant difference between controls and ES using a two-tailed, paired Student's *t*-test ($P = 0.1109$).
Conclusion Unlike the effects of brief magnetic or prolonged ES of pudendal afferent nerves on idiopathic DI and DH, prolonged ES did not significantly suppress the bladder instability secondary to obstructive BPH. These findings suggest that this type of instability does not rely on sacral reflex mechanisms and supports the view that it has a peripheral pathophysiological origin.
Funding: Grant from St Peter's Trust for Kidney, Bladder and Prostate Research

P156

Use of low-frequency surface electrical stimulation in idiopathic detrusor instability

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Introduction Low-frequency surface electrical stimulation has been proposed as an alternative treatment modality in idiopathic detrusor instability (DI). We describe a prospective randomized placebo control study.
Patients and methods Thirty-two patients with urodynamically confirmed idiopathic DI resistant to anticholinergic therapy were studied. Patients were randomized to receive treatment at the dermatomes S2–3 (11), T12 (11) or sham stimulation (10) for 3 weeks; transcutaneous electrical nerve stimulation (TENS) was used. The placebo machines were identical to the genuine machines although not functional. Patients were assessed with a validated questionnaire and a formal urodynamic study before and after treatment. The Wilcoxon signed-rank test was used to analyse the results.
Results Twenty-six patients (15 women and 11 men) completed the study (mean age 51.7 years). There was a statistically significant reduction in symptom score in S2–3 group ($P < 0.05$) and no significant change in the T12 and placebo groups. However, there was no statistically significant reduction in the urodynamic variables in all groups, see Table.

Mean change in urodynamic variables	*Dermatome S2–3*	*T12*	*Sham*
Symptom score	−9.5	−6.6	+10.7
Maximal cystometric capacity (mL)	+19.12	+53.3	+36.4
First desire to void (mL)	−10.75	−27.6	−3.4
Maximum amplitude of contraction waves (cmH_2O)	−10.7	+2.8	+24.7

Conclusion Despite a significant reduction in the symptom score in patients treated at S2–3 there was no significant change in the urodynamic variables.

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Plantar pedal neurostimulation to improve the overactive bladder

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Introduction Modulation of sacral nerve activity is effective for treating patients with intractable overactive bladders, but present techniques are invasive. Having previously shown improved bladder storage using noninvasive central sacral dermatome neurostimulation, we studied the effect of peripheral (pedal) dermatomal application.
Patients and methods The study included 38 patients (mean age 52.3 years, male to female ratio 0.6) with refractory overactive bladders (18 detrusor instability, eight detrusor hyper-reflexia and 12 sensory urgency). All patients underwent multichannel urodynamic filling cystometry at 30 mL/min fill. After emptying the patient's bladder, cystometry was repeated whilst applying neurostimulation bilaterally via the plantar pedal sacral dermatomes at 10 Hz and a pulse width of 200 ms in continuous mode at the maximum tolerated amplitude in the study patients (19), whilst the control group (19) underwent a second fill with no neurostimulation. The results were assessed using a paired Student's *t*-test and the nonparametric Mann–Whitney *U*-test.
Results There were no significant differences in urodynamic values between study and control groups when not stimulated, nor were there any differences between values in the control (no stimulation) group. When neurostimulation was applied to the study patients they showed significantly increased mean (range) volumes at first desire to void (+52.1 mL, 31–49, $P = 0.01$), strong desire to void (+53.1 mL, 30–76, $P = 0.009$) and capacity (+61 mL, 45–79, $P = 0.008$) with no significant rise in filling pressure. In patients with detrusor instability neurostimulation delayed the mean (range) time to first unstable contraction by 75.3 (61–230) s ($P = 0.007$). The mean amplitude of detrusor contractions in patients with detrusor hyper-reflexia was reduced by 14.0 (1–27) cmH_2O ($P = 0.01$).
Conclusion Plantar pedal neurostimulation significantly improves bladder storage characteristics in patients with overactive bladders, suggesting that this may be an effective
treatment option for such patients.

P158

Transcutaneous electrical nerve stimulation in the disabled patient with urinary problems

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Introduction Urinary problems have an impact on the physical, psychological and economic lives of patients, more so if the disability makes toileting more difficult. Transcutaneous electrical nerve stimulation (TENS) has been used successfully to treat urinary problems arising from non-neurological causes. The aim of this study was to test its efficacy in patients with urinary symptoms secondary to neurological disorders.
Patients and methods Forty-four patients (mean age 50.8 years) with varying neurological problems (multiple sclerosis being the most common) were prospectively recruited into the study. All patients kept records of the frequency of micturition, incontinence, pad use and change of clothing, completed Frimodt-Moller urinary symptom

questionnaires, quality-of-life scores before and after treatment, and underwent urodynamics before and 6 weeks after treatment.
Results Thirty-four patients completed the study; irritative symptom scores showed a significant reduction ($P = 0.003$) after TENS. The diaries showed a reduction in 24-h frequency of micturition ($P = 0.013$), incontinence episodes ($P = 0.04$) and changing of clothes ($P = 0.028$). The only significant urodynamic changes were an increase in postvoid residual volume ($P = 0.03$) and increase in volume leaked when TENS was on ($P = 0.003$). There were no significant changes in quality-of-life scores.
Conclusion TENS applied to sacral dermatomes had a minimal effect on urodynamic values but significant effects on irritative voiding symptoms, episodes of incontinence and changing of clothes. Eighteen patients continue to use TENS one year after the study. We have shown TENS to be a useful method of treatment in disabled patients with problematic urinary symptoms.

P159

Resolution of detrusor hypertrophy after relief of BOO: a clinical study

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Introduction The lack of a quantitative measure of detrusor hypertrophy has meant that little is known about the natural history of the process in man. An ultrasonographic technique for estimating bladder weight was recently described [*J Urol* 1997; 157: 476–9] and has many potential applications. The aim of this study was to determine a reduction in ultrasonographically estimated bladder weight (UEBW) after the relief of BOO.
Patients and methods Serial measurements of UEBW, flow rate (where possible) and IPSS were made in seven men presenting with acute painful retention of urine and seven men undergoing elective prostatectomy for LUTS. In the former group all men were assessed within 72 h of catheterization and were followed at 2, 6 and 12 weeks regardless of whether the catheter remained. Any intervening medical or surgical treatment was documented. The latter group were assessed before and at the same intervals after surgery.
Results For patients presenting in acute retention the median (range) age was 67 (53–85) years and the residual volume 949 (500–1600) mL. One patient had a successful trial without catheter after commencing α-blockers, five men underwent TURP and the patient with the highest residual volume retained an indwelling catheter throughout the study period. The mean UEBW decreased from a retention value of 140 g to 83 g at 12 weeks (59% reduction). For those with LUTS, the median age was 73 (59–75) years, the IPSS 24 (5-31), the maximum flow rate 7 (3–12) mLs, the postvoid residual 115 (0–1000) mL and the Abrams-Griffiths number 92 (26-135). Six patients had had a successful trial without catheter by one week after surgery and all were voiding satisfactorily at the 12-week follow-up. The UEBW fell from a mean before surgery of 148 g to 93 g (63%) at 12 weeks.
Conclusions These results suggest that detrusor hypertrophy resolves rapidly after both elective prostatectomy and the relief of acute urinary retention. It seems likely that this corresponds to an improvement in contractility, as seen in the rabbit bladder [*J Urol* 1990; 143: 600–6] and raises the possibility that UEBW could be used as a marker of bladder function. However, the marked variability of UEBW values seen in this study precluded the attainment of statistical significance and further development of the test is required.

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A prospective study of PGE2 and bethanechol for the treatment of detrusor hypocontractility

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Introduction PGE2 and bethanechol chloride (BC) have been used in isolation for the treatment of detrusor hypocontractility, with little clinical benefit. This prospective randomized double-blind study aims to test the hypothesis that the combination of intravesical PGE2 and oral BC are additive or synergistic in improving bladder emptying.
Methods Nineteen patients with detrusor hypocontractility (17 men and two women) were eligible and were randomized to one of two treatment groups. All had residual urine volumes (PVR) consistently > 300 mL, and most were reliant on CISC. The experimental treatment group (nine patients) received once weekly intravesical PGE2 (1.5 mg in 20 mL 0.9% saline) plus BC 50 mg four times daily, for a total of 6 weeks. The second group (10 patients) received a once weekly instillation of saline together with placebo tablets, again for 6 weeks.
Results Before treatment the median (interquartile range) PVR was 426 (405–480) mL for those receiving the experimental combination. This decreased to 325 (290–352) mL after completing the treatment ($P < 0.015$). In the placebo group the median pretreatment PVR was 538 (350–775) mL and 538 (350–775) mL after completing the 6-week course ($P = 0.09$). Four of the patients receiving the active combination reported a symptomatic improvement and were able to reduce the frequency of CISC.
Conclusion The combination of BC and PGE2 had only a modest therapeutic effect compared with a placebo combination. Whilst we would not recommend this treatment on a routine basis, it may be useful for the occasional treatment of patients with hypocontractility. Interestingly, the modest reduction in PVR appears to be maintained at 1 year.

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The ultrastructure of the hypocontractile detrusor

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Introduction Qualitative electron microscopic studies of the human detrusor have identified precise structural changes for various voiding dysfunctions, including impaired detrusor contractility [*J Urol* 1997; 157: 1783–1801]. It is proposed that the criteria used to define these ultrastructural patterns are precise and reproducible. The specific morphological features present in those with detrusor hypocontractility have been termed the degeneration pattern. This prospective study aims in part to test these proposals.
Patients and methods Twenty patients (18 men and two women, mean age 63 years, range 32–87) with hypocontractility were biopsied, as were six controls (mean age 57 years, range 35–73). Multiple muscle biopsies were taken from each patient using the cold-cup technique. Specimens were processed for electron microscopy (EM) using standard methods.
Results The criteria of the degeneration pattern were present in all patients with hypocontractility. These included the presence of widespread disruptive muscle cell profiles with disruption of cell organelles and ultimately cell lysis. These features were present in over half of randomly studied fields. In addition, seven patients (all with a bladder capacity of > 1200 mL) had indistinct muscle fascicle cell arrangement with excessive deposits of collagen and elastic fibres between widely separated muscle cells, and in the interstitium. It has been suggested that this represents the hyperelastosis pattern found in chronic overdistension. These morphological appearances were not present in any of the controls.
Conclusion This early work appears to support a morphological basis for detrusor hypocontractility and reinforces the feasibility of EM as a potential diagnostic tool. The hypocontractile detrusor has distinct ultrastructural appearances that are easily recognisable

from the normal age-matched detrusor. Detailed quantitative studies are forthcoming.

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Can oral cimetidine influence bladder histopathology in patients with painful bladder syndrome: a prospective, randomized, double-blind, placebo-controlled trial

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Introduction Painful bladder syndrome (PBS), part of the spectrum of painful bladder disease, is a condition of protracted symptoms of suprapubic pain, frequency and nocturia, with no evidence of infection. Mucosal angiogenesis and a chronic inflammatory infiltrate are constant histological features. Oral cimetidine has been shown to be effective in the symptomatic treatment of PBS. The aim of this study was to assess whether cimetidine treatment has a measurable effect on the histopathology of the bladder mucosa when compared with placebo.

Patients and methods Thirty-six patients (mean age 42 years, range 23–73, 35 women) diagnosed with PBS were entered into a prospective, randomized, double-blind study with placebo and cimetidine. Treatment comprised 400 mg cimetidine twice daily for 3 months. Bladder biopsies were taken before and after treatment. Specimens were routinely processed, stained with haematoxylin and eosin, EVG to detect fibrosis and muscle, toluidine blue for mast cells, periodic-acid Schiff/Alcian Blue for glycosaminoglycan (GAG) layer and by immunostaining for B and T cells.

Results At 3 months, 34 of the 36 patients were available for follow-up. There was no significant qualitative change in the GAG layer, basement layer or detrusor muscle collagen deposition when the two groups were analysed. The number of submucosal blood vessels remained unchanged between the groups, both before and after treatment. At the end of the study, the T cell infiltrate was reduced in the cimetidine group; the median (range) before and after treatment were 203 (142–390) and 193 (86–367), and was marginally increased in the placebo group, at 243 (172–515) and 250 (135–397), respectively. These results were not significantly different ($P > 0.3$ and $P > 0.2$, respectively).

Conclusion Oral cimetidine remains an effective symptomatic treatment for patients with PBS. There appears to be no convincing evidence that histological changes occur as a result of treatment at the cell level. Cimetidine is known to have an immunosuppressive action and it is proposed that this may be one way in which this treatment exerts its effect without altering the cell/tissue composition of the bladder wall.