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Tuesday 26 June 10.30–11.45
Surgical Techniques

18

Applied anatomy for laparoscopic access

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Introduction The incidence of complications for urological laparoscopic procedures in our institution is ≈ 9.2% (35/140). Almost half of these were vascular injuries and could in retrospect have been avoided with a more detailed knowledge of anatomical variations of the inferior epigastric and the bifurcation of the great vessels.
Material and methods Two hundred randomly selected post-contrast medium CT scans of the abdomen and pelvis were assessed with the help of two radiologists. The site of the umbilicus, anterior superior iliac spines (ASIS) and the various relationships of this mobile and fixed point, with the great vessels were measured. Eighty-nine patients undergoing abdominal ultrasonography for various indications were also assessed with colour Doppler ultrasonography to identify the position and course of the inferior epigastric arteries (IEA).
Results The median (interquartile range) of the distances between the umbilicus to the aortic bifurcation (AB), from the ASIS to the AB and from the umbilicus to the venous confluence were respectively −8.0 (28.8), 48 (16) and −24.9 (32) mm; the mean (range) angle of the umbilicus with the AB was 21.6 (14–34)°. The mean (range) distance from the IEA to the midline was 36.2 (10–48) mm and from the IEA to the ASIS was 100 (80–140) mm.
Conclusion The position of the umbilicus is variable and should not be relied upon for access planning. The relationship between the level of the ASIS and the AB is more consistent. Using this landmark will reduce the risk of vascular injury. Secondary port injury will be minimized by port insertion >15 mm lateral to the midline. While we recommend the Hasson approach for the primary port, major vascular injury will be further minimized if the trocar (or, if used, the Veress needle) is inserted at an angle of >34° to the vertical.

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Long-term outcomes of brachiobasilic transposition fistulae for haemodialysis

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Introduction The transposed basilic vein to brachial artery arteriovenous fistula provides secondary vascular access for haemodialysis. We report the long-term results of such fistulae and assess the influence of patient-related variables.
Patients and methods Eighty brachiobasilic fistulae were created in 77 patients (mean age 48.4 years, range 8–77). The mean (median, range) follow-up was 13 (8, 0.03–49) months.
Results In all, 72 (90%) fistulae developed primary patency and 77 (96%) secondary patency; 69 (86%) were used for dialysis while 11 (14%) were never used. Of the 80 fistulae 48 (60%) were patent at follow-up, including 36 (45%) that are still in use. Seven patients died with functioning fistulae, four were transplanted and one fistula was not needed. Cumulative secondary patency was 70% at 1 year, 52% at 2 years and 40% at 3 years; 41 (51%) patients developed complications, e.g. thrombosis, infection, stenosis, arm oedema, bleeding, steal syndrome and microaneurysm formation.

Characteristic	*Patent*	*Occluded*
N (%)		
Women	26 (54)	15 (47)
Hypertension	15 (31)	9 (28)
Cardiovascular disease	13 (27)	14 (44)*
Diabetes	8 (17)	4 (13)
Aspirin	8 (17)	7 (21)
Warfarin	7 (15)	5 (16)
Erythropoetin	35 (73)	17 (53)†
Mean (SD)		
Haemoglobin (g/L)	101 (16)	95 (16)
Albumin (mg/L)	37 (5.6)	34 (6.4)
N (%)		
Smoker	15 (31)	10 (31)
Mean (range) previous access	1 (0–5)	1 (0–4)

*$P = 0.02$; †$P = 0.01$, chi-squared test.

Conclusions Brachiobasilic transposition fistulae have good long-term patency rates but tend to fail in those with associated cardiovascular disease. The complication rate, although high (50%) is lower than that reported for PTFE grafts (60–100%). Brachiobasilic fistulae should be used in preference to PTFE grafts for difficult vascular access.

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Self-expanding permanent endoluminal stents in malignant extrinsic ureteric obstruction: 10 years' experience

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Introduction The use of self-expanding permanent endoluminal stents (SPES) in patients with late-stage cancer and malignant extrinsic ureteric obstruction was developed at our institution in 1990, to spare these patients the discomfort of a frequent exchanges of JJ catheters or a permanent nephrostomy tube. This tool provided a useful alternative to JJ catheters and a percutaneous nephrostomy; herein the 10-year experience is reported.
Patients and methods From April 1990 to December 2000, 74 malignant extrinsic ureteric obstructions in 58 patients (16 bilateral) were treated by implantation of a SPES. A Wallstent® was used in 59 ureters and a Nitinol® stent in 15. For good results an exact and standardized technique of implantation is required.
Results In all, 42 SPES (57%) remained patent with no reintervention until the death of the patient, or to date; in 25 SPES (34%) the patency could be maintained by secondary interventions. Only seven renal units had to be abandoned because of rapid tumour progression. In the 26 patients who survived with their cancer for >1 year the median duration of patency was 30 months. There were no infections, no compression of the SPES by the tumour and no erosion of other organs, or any allergic reaction.
Conclusions These results show that SPES are a valuable, safe and effective minimally invasive alternative in the palliative treatment of malignant extrinsic obstruction of the ureter in patients with late-stage cancer.

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Sacrocolpopexy with anterior and posterior PTFE mesh extensions

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Introduction Vault prolapse (VP) after hysterectomy is a common problem and may present with concomitant anterior (cystocele) and posterior (rectocele) pelvic compartment prolapse. The video will demonstrate a new surgical approach to this problem, i.e. sacrocolpopexy with anterior and posterior PTFE mesh extensions (SAPM).
Patients and methods The patient is placed in a modified lithotomy position with their legs in Allen stirrups. A Hegar dilator is placed to position the vaginal vault. A 10–12 cm Pfannenstiel incision is made using a ring retractor. The posterior vaginal wall (PVW) is dissected from the rectum down to the perineal body. A 4×20 cm mesh is sutured distally to the PVW with 1/0 polyester/polybuterate and to the lateral edges of the perineal body bilaterally, alongside the vault and midway in between. The base of the bladder is mobilized 5 cm off the anterior vaginal wall (AVW). Another 4×20 cm mesh is sutured to the AVW and vault. The peritoneum overlying the sacrum S1–2 is incised in the midline. The anterior longitudinal ligament (ALL) is identified between S1–2 and two sutures of 1/0 polyester/polybuterate inserted. The length of the mesh is gauged so that it lies on the curve of the sacrum with no tension and excess mesh is then trimmed. The mesh is then sutured to the ALL and the peritoneum closed over it with 1/0 polyglactin. Nine patients (median age 60 years, range 39–68) underwent SAPM, with a median (range) follow-up of 22 (15–40) months.
Results There were no episodes of recurrent VP. One patient had a recurrent grade 1 cystocele and another a grade 1 rectocele. There were no patients with de novo urgency but one patient had de novo stress incontinence. Two of three patients no longer needed to splint or digitate to empty their rectum. There was no dyspareunia, while two patients had improved vaginal lubrication. There were two patients with a total of three episodes of mesh erosion through the PVW.
Conclusion SAPM is an effective treatment for triple compartment prolapse and incomplete rectal emptying.

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Outpatient ureteroscopy: a practical approach

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Introduction Ureteroscopy is used as a diagnostic and therapeutic procedure, primarily in urolithiasis. Awareness of reduced resources have resulted in increasing pressure to undertake procedures in a day surgery setting. In this study, we evaluated the outcome of day-case ureteroscopy.
Patients and methods Between May 1995 and May 2000, 56 patients underwent 63 day-case ureteroscopic procedures (mean age 47 years, range 19–78). All patients fulfilling local day surgery criteria were scheduled to undergo day-case ureteroscopy, irrespective of stone position or size. Outcomes, including complications requiring immediate or delayed admission, and subsequent inpatient management were reviewed retrospectively.
Results Sixty-three day-case ureteroscopies were undertaken in 56 patients; nine procedures were diagnostic. Therapeutic procedures included 53 for stone disease with ultimately 97% stone clearance, and one ureteroscopy with balloon dilatation of a ureteric stricture. Most patients were discharged with a J stent *in situ*. Of nine patients requiring immediate admission, seven required simple analgesia only; all were discharged on the following day. Eight required delayed admission after discharge from the day surgery unit, of whom four were for stent-related symptoms and three because of infection. No significant predictors of immediate or delayed admission were identified, although a trend towards a beneficial effect of prophylactic antibiotics was apparent.
Conclusion This study shows that ureteroscopy can be successful as a planned day-case procedure, with few patients requiring re-hospitalization. Adherence to standardized protocols for analgesia and antibiotic prophylaxis, and a more selective approach to ureteric stenting, may result in a further reduction in the need for hospitalization after this procedure.

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Urological complications after 1200 living-donor renal transplants

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Introduction To determine the incidence and management of urological complications after 1200 consecutive live-donor renal transplants, all of which were carried out in one centre. The possible risk factors and the effect on patient and graft survival were also assessed.
Patients and methods Data were retrieved from an electronic database. The incidence of urological complications was recorded and correlated with the relevant risk factors by univariate and multivariate analysis. The effect on patient and graft survival was also determined by Kaplan–Meier statistics.
Results There were 100 complications in 96 patients (8%); urinary leaks were seen in 37 and ureteric strictures in 23. Lymphoceles causing ureteric obstruction were encountered in 17 patients. Percutaneous needle biopsy was complicated by haematuria and by clot anuria in six. Late complications included 11 cases of stones, four of bladder malignancy and two of haemorrhagic cystitis. There was evidence that the age of the recipients (<10 years), method of establishing urinary continuity (uretero-ureteric) and a high dose of steroids had an independent positive effect on the incidence of urological complications. However, their development did not influence the survival of the graft or patient.
Conclusion When there is meticulous attention to technical details, renal transplantation should be associated with a minimum of urological complications. Early intervention with percutaneous drainage reduces morbidity and the likelihood of loss of graft function. Proper and prompt management should not affect the graft and/or the patient's survival.

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Laparoscopic renal surgery: an alternative transperitoneal approach

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Introduction Laparoscopy has rapidly gained acceptance as a safe and effective approach to renal surgery. Most surgeons create a pneumoperitoneum with the Veress needle or Hasson technique via an umbilical port, with the patient semi-supine. We report our experience with a technique developed independently, which we have used with no complications in over 150 laparoscopic procedures. This technique offers a safe and effective alternative to the 'standard' approach for laparoscopic renal surgery.
Methods With the patient catheterized and in the full lateral position as for the loin approach to the kidney, a muscle-splitting incision is made ≈ 5 cm medial to the anterior superior iliac spine on the side of operation. The peritoneum is grasped between artery clips, incised

under direct vision and a 12 mm camera-port inserted. After insufflation, two further operating ports are inserted under direct vision through the lateral edge of the rectus muscle, just superior to the umbilicus and ≈ 5 cm inferior to the costal margin. A fourth port can be inserted in the flank if required.
Results There were no complications using this method for developing a pneumoperitoneum in over 150 laparoscopic procedures on the kidney.
Conclusions Our experience has established that this is a safe and effective alternative approach for laparoscopic renal surgery. Although the perspective obtained with the camera port in the iliac fossa may initially seem unusual, it is a distinct advantage for the operator to work without being inadvertently obstructed by the camera-man.

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Complications of the first 200 cases of laparoscopic nephrectomy

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Introduction Laparoscopic nephrectomy is a technically demanding procedure which requires considerable experience and training. We present the complications of the first 200 laparoscopic nephrectomies and attempt to define risk factors for complications and conversion to open surgery.
Patients and methods Between September 1992 and December 2000, 200 patients who underwent a laparoscopic nephrectomy were entered into the study. Indications for laparoscopic nephrectomy included patients requiring nephrectomy for benign pathology (152), nephroureterectomy for TCC of the upper urinary tract (28) and radical nephrectomy for RCC (20). No tumour had evidence from CT of lymphatic, vascular or perirenal invasion.
Results The overall complication rate was 19%, of which 2% were major and 17% minor. The major complications included two vascular injuries, one fatal myocardial infarction and one perforated duodenal ulcer in a patient with Zollinger–Ellison Syndrome. Of these, the first three occurred in the first 100 cases and the last in the second 100. There is a trend for the major complication rate to decrease with time. The minor complications included eight patients with fever, seven with wound infection, six respiratory and four cardiac complications, three renal haematomas, three urinary retention, two ileus and one port-site bleed. The minor complication rate remained much the same with time, suggesting that these complications may not be solely related to operator experience. There were no intraoperative port-related complications and no injuries to bowel. The conversion rate was 6.5%. Reasons for conversion were major vascular injuries in two, failure to progress in seven and extreme fibrosis in four. The conversion rate remained unchanged when comparing the first 100 with the second 100 cases. There were no conversions ascribable to major vascular injuries in the second 200 cases.
Conclusions Laparoscopic simple nephrectomy, radical nephrectomy and nephroureterectomy can be effective and reasonably safe. Proper patient selection with strict adherance to basic surgical principles helps to reduce complications and conversion during laparoscopic renal surgery. The complications and conversion rates are acceptable and we feel that many patients undergoing renal surgery should be offered the laparoscopic approach.

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Superficial TCC of the upper urinary tract can be treated primarily by endoscopic ablation and surveillance similar to superficial TCC of the urinary bladder

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Introduction Electrocautery resection and endoscopic surveillance is the treatment of choice for superficial TCC of the urinary bladder. Superficial TCC can be ablated effectively with the holmium laser; encouraging results with holmium laser resection (HoLR) of superficial TCC of the upper urinary tract (UUT) in patients with bilateral disease or solitary kidneys initiated a prospective study to evaluate whether flexible ureteroscopy combined with HoLR and endoscopic surveillance can be regarded as the primary treatment of superficial TCC of the UUT in patients with normal renal function, similar to endoscopic resection and surveillance as the primary treatment for superficial TCC of the urinary bladder.
Patients and methods Twenty-two patients underwent a total of 39 ureterorenoscopic HoLR for superficial ureteric and/or pelvicalyceal tumours; two patients had bilateral disease and six patients had a solitary kidney. Ten patients had one HoLR and 12 patients had 2–6 HoLR sessions, because they had recurrent tumour growth. The HoLR was administered with 7.5 F rigid and 8.5 F flexible ureteroscopes, a Ho:YAG laser at 5–15 W (0.5–1.0 J, 10–15 Hz) and 220 nm flexible laser fibres. The patients were followed by renal ultrasonography, urine analysis, bladder cytology, cystoscopy and retrograde pyelography every 3 months, and ureteropyeloscopy with UTT cytology and biopsy of suspicious areas every 3–6 months.
Results HoLR of tumours caused no bleeding; no UUT was perforated and no secondary ureteric stricture developed. Histology revealed pTaG1, pTaG2 and pT1G1 tumours. Patients with solitary tumours remained tumour-free (follow-up 3–25 months). All patients with multiple lesions developed recurrent TCC which were re-treated with HoLR. One patient showed progression of tumour stage and grade (pTaG1 to pT1G2) and underwent nephroureterectomy.
Conclusions Flexible ureteropyeloscopy combined with HoLR and careful endoscopic surveillance seems to be safe and effective, and can be recommended as primary treatment of superficial TCC of the UUT, even in patients with normal renal function. However, patients should be able to completely understand the risks of this approach and be fully cooperative. Nephroureterectomy can be reserved for patients with tumour progression or invasive TCC, in the same way as cystectomy is reserved for progressive or invasive TCC of the bladder.

Poster Session 1
10.30–11.30
Basic Science – Physiology

P1

Fine structural features of the deeper cells of the human bladder epithelium

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Introduction The general morphology of the cells of the urothelium have been well described. Superficial 'umbrella' cells are related on their deep surfaces to the apices of a variable number of bipolar intermediate/basal cells, and are attached to these by punctate maculae adhaerentes, as are the adjacent deeper cells one to another. The basal cells end as flattened discoid processes adherent to the basal lamina of the epithelial/lamina propria junction.
Materials and methods Flexible cystoscopic biopsies were obtained from the posterolateral urothelium, from 27 male and female patients investigated for microscopic haematuria, or bladder hyperreflexia. Samples were fixed immediately in 3% glutaraldehyde and processed for transmission electron microscopy.
Results Two additional features of the fine structure of the urothelium are reported: (i) the consistent presence within the basal processes of identifiable basal cells of scattered dense-cored vesicles 150–200 nm in diameter bounded by a bilaminar membrane; and (ii) the presence within the apices of cells attached to the deep surface of the superficial 'umbrella' cells in many, but not all biopsies of flattened or partially dilated vesicular structures, 45×300 nm, in association with numerous mitochondria, Golgi systems and large globular secondary lysosomes.
Conclusions The basal granules may be peroxisomes, or could represent a secretory product to be released into the lamina propria adjacent to the fenestrated endothelium of the subepithelial capillary plexus. The flattened apical vesicles may be primary lysosomes but also show structural similarities to the Birbeck granules of Langerhans cells. The epithelium is freely accessible to cells of the lymphoid system and inflammation of the underlying lamina propria frequently accompanies the presence of the specific vesicles described in the apices of the intermediate/basal cells; do these cells, among other functions, also serve as antigen presenters?

P2

Fine structure of the innervation of the lamina propria in normal human urinary bladder biopsies

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Introduction To characterize the fine structure and distribution of nerves in the lamina propria of the human urinary bladder epithelium.
Patients and methods Biopsies of the lining of the human urinary bladder were obtained by flexible cystoscopy from nine men and eight women (aged 26–69 years) investigated for microscopic haematuria, and in whom there was no evident bladder pathology. The specimens were prepared for transmission electron microscopy and a complete photographic survey made of all nerves, generally 60–160, observed in each sample.
Results The lamina propria innervation was divisible into four constituent elements: (i) terminal branches of peripheral nerves consisting of a few 2–3 μm diameter myelinated fibres and numerous unmyelinated strands, partially or completely invested with a single layer of perineurium; (ii) a diffuse plexus of unmyelinated fibres containing slender axons linking periodic varicosities enclosing 55 nm clear and 60–150 nm dense-cored vesicles, some apparently vasomotor to terminal arterioles, others making close contacts with the flattened smooth muscle cells of the muscularis mucosa; (iii) fine axons lacking Schwann cell ensheathment, either naked, or in intimate association with flattened cells having the cytological characteristics of fibroblasts, in the zone immediately beneath the epithelial basal lamina; and (iv) naked axons within the epithelium between the basal processes of the epithelial cells and the basal lamina, but never extending more deeply into the epithelium. The epithelial and subepithelial axons were generally filled with similar clear and dense-core vesicles with relatively few connecting axons.
Conclusions Despite considerable individual variation, a consistent pattern of innervation could be discerned in this detailed study.
Funding: Napp Laboratories

P3

The electrophysiological properties of *in vitro* generated urothelium

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Introduction The urothelium has a specialized morphology that facilitates and maintains its barrier function whilst accommodating changes in urine volume. A human *in vitro*-generated urothelium that possesses these morphological and functional properties would have a diverse range of potential applications, specifically in the fields of tissue engineering and reconstructive bladder surgery. We have measured the electrophysiological properties of *in vitro* generated urothelium to assess its barrier function.
Materials and methods Snapwell membranes were seeded with human urothelial cells, cultured from samples of normal urothelium obtained at surgery. At confluency the calcium concentration of the medium was either maintained at 0.09 mmol/L or increased to 2.0 mmol/L. The electrophysiological parameters of the urothelial monocultures were measured using a modified Ussing chamber and electronic volt-ohmmeter. The transepithelial electrical resistance (TER) was calculated from the measured transepithelial potential difference and short circuit current.
Results When cultured in low-calcium (0.09 mmol/L) serum-free medium, urothelial cells formed monolayers. Phenotypically the cells resembled the basal/intermediate cells *in vivo*. They did not form tight junctions and had a low TER (12.8, SD 6.5 Ω/cm^2). Increasing the exogenous calcium concentration upregulated desmosome and tight-junction formation. The stratified monocultures expressed an altered cytokeratin profile and developed an increased TER of 42.0 (11.0) Ω/cm^2.
Conclusion The results show that cellular organization and the acquisition of tight junctions contribute to the barrier function of *in vitro* generated urothelium.
Funding: BUF, Ralph Shackman Trust

P4

Elective ureteric manipulation and recovery of ureteric peristalsis: a chronic pig study

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Introduction Ureteric manipulation or surgery can result in temporary loss of peristalsis. There are no published values for the recovery times; thus recovery in a chronically instrumented pig model was assessed.
Materials and methods Through a percutaneous nephrostomy, a flexible 7 F twin pressure-transducer catheter was placed in five pigs (55–62 kg), with its distal sensor located in the juxtavesical ureter. Peristaltic activity was studied using pressure change (wall tension) recorded from ≈ 4 h (after awakening from anaesthesia) to the 21st postoperative day, in daily 1-h sessions.
Result Nephrostomy urine leakage ceased within 24 h; there was no postoperative dilatation or urinary infection. Measurements at 4 h showed mean (SD) peristaltic frequencies of 1.6 (0.1)/min and an intra-ureteric peak pressure of 3.2 (0.1) kPa. This disappeared 1 and 2 days afterward; the peak pressure reappeared at 3 days and progressively increased until 7 days. The frequency was similarly zero for 2 days and gradually increased to 1.3 (0.1)/min at 7 days; a steady state then ensued. Peristalsis was irregular and in clusters of four waves followed by long inactive intervals; this pattern persisted for up to 5 days but from 7 days a single wave pattern ensued. with peristalsis returning antegradely. The renal pelvic hydrostatic pressure was a continuous 0.1 kPa with only minor irregular peaks at 1–3 days. Rhythmicity with peaks of 0.7 kPa and troughs to 0.1 kPa was established from 4 days.
Conclusion Peristalsis persists initially after manipulation but only after 7 days is normal function re-established. Recovery follows a gradual and hierarchical pattern from proximal to distal.
Funding: Dutch Academy of Sciences

P5

Effects of β-adrenergic stimulation and inhibition on ureteric peristalsis

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Introduction Ureteric peristalsis requires myogenic activity which presumably is autonomically neuromodulated. Evidence of β-adrenergic control is presented.
Materials and methods Five pigs (55–62 kg) were used in a chronically instrumented model. Through a percutaneous nephrostomy, a flexible 7 F twin pressure-transducer catheter was positioned with the distal sensor located in the juxtavesical ureter. From 1 week after surgery a daily 5 h drug study session using a pre-planned random schedule was undertaken. Several sessions were carried out and results recorded. Intravenous isopreterenol (0.005 mg/kg) and propranolol (5 mg) were used; the pigs were then killed at the end of the study.
Result There was no postoperative infection or dilatation. Isoproterenol resulted in rapid hypotension, with a mean (SD) pressure of 14.6/8.0 (0.5/0.3) kPa, and in the control 20.0/12.0 (0.3/0.3) kPa ($P < 0.05$), a tachycardia of 180 (9)/min, control 75 (7)/min ($P < 0.05$), and extreme dermal vasodilatation; ureteric peristalsis ceased. Propranolol also resulted in a hypotension of 16.6/7.9 (0.4/0.1) kPa; control 20.6/11.3 (0.3/0.5) kPa ($P < 0.05$) but with bradycardia of 65 (3)/min; control 80 (2)/min ($P < 0.05$). Increased ureteric wall tension was manifested by a rise in the amplitude of peak ureteric pressure, at 5.6 (0.1) kPa; control 5.3 (0.1) kPa ($P < 0.05$), and peristaltic frequency, at 2.0 (0.3)/min; control 1.3 (0.1)/min ($P < 0.05$).
Conclusion In this conscious-pig model, β-adrenergic stimulation resulted in a dramatic down-regulation of ureteric peristalsis, while inhibition caused an up-regulation. This study confirms the presence of autonomic neuromodulation of ureteric peristalsis.
Funding: Dutch Academy of Sciences

P6

The first experience of magnetic ureteric stimulation

A.J. Young, R.A. Miller*, M.J. Kellett† and B. Lynn *Department of Physiology, University College London, *Whittington Hospital, and †Institute of Urology and Nephrology, London, UK*

Introduction Electrical stimulation of the renal calyces/pelvis causes release of tachykinins from unmyelinated sensory nerve endings. These act as neurotransmitters and are powerful stimulants of pelviureteric motility. In theory, the effect of electrical stimulation on the upper renal tract should be repeatable with magnetic stimulation. The aim of this study was to investigate whether a high-power magnetic stimulator (HPMS, Digitimer Ltd.) could produce ureteric peristalsis in a pig model.
Materials and methods A midline laparotomy and cystotomy were performed under general anaesthesia in four female Large White pigs (body weight 40–48 kg). A dual sensor, 4 F ureteric pressure catheter (Gaeltec Ltd.) was inserted along the left ureter to record peristalsis. A 'figure-of-eight' coil was then placed anterior to, but not in contact with, the kidney. Magnetic stimulation at various intensities (up to 7.2 V/cm, 270 ms) was then applied.
Results Ureteric peristalsis was consistently produced with the device at 100% output in all experiments. The threshold for peristalsis was 65–100% of HPMS output between experiments. Magnetic stimulation caused strong body-wall contraction. However, control experiments indicated that these contractions alone were unlikely to be indirectly triggering peristalsis.
Conclusions This study showed that HPMS can initiate ureteric peristalsis. This is most likely through the release of tachykinins, as occurs with electrical stimulation. Therapeutic possibilities in upper tract stone disease can now be explored.
Funding: DTI SMART grant

P7

Impairment of ATP-mediated cavernosal smooth muscle relaxation providing further evidence linking erectile dysfunction to BOO

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Introduction There is growing evidence to suggest that patients with a high symptomatic score of BPH have an increased risk of erectile dysfunction (ED). ATP potently relaxes both human and rabbit cavernosal smooth muscle (CSM) via P2Y receptors, and some cavernosal nerves are known to release ATP. We have shown that cavernosal nitric oxide signalling is impaired in a model of BPH. To establish further evidence of a functional link between BPH and ED we compared the ATP-response of CSM from rabbits with partial BOO to controls.

Materials and methods Partial BOO was surgically produced in six adult male New Zealand White rabbits. Six weeks later, after cervical dislocation, CSM strips were mounted in organ baths and pre-contracted with phenylephrine (10 μmol/L) in the presence of atropine (1 μmol/L), guanethidine (5 μmol/L) and indomethacin (10 μmol/L). ATP was added, concentration–relaxation curves produced and the IC_{50} calculated. Experiments were repeated in six normal controls and in the presence of L-NAME, a nitric-oxide synthase inhibitor.
Results The IC_{50} for ATP-induced relaxation in CSM of rabbits with partial BOO was 2.9 mmol/L, compared with 1.7 mmol/L in the control group. ATP-induced relaxation of CSM was significantly impaired ($P = 0.01$) compared with the control group. The addition of L-NAME did not significantly affect the IC_{50}.
Conclusion These results provide evidence that impairment of ATP-induced CSM relaxation may be involved in the pathogenesis of ED associated with BPH and that in the rabbit CSM, ATP acts independently of nitric oxide.

P8

The functional urothelium: an underestimated quantity

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Introduction It is generally accepted that the ureter is a simple conduit for the passage of urine, the bladder an organ for the storage of urine with controlled emptying, and the urothelium an inert barrier to contain the urine. We propose that the urothelium is an active interface between the urine and the extracellular space. By sampling renal pelvic and bladder urine, a simple biochemical comparison between these urine sample should provide supporting evidence.
Materials and methods Adult patients (42) undergoing upper urinary tract surgery for stone disease were included in the study. Paired renal pelvis and bladder urine samples were obtained in 30 patients; the urine analyses included culture, pH and osmolality measurements.
Results The mean (SD) pH of the renal pelvic and bladder urine was 6.36 (0.84) and 6.61 (0.61), respectively ($P = 0.03$); the osmolality of 18 paired samples was 343 (182) and 477 (175) mosmol/kg, respectively ($P = 0.016$). These data support the hypothesis. Six paired pelvic urine specimens were collected; there was no significant difference in pH or osmolality between left and right samples.
Conclusion These data suggest a dynamic movement of solutes along the urinary tract distal to the collecting ducts. Urinary tract disease in adults and children is multifactorial and the associated problems are not always explained in terms of neuromuscular physiology. The work described here forms the basis for further investigations into the effect of the functional urothelium and urine biochemical composition on urodynamics and urinary tract disorders such as VUR and detrusor instability.

P9

The influence of low-power laser irradiation on testicular microvascular blood flow in an experimentally cryptorchid rat model

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Introduction Testicular microvascular blood flow (TMBF) is known to induce vasomotion; the aim of this study was to investigate the effect of experimental cryptorchidism on TMBF and its possible response to low-power laser irradiation (LPLI).
Materials and methods Unilateral cryptorchidism was induced experimentally for 14 days in 20 immature Wistar rats; at 15 days the testes were replaced surgically into the scrotum. The animals were then prepared for testicular micromanipulation, with the contralateral testicles used as the control. TMBF was monitored continuously in real time using a laser Doppler flowmeter. Cryptorchid testes were then irradiated by a low-power helium-neon laser at a power density of 12.72 mW/cm^2 and 8.5 J/cm^2.
Results After 14 days the cryptorchid testes showed a significant decrease in mean (SD) microvascular flow, at 6.2 (1.9) PU; in the contralateral testes the flow was 14.8 (1.4) PU ($P < 0.01$). Immediately after LPLI the microvascular flow increased to control values of 13.2 (1.7) PU within 2 h ($P < 0.01$) and then returned to the initial value. Only on the third day and after three courses of LPLI was the microvascular flow stable and no different in the contralateral and ipsilateral testicles.
Conclusion Experimental cryptorchidism for 14 days leads to a significant decrease in TMBF. The use of LPLI on the affected testicles increases the TMBF, showing that TMBF changes are reversible after this period of cryptorchidism. The mechanism underlying changes in TMBF remains unknown.

Poster Session 2
Andrology

P10

Cycling and penile oxygen pressure: the type of saddle matters!

U. Schwalzer, F. Sommer, C. Cremer, T. Klotz and U. Engelmann *Department of Urology, University of Cologne, Germany*

Introduction Temporary genital numbness is a common side-effect of long-distance cycling and cases of impotence have been reported. Recent reports suggest the cause is irritation of the penile nerves, by compression against pelvic bones, but a second cause of sexual dysfunction could be the decrease in penile blood flow by perineal compression of the vulnerable vessels during bicycling while seated. We tested four different bicycle saddles to assess their influence on penile perfusion.
Subjects and methods The study included 20 healthy athletic young men (mean age 26.8 years, range 21–31) with no history of erectile dysfunction. The transcutaneous oxygen pressure (which correlates with arterial and tissue oxygen pressure at the glans of the penis) was measured using a transcutaneous measurement device. All men had the oxygen pressure measured while standing before cycling and then during cycling while seated on a stationary bicycle. Four different designs of saddle were used: (A) a narrow heavily padded seat; (B) a narrow medium-padded saddle with a V-form groove in the saddle nose ('body geometry'); (C) a wide unpadded leather saddle; and (D) a wide medium-padded special seat for women, with no saddle nose.
Results During cycling on all saddles there was a decrease in penile oxygen pressure, reflecting perineal compression; however, there were significant differences. The mean minimum oxygen pressure (mmHg) was 11.8, 20.8, 25.3 and 62.3 for saddles A to B, respectively; the respective decrease from the initial pressure was 82, 72, 64 and 20%.
Conclusions Cycling while seated leads to compression of the perineal and penile arteries, with a consecutive decrease in penile perfusion but there are significant differences among different saddle types. The most important factor in protecting penile perfusion is not the extent of padding but the width of the saddle, whereby sufficient support to the pelvic bones avoids compressing the perineal soft tissue.

P11

A conservative treatment option for curing venous leakage in impotent men

F. Sommer, A. Eusan, T. Majd, T. Klotz and U. Engelmann *Department of Urology, University of Cologne, Germany*

Introduction The incidence of impotence after the age of 40 years increases rapidly, from 5.6% to 61% in men >70 years old. Investigations show that 35–60% of these men have venous leakage or insufficiency of the veno-occlusive system. Our study group has shown that contractions of the ischiocavernosal (IC) and bulbocavernosal (BC) muscles are important in the process of penile rigidity. The aim of the present study was to assess the influence on penile rigidity of a specially designed IC and BC (pelvic floor) exercise programme (VigorRobic®) in patients with mild to medium venous leakage or insufficiency of the veno-occlusive system.
Patients and methods Fifty-two impotent men entered the placebo-controlled trial. All patient were assessed using a standard protocol which included a history and examination, colour flow duplex Doppler ultrasonography, and where indicated, Rigiscan® nocturnal penile tumescence testing and/or dynamic infusion caversonometry and caversonography. The VigorRobic training programme was given three times, in weekly sessions. The potency of each man was evaluated using a German questionnaire on ED (KEED) at the first visit, after 4 weeks and after 3 months. Cavernosometry was performed after 3 months to obtain penile rigidity values.
Results Twelve patients chose other treatment options (one in the VigorRobic group and 11 from the placebo group) so 25 patients were assigned to VigorRobic exercises and 14 to placebo. There was a significant difference in the subjective results of the VigorRobic group (68% increase in potency) compared with placebo (14% increase). There was also an improvement in penile rigidity in the VigorRobic group (mean 42%) after 3 months.
Conclusion Pelvic floor exercise is a realistic conservative alternative treatment option in patients with mild to medium degrees of venous leakage or insufficiency of the veno-occlusive system.

P12

The management of idiopathic stuttering priapism

R. Rees, S. Goorney, J. Pryor and D. Ralph *Institute of Urology, Middlesex Hospital, London, UK*

Introduction Idiopathic 'stuttering' or recurrent priapism is a distressing problem and presents a difficult management problem which is often refractory to conventional treatment. It is a well-described complication of sickle-cell disease (42% of patients), where stilboestrol has been shown to be effective in preventing attacks. However, we now present 12 cases of idiopathic stuttering priapism who presented over a 5-year period, and underwent successful treatment with medical or surgical therapies.
Patients and methods The notes of 12 consecutive patients presenting with recurrent priapism were retrospectively analysed. Their mean (range) age was 49 (28–71) years and mean duration of symptoms 4 (2–10) years. All patients had a normal haematological picture and a low-flow picture on Doppler assessment.
Results Priapism was treated successfully in all patients at a mean follow-up of 12.2 (2–24) months. Four were stabilized on goserelin, although one later opted for a prosthesis to protect fertility. Three patients achieved a good result with cyproterone acetate, and oral procyclidine was successful in two. However, initial procyclidine was unsuccessful in four patients, one of whom underwent insertion of an intrascrotal phenylephrine-delivery pump. One patient opted for orchidectomy (and developed mild gynaecomastia), and a further patient had a penile prosthesis inserted.
Conclusion Stuttering priapism is a debilitating condition for which we describe several novel successful treatment options.

P13

Management of low-flow priapism with the immediate insertion of a penile prosthesis

R. Rees, S. Goorney, J. Peters and D. Ralph *Institute of Urology, Middlesex Hospital, London, UK*

Introduction Failed conservative management of low-flow priapism usually results in severe cavernosal fibrosis. The penis is subsequently strictured and the delayed insertion of a penile prosthesis difficult. This paper reports the management of this condition by the immediate insertion of a penile prosthesis.

Patients and methods Three Caucasian patients presented with low-flow priapism of a mean (range) duration of 47 (32–60) h. All had failed conservative management with the instillation of α-adrenergic agents, and one patient had already had a Winter shunt placed elsewhere. The immediate management consisted of the insertion of a Mentor malleable prosthesis in two patients, and an AMS 700CX in the third. One of the malleable prostheses was subsequently changed to an inflatable prosthesis as a planned procedure. Extensive antibiotic prophylaxis was given.
Results There were no postoperative complications in any patient, and none of the patients has lost any penile length. Two of the three patients are sexually active at 6 months follow-up.
Conclusion The immediate insertion of a penile prosthesis for prolonged low-flow priapism is simple and maintains penile length. This should always be offered to the patient at the initial presentation, as the outcome is better than a delayed insertion.

P14

Priapism in sickle-cell anaemia: an international multicentre study

A.B. Adeyoju, A. Olujohungbe, A. Yardumian, D. Bareford, A. Akenova, O. Akinyanju, K. Cinkotai *Department of Urology, Blackburn Royal Infirmary, Blackburn, UK*

Introduction Priapism is known to be common among patients with sickle-cell anaemia. However, the precise characteristics of the condition in this population is poorly documented. We set out in this international multicentre study to define the incidence, risk factors and complications of priapism in a large population of patients with sickle-cell anaemia taken from five centres in the UK and Nigeria.
Patients and methods A questionnaire was developed and administered to patients with sickle-cell anaemia. Questions were designed to define the occurrence, nature, precipitants, frequency, duration, treatment and complications of priapism. Acute (severe) priapism and the recurrent 'stuttering' type were distinguished.
Results In all, 130 patients from the five participating centres completed the questionnaire (mean age 25 years, SD 11, range 4–66); 102 (78.5%) patients were homozygous HbSS genotype, 19 (14.6%) were HbSC genotype and two (1.5%) were Hb SbThalassaemia. Overall, 46 (35%) patients reported a history of priapism; of these, 33 (72%) had a history of 'stuttering' priapism, while 24 (52%) had had an acute episode of priapism. The mean age of onset of priapism was 15 years, with 75% of patients having the first episode before their 20th birthday. Sexual activity was the most frequent precipitating factor, with fever and/or dehydration being the next most common. Of 46 patients, 10 (21%) with a history of priapism reported having erectile dysfunction. A similar proportion reported dissatisfaction with sexual intercourse, including a fear of engaging in sexual activity.
Conclusion The incidence of priapism among patients with sickle-cell anaemia is high (35%). The treatment of this condition in this population of patients remains unstandardized. The implications of priapism for erectile and sexual function are significant, and is documented in this large series. This study highlights the need for an increased awareness of the problems associated with priapism among patients, families and medical professionals.
Funding: Pfizer Pharmaceuticals

P15

Circumcision: a refined technique and 5-year review

S.C. Tucker, J. Cerqueiro, G.D. Sterne and A. Bracka *Department of Plastic and Reconstructive Surgery, Wordsley Hospital, Stourbridge, West Midlands, UK*

Introduction The vast majority of circumcisions currently undertaken in the UK are for phimosis or balanitis, and the patients are not seeking the 'denuded glans' appearance of a ritual circumcision. We present a refinement of the sleeve technique of circumcision, which involves Horton's test to define the proximal incision margin (thus preventing excessive excision of foreskin), and bipolar electrodissection. It is suitable for both adults and children.
Patients and methods The 204 patients undergoing circumcision at our unit in a 5-year period were reviewed.
Conclusion This technique is safe, with a haematoma rate of only 1.4% and an overall complication rate of 3%.

P16

Squamous cell carcinoma-associated antigen levels follow the course of disease in patients with penile carcinoma

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Introduction In cervical carcinoma, serum levels of squamous cell carcinoma (SCC)-associated antigen have been useful in following the course of the disease. However, only one group has reported the use of the SCC antigen in penile carcinoma [*Urology* 1990; 36: 315–7]. We monitored levels of SCC antigen in the management of localized and metastatic penile SCC.
Patients and methods SCC-associated antigen levels were measured using a microparticle enzyme immunoassay in patients presenting with penile carcinoma and followed sequentially during treatment.
Results Two patients with a localized tumour and no recurrence on follow-up had normal marker levels after treatment (<1.5 μg/L). The mean and median (range) SCC antigen levels were 3.6 and 3.5 μg/L (0.6–4.5, $n=5$) in patients with nodal metastases. In one patient, the SCC antigen level was less than normal after removing the primary tumour but increased sequentially before metastases were found on imaging in the lymph nodes, declined after lymph node dissection and increased again after metastases developed elsewhere.
Conclusions SCC antigen levels were raised in three of five patients with nodal metastases from penile SCC and normal in three patients with no metastases after treating the primary lesion. These early data suggest that a raised SCC antigen level may herald nodal metastases before they can be found on CT or MRI, and follow the response to treatment.

P17

Dynamic MRI for staging penile cancer

S.R. Goorney, C. Hare, R. Rees and D.J. Ralph *The Institute of Urology, The Middlesex Hospital, London, UK*

Introduction This study assesses the accuracy of dynamic MRI in the staging of penile carcinoma.
Patients and methods Eleven patients with biopsy-confirmed penile carcinoma (mean age 51.4 years, range 43–63) were assessed. Of these, six patients had had previous surgery or radiotherapy with a glans recurrence confirmed. The dynamic MRI was performed immediately before and after injection with 20 mg PSE (nine), where possible, in combination with both intra-arterial or intravenous

contrast medium, and images taken (T1-flash coronal and transverse dotarem). Surgery consisted of total glans excision in four patients, partial amputation in three, total amputation in three and topical chemotherapy in one, depending on the MRI findings. Histology, clinical and MRI staging were compared using the TMN classification.
Results Five patients were considered to have T1 disease of the glans on MRI that was confirmed both clinically and histologically. Three patients were considered to have T2 disease confirmed by MRI and histology. Three patients were shown to have T4 disease on MRI and therefore they had a total amputation, confirmed histologically.
Conclusion There was a good correlation between the clinical, histological and MRI findings. Using dynamic MRI in the presence of an erection gave better definition between the glans and corpus cavernosum, and thus allowed more conservative surgery. Dynamic MRI is the imaging of choice for staging penile cancer preoperatively.

P18

Cystic fibrosis gene mutation, urogenital anomalies and fertility assessment in patients with congenital bilateral absence of the vas deferens

M.Y. Hammadeh, D.J. Ralph and J.P. Pryor *The Institute of Urology and Nephrology, London, UK*

Introduction We investigated the frequency of cystic fibrosis (CF) transmembrane conductance regulator (CFTCR) gene mutation and genitourinary anomalies (by ultrasonography or IVU and TRUS) in patients with congenital bilateral absence of the vas deferens (CBAVD) who presented with azoospermia and infertility. The outcome of the infertility treatment was also assessed.
Patients and methods Over a period of 12 years, we reviewed 82 patients (mean age 33.9 years, range 22–52) with CBAVD; only 10 (12%) had clinical symptoms of CF.
Results All 12 patients with symptoms of CF were homozygous for CFTCR gene mutation, while 36 patients (50%) with no symptoms were heterozygous for CFTCR gene mutation. The most common gene mutation was F508 (72%). Renal anomalies were found in five patients (12%), the most common being renal agenesis in four. Seminal vesicle (SV) anomalies were found in 24 patients (71%), the most common being SV agenesis and hypoplasia (in 46% each). Renal agenesis was found in one patient (5%) and SV anomalies in six (29%) of those with CFTCR gene mutation (46 patients). Sperm were retrieved and ICSI undertaken in 48 patients (59%). A total of 77 ICSI cycles were carried out and clinical paternity achieved in 29 patients (38% per cycle) with 22 live births (29% per cycle).
Conclusion CFTCR gene mutations are frequent in patients with CBAVD. Sperm retrieval and assisted reproductive techniques are practical, effective and feasible in patients with CBAVD.

P19

Effect of flushing the vasa deferentia at the time of vasectomy on the rate of azoospermia

F. Sommer, A. Eusan, H.-P. Caspers, K. Esders, P. Reddy and U. Engelmann *Department of Urology, University of Cologne, Germany*

Introduction More than 30 million couples throughout the world are using vasectomy as a method of birth control. The aim of this study was to determine whether irrigation of the vas deferens during vasectomy could shorten the time needed to reach azoospermia.
Patients and methods In 59 consecutive vasectomies for the purpose of sterilization, half the patients (chosen by random numbers) had the vas deferens irrigated with 40 mL of sterile water on each side. Afterwards, the men sent in every fourth ejaculation, until two consecutive samples were without spermatozoa. The postoperative sperm samples were examined microscopically while unaware of whether the man belonged to the treated or the control group.
Result The median number of ejaculations before azoospermia was 25–30 in the irrigated group; the control group required 50–65 days before becoming azoospermic.
Conclusion Flushing the vasa deferentia at the time of vasectomy is easy to do, safe, and can be used in clinical practice to reduce the time needed to reach azoospermia.

P20

Irrigation of the vas – does it accelerate the clearance of sperm after vasectomy? The results of a randomized trial

R.G. Mason, L. Dodds and S.K. Swami *Department of Urology, Aberdeen Royal Infirmary, Aberdeen, UK*

Introduction Vasectomy is a safe and reliable method of contraception. Sterility is often declared after the production of two consecutive azoospermic semen samples. In some men many months may elapse before this is achieved. Nonmotile, lingering sperm are usually responsible for the continuing positive results. The purpose of this study was to determine whether irrigation of the distal vas at the time of vasectomy could accelerate the clearance of sperm and the onset of sterility.
Patients an methods In all, 200 men attending for vasectomy were randomized into the study. Patients in the control group underwent standard vasectomy and those in the 'flushed' group underwent vasectomy with irrigation of each distal vas with 10 mL of sterile water via a 24 G cannula. Semen was analysed at 6 and 12 weeks, and every 4 weeks until two consecutive specimens were negative. The interval between vasectomy and clearance was recorded.
Results Of the initial group, 37 men failed to return sufficient samples, leaving 87 in the control group and 76 in the flush group. The two groups were well matched for age (control mean 36 years, flush 35.1). There was no significant difference in the mean time to clearance (184 days in the control and 200 days in the flush group, $P = 0.36$), the percentage who achieved clearance at 16 weeks (29% vs 21%, $P > 0.5$), or the percentage with lingering sperm at >40 weeks (22% vs 26%, $P > 0.5$). In all, five patients underwent repeat vasectomy (three control and two flush) but only one had confirmed recanalisation.
Conclusion Irrigation of the vas with sterile water at vasectomy does not accelerate sperm clearance and hence does not hasten the onset of sterility. Patients must be counselled about the possibility of persistent lingering sperm.

P21

Patient selection in extracorporeal shockwave therapy for Peyronie's disease

O.F. Awogu, A.J. Ball, T.W. Carr, R.N. Lodge and P.M. Lester *Southend Hospital Trust, Westcliffe-on-Sea, Essex, UK*

Introduction Several reports have emerged of the efficacy of extracorporeal shockwave therapy (ESWT) in the treatment of Peyronie's disease as a safe, minimally invasive and easily tolerated treatment option. We have attempted to increase the success rate by careful patient selection.
Patients and methods ESWT was limited to patients having Peyronie's disease for at least 12 months, whose plaques were mature and whose curvature had stabilized for at least 6 months. Patients having normal intercourse despite their curvature and with no pain were excluded. A Storz Minilith SL 1 machine delivered 3000 shock waves at power setting 4–5. Three treatment sessions

were given at 1-month intervals and patients assessed 3, 6 and 18 months after the last session.

Results Twenty-seven patients completed three treatments, 10 of whom had a further three treatments after 6 months. All 17 patients with pain on erection were pain-free at the end of the therapy. Twenty patients (74%) had reduced angulation (mean 40°) sufficient to resume sexual intercourse. The improvement in angulation and plaque size was sustained in all patients during the review period. Of 10 patients who had a second treatment, seven had calcified plaques. A further reduction in angulation (mean 22°) was noted in these and six of these patients have resumed normal intercourse.

Conclusion ESWT is a safe treatment option for Peyronie's disease. Calcification of the plaques indicates the need for more treatment sessions. Pain was successfully relieved and treatment benefit maintained for 18 months. Further study is needed with a longer follow-up and more patients.

14.00–15.00
PUJ Obstruction

32

Balloon rupture of PUJ obstruction through a percutaneous approach: 8 years' experience

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Introduction Adult PUJ obstruction is increasingly managed by incisional or balloon-rupture techniques, through an antegrade or retrograde approach. The reported experience with percutaneous balloon disruption of PUJ obstruction is limited. We evaluated our results using this procedure over the last 8 years.
Patients and methods The symptomatic and renographic results of 53 patients who underwent percutaneous balloon disruption of PUJ obstruction were reviewed. The procedure was undertaken on 55 renal units (45 primary and 10 secondary PUJ obstructions). A high-pressure balloon (Uromax) was used to disrupt the PUJ under fluoroscopy, via the percutaneous route. The outcome was regarded as successful if the patient became asymptomatic, with improvement in drainage and stable/improved function on renography.
Results Of the 55 procedures 38 (69%) were successful and 17 failed (31%), with a median follow-up of 30 months. Of the 17 failures eight underwent repeat balloon disruption with a successful outcome in six. Among the 17 failures in 12 there was a poor rupture of the 'waist'. Five of eight patients with a split renal function of $<25\%$ showed stable or improved renal function. Perioperative complications were mainly stent-related. Of 10 failures, five underwent open pyeloplasty, three nephrectomy and two died from unrelated causes.
Conclusions This series, the largest of its kind to our knowledge, shows that percutaneous balloon disruption for adult PUJ obstruction is a safe and reasonably effective procedure, giving results comparable with those of other reported endoscopic techniques but with less potential for injury to crossing vessels. Poor rupture of the 'waist' during the procedure was associated with a high failure rate.

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Secondary pyeloplasty after failed retrograde balloon dilatation for PUJ obstruction in adults: assessment of outcome and role of crossing vessels

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Introduction Retrograde balloon dilatation is an accepted treatment for PUJ obstruction in adults. To date, 110 patients with PUJ obstruction have been treated in our unit using this technique, with a success rate of 70%; 22 patients in whom the endoscopic treatment failed subsequently underwent open pyeloplasty. In the present study we assessed the outcome of secondary pyeloplasty and the role of anatomical factors like crossing vessels on the outcome of the primary endoscopic procedure.
Patients and methods The medical records of all 22 patients (23 kidneys) who underwent pyeloplasty for secondary PUJ obstruction were analysed. Patient demographics, secondary procedures, operative findings and outcome were evaluated.
Results Five patients underwent a repeat balloon dilatation before the pyeloplasty and in three this was performed twice; 19 kidneys continued to be obstructed and in four the function deteriorated after primary balloon dilatation. Dismembered pyeloplasty was carried out in 17 patients and nondismembered pyeloplasty in the remainder. The mean operating time was 110 min. None of the patients required blood transfusion. A crossing vessel across the PUJ was identified in 10 (43%) patients. Eighteen patients (78%) had symptomatic improvement and 16 (69%) kidneys showed unobstructed drainage after pyeloplasty; five (22%) kidneys continued to be obstructed. Five patients underwent further procedures (repeat pyeloplasty in two, repeat balloon dilatation in two and a long-term stent in one).
Conclusions In our experience, crossing vessels over the PUJ are a common finding in patients in whom primary balloon dilatation has failed. Secondary pyeloplasty is technically no more difficult and the morbidity is not increased. However, the overall outcome may not be as good as that reported for primary pyeloplasty.

34

Acucise™ endopyelotomy: its role in managing pelvi-ureteric junction obstruction

S. Minhas, S. Biyani, G. Cooksey, D. Almond and J.W. Hetherington *Princess Royal Hospital, Sutton, Hull, UK*

Introduction Open pyeloplasty has been the gold standard for correcting PUJ obstruction (PUJO), although endourological management has gained increased acceptance. The aim of this study was to determine the effectiveness of Acucise™ endopyelotomy (AE) in treating PUJO and to identify factors affecting the surgical outcome.
Patients and methods Forty-two patients (34 with primary and eight with secondary PUJO) underwent AE. The preoperative evaluation included ultrasonography and IVU with diuretic renography. Hydronephrosis was graded in 36 patients, of whom four, 14, nine and nine had grades I, II, III and IV, respectively. Objective success was defined as the patient being clinically pain-free with no evidence of obstruction on diuretic scan.
Results The mean hospital stay was 2.7 days and the follow-up 27 months (range 6–55). The objective success rate was 45%, although subjectively 27 (64%) of patients were pain-free; five (12%) of patients required open pyeloplasty and three (7%) nephrectomy. The success rate for those with grade I/II hydronephrosis was 55%, but was only 28% for those with grade III/IV. The renograms were normal in 12 (48%) of those with perioperative extravasation, compared with three of 12 without. Only one patient with secondary PUJO had a normal postoperative renogram.
Conclusions AE is a safe and minimally invasive procedure for managing PUJO, with favourable long-term results. Patients with grade III/IV hydronephrosis, poor preoperative renal function and secondary PUJO are more likely to have treatment failure. Pre-selection of these patients will improve the results of AE.

35

Dismembered pyeloplasty: experience with a transperitoneal laparoscopic approach

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Introduction The benefits of laparoscopic approaches to urological surgery are increasingly apparent; we report our initial experience of laparoscopic dismembered pyeloplasty.

Patients and methods Fifteen consecutive patients with PUJ obstruction were offered laparoscopic pyeloplasty. All procedures were undertaken by or under the supervision of one surgeon. Two patients had had previous procedures (one antegrade endopyelotomy, one balloon dilatation). The mean (range) age of the patients was 41 (15.7–79.9) years. A three- or four-port transperitoneal technique was used, with a sutured anastomosis (interrupted 4/0 polyglactin) over a 6 F JJ stent. Urethral catheter drainage was continued for 5 days after surgery.
Results The procedure was successful in 12 patients whilst laparoscopy revealed extensive scarring requiring conversion in the patient with a previous endopyelotomy. Six patients had an anterior crossing vessel, requiring transposition of the pelvis before anastomosis, and a ureteric stent had been present for a mean (range) of 7 (4–12) months in seven patients. The mean (SD, range) operative duration was 223 (30.3, 180–290) min, including cystoscopic insertion or a change of stent. The mean morphine requirement after surgery was 27 (22.2, 0–60) mg and the median stay 6 (4–17) days. Five patients had complications after surgery; three pyrexia, one prolonged drainage from the anastomotic drain and one the onset of atrial fibrillation. Of the six patients completing the 3-month follow-up, all have improved drainage on renography and are symptom-free.
Conclusions These encouraging initial results provide further evidence that this technique is effective and will bear comparison to a standard open pyeloplasty in the longer term.

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Early experience and results after laparoscopic pyeloplasty

J.S. McGrath, F.X. Keeley and A.G. Timoney *The Bristol Urological Institute, Southmead Hospital, Bristol*

Introduction Since Wickham first reported percutaneous pyelolysis in 1984, a variety of minimally invasive approaches to PUJ obstruction has been described. These include balloon dilatation, retro-endopyelotomy and Acucise™ incision. Despite the clear advantages of a minimally invasive approach, the success rates of these procedures have not equalled that of the standard Anderson-Hynes pyeloplasty. However, recently the development of laparoscopic urology has combined the success rates of dismembered pyeloplasty with the advantages of minimally invasive surgery. We describe our initial experience in 13 patients.
Patients and methods Surgery was carried out at one centre by two urological surgeons between April 1998 and December 2000. All patients had renographic evidence of PUJ obstruction and had previously undergone ureteroscopy with a view to endopyelotomy. Contraindications to endopyelotomy included complex crossing vessels or a sizeable PUJ requiring reconstruction. Surgery comprised an extra-peritoneal approach with the placement of three laparoscopic ports. Postoperatively, a JJ stent was left and renography repeated at 3 months. The mean (SEM) follow-up was 10.1 (1.8) months.
Results A dismembered Anderson-Hynes pyeloplasty was carried out laparoscopically in 11 of the 13 patients. The two conversions occurred early in the series as a result of bleeding in one and the size of the renal pelvis in one. There were no intraoperative complications. The mean (SEM) hospital stay was 3.7 (0.4) days. All patients were pain-free at 3 months, with renographic confirmation of free drainage on the affected side.
Conclusions A laparoscopic Anderson-Hynes pyeloplasty is safe in patients with PUJ obstruction. In our experience, the early results are equivalent to those from open pyeloplasty. There are significant advantages to both the patient and healthcare provider as a result of a minimally invasive approach.

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Laparoscopic dismembered pyeloplasty: 50 consecutive cases

C.G. Eden, D. Cahill and J.D. Allen *The North Hampshire Hospital, Basingstoke, Hampshire, UK*

Introduction The best long-term results for the treatment of PUJ obstruction are obtained by dismembered pyeloplasty. Laparoscopic dismembered pyeloplasty aims to reproduce the same excellent results as open surgery but without the disadvantages of the wound.
Patients and methods Fifty consecutive consenting patients presenting with PUJ obstruction underwent laparoscopic dismembered pyeloplasty by one surgeon at his own hospital. The mean (range) patient age was 39.0 (9–77) and weight was 71.0 (27–110) kg. A four-port balloon-dissecting extraperitoneal laparoscopic technique was used in all cases.
Results Two cases were converted to open surgery (4%). The mean operative duration was 164 (120–240) min. Nine patients had their ureter transposed anterior to a crossing lower pole vessel. Eleven patients had a separate renal pelvic suture line. The mean postoperative parenteral analgesic requirement was 19.1 (0–111) mg morphine sulphate; the mean hospitalisation was 2.6 (2–7) days. Two patients had complications; one had a sub-endocardial 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. Normal upper tract drainage was noted in 41 (82%) patients; equivocal excretion curves were obtained in eight (16%) patients, all of whose anastomoses were widely patent on retrograde ureteropyelography and/or ureteroscopy. All of these patients were symptom-free. The patient who had failed endopyelotomy had a normal renogram and was symptom-free at 3 months but developed pain and an obstructive renogram at 9 months after secondary pyeloplasty.
Conclusions These results suggest that a loin wound is not necessary for a successful outcome after dismembered pyeloplasty and that laparoscopic dismembered pyeloplasty should now be considered the standard of care.

14.00–15.00
Prostate cancer 1

38

Patient access to inaccurate Internet-based medical information on PSA testing – a possible source of doctor–patient conflict

P.W. Foster and R. Persad *Bristol Royal Infirmary, Bristol, UK*

Introduction As more members of the public become connected to the Internet their access to medical information becomes easier than ever. Information found on the Internet is often unsolicited and possibly inaccurate. Patients accessing this information often do not have the ability to decide which sources are reliable. PSA testing and prostate-cancer screening is a much-debated issue. We sought to evaluate the accuracy of information available to the general public relating to PSA testing on the Internet.
Methods Using Hotbot™ search engine the results for the search words 'PSA test' were found. Each of the 50 top sites for this search were visited and details documented about the information stated on key aspects of PSA testing and related issues. Information about site sponsorship was also sought.
Results The search 'PSA test' revealed over 1000 references; eight sites needed registration or were inaccessible, and therefore 58 sites were visited in total. Of the 50 sites analysed all were relevant to patient information about the subject; 17 sites (34%) suggested that PSA testing was relevant in the screening of prostate cancer; 34 sites (68%) gave accurate information about the role of prostatic biopsies and DRE. Thirty-two sites (64%) gave information on the epidemiology of prostate cancer. It was only possible to be certain of reputable unbiased ownership of the site in 10 cases (20%). One site offered the unconditional sale of PSA tests.
Conclusions Information about PSA testing on the Internet varies in quality and indeed is often misleading. It is also evident that information about site sponsorship, possible bias and the validity of authors is difficult to accurately obtain. As Internet access becomes the norm in the household, patients will have easy access to a wealth of inaccurate information that could lead to a clash of opinions in the consultation room.

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PSA and the risk of prostate cancer diagnosis: a 10-year observational study after a screening study

C. Lynch, S. Pandian, M. Hehir and the Stirling Prostate (Natural History) Study Group *Urology Department, Stirling Royal Infirmary, Stirling, UK*

Introduction In a community study into BPH in 1989/1990, a total of 492 men living in two GP areas were screened for prostate disease using the AUA symptom score, PSA, DRE and TRUS. The 10-year cumulative risk of cancer was examined in a retrospective analysis. The aim of the present study was to determine whether a low-risk group could be identified from the original cohort, e.g. those with an undetectable PSA or a low PSA.
Methods A urology department cancer database was cross-checked with the community-study database.
Results Of the 492 men, 33 developed carcinoma of the prostate; 20 were diagnosed at the initial screen and 13 subsequently. (Of the 20 diagnosed initially, 12 were found incidentally at TURP and eight on transrectal biopsy because of an abnormal PSA, DRE or TRUS.) The cumulative risk (at 10 years) of developing a carcinoma in patients with values below, in and above the normal range

No. cancers/no. men (% per group)		*No. (%) with PSA (ng/mL) of*		
		<2	*2–4*	*>4*
Age group (years)				
40–49	1/91 (1.1)	0	0	1
50–59	6/146 (4.1)	3	3	0
60–69	14/176 (7.9)	6	4	4
70–79	12/78 (15.4)	7	2	3
Total	33/492 (6.7)	16 (5.4)	9 (7.8)	8 (9.4)

Conclusions Those men identified as having carcinoma of the prostate after 10 years had a broad range of PSA values, from undetectable, through the normal range and above. There was a moderate rise in cancer risk with increasing PSA level, the risk at a baseline PSA of <2 ng/mL (5.4%) being about half the risk with at a PSA of >4 ng/mL (9.4%). It was not possible to identify a low-risk group from this series. Using Oesterling threshold and bisected Oesterling ranges there appeared to be no age-specific value which was predictive of cancer of the prostate after 10 years of observation.

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Longitudinal study of bone turnover in patients with metastatic prostate cancer started on LHRH agonists

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Introduction Cross-sectional studies have shown greater bone turnover in castrated patients than in matched controls. Prostate cancer metastases can increase bone resorption and castration can induce the regression of metastases, which makes the combined effect unpredictable. The objective of this study was to determine longitudinally the change in bone turnover after LHRH-agonist therapy in patients with metastatic prostate cancer.
Patients and methods A prospective cohort of patients with metastatic prostate cancer in a London teaching hospital was studied from before LHRH agonist therapy to 1 year after treatment. Bone alkaline phosphatase and urinary cross linked N-telopeptides (NTX) were used as indices of bone turnover and their natural logs (ln) compared by paired *t*-tests over the first 3 months of treatment for which data are so far available.
Results The mean (SD) ln NTX levels decreased from 3.58 (0.64) to 3.33 (0.91), with a mean difference of 0.25 ($P=0.14$; $n=10$; 95% CI -0.11 to 0.60). The ln BALP increased from 3.37 (0.40) to 3.41 (0.39), with a mean difference of 0.17 ($P=0.26$; 95% CI -0.15 to 0.49). The PSA level declined significantly after starting LHRH agonists.
Conclusion This is the first longitudinal study after the change in bone turnover from before hormone deprivation up to 1 year after treatment. Data up to 3 months do not confirm an increase in bone turnover and may even show a decrease with a longer follow-up. Unexpected changes in bone turnover may occur after LHRH agonists, including a decline if metastases regress; the balance may

depend on the extent of metastases. This study indicates the necessity for longitudinal studies.

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Immediate DEXA scanning reveals a high incidence of osteoporosis in advanced prostate cancer before hormonal manipulation

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Introduction Osteoporotic fractures are more frequent in patients with prostate cancer who have undergone either medical or surgical castration, because there is rapid loss of bone mass. However, there is also biochemical evidence of generalized acceleration in bone resorption in patients with advanced disease, even before hormonal manipulation (HM). This study examined the incidence of osteoporosis in patients with locally advanced and/or metastatic prostate cancer, using forearm DEXA scanning before commencing HM. These scanners are portable and provide a rapid method of diagnosis. Osteoporosis risk factors (ORF) were also assessed.
Patients and methods Fifty patients (mean age 73 years, range 46–88) with prostate cancer presented over a 12-month period.
Results Of the 50 patients, 21 (42%; mean age 76 years) were osteoporotic (T score $\leqslant -2.5$) and 19 (38%; mean age 72 years) were osteopenic (T score -1.5 to -2.4). The median (range) PSA level was 87 (20–2020) ng/mL in the osteoporotic group, 57 (29–426) ng/mL in the osteopenic group and 76 (32–242) ng/mL in the normal group. There were also no significant correlations between Gleason score, stage, alkaline phosphatase, serum calcium and the presence or absence of osteoporosis. Only five patients with osteoporosis had one or more ORF, four in the osteopenic group and one in those with normal bone density.
Conclusions Patients with advanced prostate cancer requiring HM have a high incidence of osteoporosis before treatment and this cannot be attributed to other ORF. In addition, osteoporosis in these individuals cannot be predicted from clinical or biochemical values. Therefore, bone densitometry should be measured in all patients with advanced prostate cancer requiring HM, as the results have implications for the choice of cancer therapy. Furthermore, it identifies which patients require initiation of treatment for osteoporosis or those requiring prophylaxis.

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Nuclear texture analysis in predicting response to hormonal therapy in prostate cancer

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Introduction Computerized nuclear texture analysis refers to objective measurements of the spatial distribution of chromatin within nuclei. The aim of this study was to explore its role in predicting the response to hormonal therapy in prostate cancer.
Materials and methods The study included 23 patients with advanced prostate cancer and on anti-androgen treatment. The follow-up PSA data was plotted and patients divided into five groups, i.e. 1, hormone-resistant (one man); 2, early escape with rapid progression (two); 3, late escape with rapid progression (10); 4, late escape with slow progression (four); and 5, long-term responsive (six). Digital images of the nuclei were captured and nuclear texture analysed using software developed in our laboratory. At least 30 nuclei were measured in each sample and 41 textural features measured on each nucleus. In addition, DNA ploidy was measured using flow cytometry.
Results Nuclear texture analysis revealed distinct statistical differences between the five prognostic groups (Kruskal-Wallis test, $P < 0.001$). A discriminant analysis between groups 1 and 2 combined and group 5 identified 11 texture features most important for their distinction, providing 68% correct classification of nuclei into the respective groups. The flow cytometry/DNA ploidy showed a higher incidence of tetraploidy in the hormone-responsive group than in the other groups.
Conclusion Nuclear chromatin has different texture patterns in tumours with varying responses to hormonal therapy. A nuclear texture-based score may allow more accurate prediction of hormone sensitivity in patients with advanced prostate cancer.

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A randomized trial of periprostatic local anaesthetic for transrectal biopsy

K. Walsh, A. Salemi, T. O'Brien and R. Popert *Guy's Hospital, London, UK*

Introduction TRUS and biopsy are increasingly being used to detect prostate cancer. Recent reports suggest that the use of periprostatic injection before prostatic biopsy could reduce the discomfort for a patient during this procedure. We conducted a randomized trial to evaluate this claim.
Patients and methods Sixty-four patients who attended a specialized prostate clinic and who were being evaluated for an elevated PSA level agreed to participate in the trial; they were randomly allocated to two groups. The intervention group received 10 mL of 1% lignocaine in the periprostatic tissue before biopsy and the control group underwent a standard biopsy. All patients had a sextant biopsy taken under TRUS guidance. After the procedure they were asked to determine the severity of the pain on a scale of 0 to 10, and whether the quality of the pain was mild, moderate or severe.
Results The responses were distributed normally; the groups were compared using the Student's *t*-test. There was no significant difference in the severity of pain between the groups ($P = 0.14$) but there was a trend toward a statistical difference ($P = 0.07$) on the qualitative pain scale.
Conclusion No significant difference was detected between the groups, suggesting that the administration of local anaesthetic is not as valuable as earlier reports suggested.

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Periprostatic nerve block gives better analgesia in prostate biopsy

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Introduction Transrectal prostate biopsies are usually taken with no anaesthesia, with significant (although considered acceptable) pain. However, the advent of multiple biopsy techniques has focused the need for analgesia/anaesthesia during this procedure. We prospectively compared two local anaesthetic techniques.
Patients and methods The study group consisted of 86 consecutive men (median age 67.7 years, range 48–88) undergoing prostatic biopsy because of either an abnormal PSA level or DRE. They were randomized into three groups; men in first group (30) received 10 mL of 1% lignocaine infiltrated into the periprostatic nerve plexus bilaterally [*J Urol* 2000; 163: 172–3] and men in second group (27) received 11 mL of 2% lignocaine gel rectally 30 min

before the procedure. Men in the third group were recruited as controls and were either given a saline injection into the periprostatic nerve plexus (15) or plain gel rectally (14). Sextant prostatic biopsies were then taken in all, using a standardized protocol. Immediately after the procedure patients were asked to indicate the degree of pain on a 10-cm visual analogue scale (VAS). The Kruskal–Wallis test was used to analyse the results.

Results The median (range) score on the VAS was 1.9 (0.0–9.7). Men in group 1 significantly less pain than the others, at 0.5 (0–2.8) ($P < 0.001$). There was no statistically significant difference in pain between men in group 3, at 4.8 (0.5–9.4) or group 4, at 4.3 (1.0–6.3) ($P = 0.35$). The rectal instillation of 2% lignocaine gel did not reduce pain significantly ($P = 0.186$), at 2.7 (0–9.7) from that in the controls.

Conclusion A periprostatic nerve block with 1% lignocaine was associated with significantly less pain during prostatic biopsy than was rectal lignocaine gel and placebo.

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Nurse-performed TRUS and biopsy: do patients mind?

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Introduction Because of the increased demand for prostatic biopsies, a Nurse Specialist was trained to carry out TRUS-guided biopsies; to date 87 procedures have been conducted. It is important to establish the patient's perspective of this Nurse-led service.

Patients and method A questionnaire was sent to the 87 patients whom the nurse had biopsied, to establish if the patients were happy with the Nurse-run service and to assess how patients would feel about the Nurse Specialist giving them the results of their biopsies before they had seen a Consultant.

Results Seventy-two completed questionnaires were returned (83% response rate); in this group 30 (42%) of patients had had a previous biopsy and 42 (58%) were experiencing their first. Most (93%) were not worried about the nurse undertaking the procedure and only 4% were worried (3% gave no response). When asked whom they would prefer to take any future biopsies, 79% replied that they did not mind; 18% would prefer the Nurse Specialist and only 3% the doctor! Most (86%) of the patients would be happy to hear their results from the Nurse Specialist, whereas only 11% would be unhappy (3% gave no response).

Conclusion Overall, the results indicated strong support for Nurses undertaking TRUS and biopsy. This evidence should encourage the establishment of more Nurse-led assistance in the management of patients with suspected prostate cancer.

15.15–17.00
Clinical Governance

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Near-misses in bladder cancer – an 'airline safety' approach to urology

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Introduction Traditionally, surgical audit has identified and highlighted the incidence of adverse events complicating patients' care. The airline industry has taken this concept a step further back by identifying and studying 'near misses', i.e. an event that has the potential to do harm. We decided to apply this approach to patients with known or suspected bladder cancer.
Patients and methods A prospective study was conducted by two urology firms on all patients with known or suspected bladder cancer over a 3-week period. Patients presented to either the central (hub) hospital, or to an associated (spoke) hospital. Four stages in bladder cancer care were considered, i.e. diagnostic or check flexible cystoscopy, admission to hospital before TURBT, the operative and perioperative period and the first outpatient consultation. A separate proforma, comprising various aspects of management, was used for each of these stages of care. Each completed proforma was regarded as an 'episode'. If any one criterion was not met, the episode was recorded as a 'near miss'. Near misses were classified as those caused by limitations in the capacity of the system, clerical error, equipment failure and patient failure.
Results In all, 115 completed episodes were recorded; there were 65 (57%) near misses with 54% caused by capacity limitations and 23% by clinical error. In addition, 16% were secondary to clerical error, 5% to patient failure and 2% as a cause of equipment failure. Of particular note is that near misses relating to diagnosis were more common at the spoke hospital; delayed referral accounted for more than half of the clinical error, and the availability of upper tract imaging was a problem at all phases of patient management.
Conclusions Near misses are very common in the management of patients with bladder cancer and their identification should provide a useful framework for identifying potential areas for improvement in patient care.

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Two weeks' wait for urological cancer – myth or reality?

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Introduction Patients suspected of having cancer need urgent referral to a specialist and rapid investigation for an early diagnosis. The tumour then needs to be staged quickly and if radical surgery is contemplated with a curative intent, that has to be carried out without delay. The NHS 2-week deadline, which became applicable to urological cancers from December 2000, is directed solely at the first phase of this journey, from the time of referral to the point hospital consultation. This retrospective study on 100 patients with potentially curable urological cancers traces the patients' journey from the time of first consultation with a medical practitioner to the time of definitive surgery.
Patients and methods We reviewed the hospital records of 100 patients, comprising four groups of 25 consecutive cases each, who underwent radical surgery for cancers of the kidney, testis, bladder and prostate before December 2000. The time intervals from referral to urology appointment, appointment to confirmation of diagnosis, and diagnosis to staging and radical surgery were noted. The mean (95% CI) intervals were calculated for each group and for the whole population.
Results The results show that in patients deemed suitable for radical surgery for urological cancer, a significant proportion of time is spent awaiting staging investigations and the surgical procedure. The shortest wait was for patients with testicular tumour and the longest for bladder cancer.

Organ involved	*Mean (95% CI) time (days) from:*		
	*referral to 1UA**	*1UA to D*	*D to surgery*
Kidney	41 (18–64)	29 (8–50)	27 (19–35)
Testis	35 (21–50)	14 (0–28)	11 (3–18)
Bladder	49 (30–67)	29 (18–41)	94 (54–135)
Prostate	59 (41–76)	180 (77–284)	75 (60–90)
Total	46 (37–55)	64 (35–92)	57 (42–71)

*1UA, first urology appointment; D, diagnosis.

Conclusions The 2-week wait will decrease the waiting time to see a specialist, but tangible progress in delivery of cancer care can only be achieved with improvement in diagnostic facilities and theatre throughput, which would require financial and manpower investment in these areas.

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An audit comparing Minimum Standards for urological cancer services, set by the Cancer Services Co-ordinating Group (CSCG) for Wales, with what is currently being achieved

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Introduction The CSCG Urological Cancer Minimum Standards define the essential aspects of the service that should be provided for cancer patients throughout Wales. These cover six aspects: organization, communication, diagnosis, treatment, follow-up and clinical information. We focused on the diagnostic standards: (i) urgent GP referrals must be seen within 10 working days; (ii) the diagnosis of cancer should be confirmed within 20 working days; (iii) after confirming the diagnosis, full staging and discussion of a definitive treatment plan with the patient should occur within 20 working days.
Methods The case-notes of patients with confirmed urological cancer, in a Welsh district general hospital, diagnosed between January 1998 and December 1999 were analysed retrospectively.
Results In all, 98 cases were identified and 85 were available for analysis, comprising prostate (50%), renal (22%), bladder (20%), bladder and renal pelvis (4%) and testicular (4%) cancer. The results for each standard were: (i) 21 patients (25%) seen within 10 working days, 21 (25%) at 10–30 days, 28 (33%) at 1–2 months, 11 (13%) at 2–3 months, four (5%) at 3–4 months; (ii) 57 patients (67%) diagnosed within 20 working days, 14 (16%) at 1–2 months, four (5%) at 2–3 months, three (4%) at 3–4 months and seven (8%) at 4–11 months; (iii) the full staging and treatment plan was achieved in all patients within 20 working days.

Conclusions Only 25% of patients eventually diagnosed as having cancer were seen within the CSCG recommended time. Although an improvement in highlighting urgent cases can be achieved by the future introduction of a standard referral letter for GPs, it is unrealistic to expect CSCG minimum standards to be achieved without increased manpower, including help with collecting data and more rapidly available diagnostic investigations. This study only assessed patients diagnosed as having cancer; we are currently auditing the larger population found to have benign disease, which may reveal longer delays.

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Improving the quality of service for patients diagnosed with a urological malignancy

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Introduction Patients with a urological are entitled to the highest possible quality of care throughout their disease course. Traditionally (in the author's opinion) patients are often denied of the most efficient and effective care at this most vulnerable and sensitive time. By introducing a nurse-led service which concentrates on patients' specific and overall needs, the author has developed a strategy of care which provides a significantly improved high-level quality approach to coordinating care from diagnosis through treatment planning and intervention, and ultimately follow-up care.
Patients and methods *Nurse-led histology clinic*: Inherently, it is exclusively doctors who inform patients of their cancer diagnosis. Using the protocols and guidelines agreed by specialist Nurses and Consultants, patients received their diagnosis from a Specialist Nurse who then coordinated further investigations, results and appointments. Subsequently the patient consultation with the consultant is more productive and meaningful for both. *Nurse-led follow-up clinic*: Patients assessed by consultants as having stable disease were referred to the nurse to co-ordinate their follow-up care on their behalf.
Result Patient questionnaires showed overwhelming satisfaction and acceptance. The time to receiving the diagnosis halved with the coordination of investigations, results and appointments, allowing for an earlier definitive treatment plan. Patient information was increased and simultaneously patient anxiety reduced. After the diagnosis a much required but often much neglected continuity of care was provided. Patients were removed from a busy general consultant clinic and reviewed regularly by the Nurse who provides a more holistic consultation. Overall the use of resources was better.
Conclusion With the introduction and development of the role of the Specialist Nurse in urological oncology these patients within this Trust now receive a radically different, more patient-centred and significantly better quality of care.

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Audit reviewing the urological cancer 2-week referral scheme

L.A. Grant, O.J. Cole and D.R. Harriss *Department of Urology, Nottingham City Hospital, Nottingham, UK*

Introduction The Government guarantees that a specialist will see patients with suspected cancer within 2 weeks of seeing their GP. This prospective audit assessed the impact of its introduction on the urology service of a busy teaching hospital.
Patients and methods From July 2000, GP referrals were faxed to a central booking point with no consultant triage. Adherence to guidelines and times to diagnosis and treatment including outcome were audited.
Results The progress of the first 100 patients (mean age 63.4 years) were analysed; all were seen within 2 weeks of referral. Their presenting symptoms were:

Referral criteria	*No. patients*	*No. with cancer**
Macroscopic haematuria	45	8
Microscopic haematuria	13	0
Testicular swelling	16	1
Raised age-specific PSA	5	4
Symptomatic raised PSA	3	3
Suspected penile cancer	2	0
Renal mass	1	1
Outside referral criteria	15	5

*Some patients still awaiting further investigation.

There was a significant delay (up to 20 weeks) to investigation after the initial consultation. Overall, 22% of patients were found to have cancer. This represents 42% of all urological cancers reported at this hospital during the same period.
Conclusions We have shown that a urological service can be reorganized to accommodate the 2-week cancer wait. However, this scheme is undermined by the subsequent long wait for investigation. Additionally, the cancer detection rate is low and therefore it is debatable whether this is an efficient use of resources.

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Risk and informed consent – the patient's view

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Introduction Clinicians worry that patients are not given enough detail about surgical procedures. They also perceive that better-educated patients are more likely to question or express dissatisfaction with their treatment. A 1% threshold complication rate is commonly used when deciding how much information to give for purposes of informed consent.
Patients and methods Patients attending an outpatient clinic completed an anonymous questionnaire about consent for previous operations and about information they would like for potential future procedures. The answers were analysed with regard to the social class of the respondent using the Registrar General's definitions.
Results At submission, 85 patients had completed the questionnaire (mean age 67.5 years); social classes 1 and 2 accounted for 49% (compared with a national average of 23%); 67% had undergone a previous urological procedure; 19% were dissatisfied with the information they had been given and 60% were satisfied; 30% of patients wanted to know about remote complications and only 23% wanted information restricted to frequent complications alone. In 52% of patients the degree of information desired about a potential complication did not vary whether that complication was severe, moderate or mild. There was no difference in the quality or quantity of information desired by patients in higher socio-economic groups.
Conclusions A significant proportion of patients is dissatisfied with the information they are given about surgical procedures. A significant number want to know about even the remote possibilities of minor complications. Higher socio-economic status does not mean a greater desire for information.

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The outpatient clinic – how many patients on a list?

T.M. Lane, H. Hashim, T. Limbin, E. Ford, J. Masood, N. Shah and J.T. Hill *Harold Wood Hospital, Romford, Essex, UK*

Introduction Royal College of Surgeons guidelines suggest that a Consultant clinic should ideally comprise seven new and seven follow-up patients (within a 3-h period). BAUS are soon to follow suit and are likely to suggest a greater number than has hitherto been declared [Fawcett D. Consultant workload – are guidelines necessary or desirable? *BAUS Today* 2000; 3: 391]. However, any advice given will be in the absence of appropriately robust data which might reasonably be used to prescribe clinic composition. With this in mind we recently undertook a review of outpatient consultations to determine optimum scheduling levels in our urological practice.
Patients and methods Two hundred outpatient clinic appointments were studied over a 6-month period. All aspects of these clinic episodes were timed from the moment the patient entered the consulting room to the time they left. Thus allowed an accurate assessment of the proportion of time clinicians spent eliciting clinical histories, performing physical examinations, seeking results, documenting findings or dealing with interruptions. Both Consultant and trainee were examined alike, with all timings recorded by a pre-registration house-officer.
Results The mean time taken to a see a new referral in clinic was 23 min, compared with 12 min for those with a follow-up appointment. Less than 20% of this clinic time was spent either explaining results or answering patient-directed questions. The time taken to see both new referrals and repeat attendees varied according to the underlying pathology. There was no statistical difference in the time taken to see patients between trainees and Consultants (but no attempt was made to adjust for varying case-mix). Significant proportions of time were spent either in supervision or dealing with clinical matters unrelated to the outpatient department.
Conclusion With increasing demands to adhere to minimum agreed waiting times there is increasing pressure to see even more patients within clinics. Agreed standards must be established if quality of care is not to be eroded. Our study already highlights concern over the present levels of time available to discuss issues with patients and outlines the influence of a host of local factors on consultation times. We suggest that recommendations for clinic numbers should be based on those local factors which limit consultations and which may not necessarily translate to a national agenda. We think it likely that a suggestion for more patients to be seen in clinic will further erode patient care. Our data suggest that five new and five follow-up patients per 3-h clinic session is optimum if tandem clinic lists with trainees are to be appropriately supervised.

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How many cases should there be on an operating list?

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Introduction With increasing pressure to meet target waiting times there is a tendency to over-book routine operating lists. However, the consequences of list over-runs are patient cancellations and disruptions to subsequent elective sessions. Inaccuracies in list scheduling arise in part because of the rather subjective nature of case-length assessment. We undertook a 6-month review of elective surgical admissions to determine the mean operating periods and associated anaesthetic and recovery times, to help in list scheduling.
Patients and methods In all, 200 patient episodes were assessed; the operative duration for each procedure was recorded and the surgeon's grade noted. Anaesthetic and recovery times were also recorded for each case and the grade of anaesthetist responsible for each episode noted. Other aspects recorded included the time taken for patients to travel from the ward to theatres, intraoperative delays and the time taken to position, drape and transfer patients.
Results The mean operating duration was obtained for all routine procedures commonly undertaken on elective operating lists. There were no significant differences in operative duration between consultant and trainee (although case selection and allocation was routinely undertaken in determining the grade of the operative surgeon). There were significant differences in anaesthetic time between unsupervised trainees and the consultant or supervised trainee. Similarly, there were significant differences between consultants and supervised trainees in the administration of spinal anaesthetics. ASA grade influenced general anaesthesia time only when junior anaesthetists were unsupervised. Ward-to-theatre time (24 min), positioning (7 min) and transfer times (9 min) appeared remarkably consistent. Individual patient episode timings were calculated, e.g. 72 min should be allocated for a TURP (anaesthetic time 19 min, position and drape 7 min, operating time 42 min and recovery transfer 9 min.
Conclusion Surgical times were not significantly different between consultant and trainee, probably reflecting appropriate case selection and allocation. Anaesthetic times were significantly longer when junior anaesthetists were unsupervised and when anaesthetic juniors were involved with spinal anaesthesia. Mean times for each patient episode were calculated according to surgical procedure and modified to reflect junior staff balance. We recommend local audits to improve case selection for operating lists.

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Should we mark patients to indicate the side of surgery?

M.J. Henley, A. Myatt, S. Jain and C.P. Chilton *Department of Urology, Derby City Hospital, Derby, UK*

Introduction Recent events have engendered debate about the best practice to ensure that the correct organ or limb is operated upon. Within surgery there are many different views and practices, particularly on whether the patient should be marked or not. This survey was designed to assess the current practice of British urologists. Such information could be used to inform further debate, in an attempt to formulate nationally accepted guidelines, as none exist at present.
Methods A postal survey was conducted of members of the BAUS.
Results Seven hundred questionnaires were distributed; 39.2% (275) were returned and 213 (17%) respondents stated that they would always mark the side of surgery, 53 (19%) said that they would never mark the side and nine (3%) marked the side only in certain circumstances. When asked who should mark the patient, 10 (4%) felt that the consultant should do so, 33 (14%) the house officer, 184 (80%) the operating surgeon and two (1%) the patient; 205 (91%) marked patients on the ward, 11 (5%) in the anaesthetic room, four (2%) in either, three (1%) in theatre and two (1%) 'other'. In all, 207 (84%) specify the side to be operated on in the published theatre list and 40 (16%) do not. Only 23% worked in hospitals with trust guidelines on marking.
Discussion There is a considerable difference of opinion; do we need nationally agreed guidelines or should this be left to surgeon's preference?

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Auditing surgeons and their outcomes: the importance of case-mix adjustment

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Introduction Surgeons are increasingly required to justify the quality of their work to patients, peers and the government. One of the most frequently used methods to ensure high-quality clinical performance is the comparison of surgeons' outcomes with one another. However, attributing any apparent differences to surgeon rather than patient characteristics can be misleading. We describe the effects of case-mix adjustment on the apparent variation seen among urologists undertaking TURP.
Methods A multicentre cohort of patients undergoing TURP was studied prospectively. Outcomes and case-mix data were obtained via questionnaires, which were sent to the patient, surgeon and hospital. Outcomes measured were the IPSS before and after TURP, and adverse events. The outcomes for each urologist were adjusted for case-mix using two statistical methods; nonhierarchical regression and multilevel analysis
Results Over 6 months, data were collected on 4625 TURPs carried out by 107 urologists in 52 centres. Raw data showed significant differences ($P < 0.05$) among urologists for both postoperative IPSS and adverse events. The differences observed were reduced when adjusted for case mix using either nonhierarchical regression or multilevel analysis, and were not statistically significant.
Conclusions The use of appropriate statistical methods is essential when comparing outcomes between surgeons, as apparent differences may disappear when adjusted for case mix. Without case-mix adjustment there is a danger that the good surgeon may look bad, and vice versa.

15.45–17.00
Stress Incontinence

56

Extracorporeal magnetic stimulation vs sham treatment for female genuine stress urinary incontinence: a randomized trial

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Introduction, patients and methods Seventy patients were enrolled and 52 completed a 16-treatment course of either active (27) or sham (25) extracorporeal magnetic stimulation. None of the patients had undergone previous surgical treatment, all had measurable (pad-testing) and visible (video-urodynamics) stress leakage. Quality-of-life questionnaires (I-QoL), flow rates, pad usage, 20-min and 24-h pad tests were among the variables assessed; these assessments were repeated after treatment (8 weeks) and at 3, 6 and 12 months; enrolment is now complete.
Results All preoperative values were similar. In the treatment arm (27) the 20-min pad test improved from a median (range) of 34.1 (0.5–89.5) to 22.9 (0–133.5) mL at 8 weeks and the 24-h pad test improved from 22.1 (2–85.5) to 9.1 (0–61) mL. In the sham arm (25) the 20-min pad test improved from 46.3 (1–197.5) to 40.3 (0–143) mL at 8 weeks and the 24-h pad test improved from 29.7 (2–102.5) to 20.8 (2–68) mL. The I-QoL increased (improved) from a mean of 64.6 to 70.2 at 8 weeks in treatment arm and decreased (deteriorated) from 69.5 to 65.2 in the sham arm. Four patients in the active arm and two in the sham arm had no detectable leakage at urodynamics at 8 weeks.
Conclusions Magnetic stimulation results in measurable improvements in pad testing and QoL scores over sham treatment in women with stress incontinence.
Funding: Neotonus Inc.

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Pubovaginal sling for stress urinary incontinence: analysis of results and quality-of-life assessment

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Introduction In many institutions the pubovaginal sling is now the standard method of treating stress urinary incontinence (SUI). We report the medium-term results of the pubovaginal sling for treating SUI in relation to surgical outcome and impact on quality of life.
Patients and methods From July 1999 to October 2000, 56 females (aged 17 to 69 years) underwent surgery for SUI; all data were accrued prospectively. All patients had urodynamically confirmed type 2 SUI or intrinsic sphincter deficiency. Two patients had concomitant detrusor instability. Overall, the mean abdominal leak-point pressure was 101 cmH_2O.
Results All patients underwent surgery by one surgeon. Their quality of life was assessed using the King's Health Questionnaire and the SF-36. The mean length of hospital stay was 4.08 days; 10 patients had to use CISC for a mean duration of 7.7 days. At 6 weeks after surgery all patients were dry; at 6 months one patient developed recurrent SUI and six patients reported urgency symptoms. Of these, three were commenced on an anticholinergic drug. The quality-of-life questionnaires completed before and after surgery were analysed; preoperative data were available on all 56 patients, 6-week data on 27 and 6-month data on 17. As early as 6 weeks there was a significant improvement in quality of life. In particular, in relation to the categories of physical functioning and degree of pain (SF-36), there was a statistically significant improvement ($P = 0.003$ and 0.049, respectively). Analysis of the King's Health Questionnaire as early as 6 weeks after surgery showed significant improvement in the categories of role limitation, physical/social functioning and emotional status.
Conclusion In our experience pubovaginal sling surgery is effective, with a significant effect on the patient's quality of life.

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Tension-free vaginal tape sling for stress urinary incontinence: 2-year outcome

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Introduction The tension-free vaginal tape (TVT) sling is a new procedure for treating stress urinary incontinence (SUI). This study reports our early experience of treating both SUI and mixed stress and urge incontinence. We assessed safety, efficacy and complications.
Patients and methods We prospectively assessed 35 consecutive patients who underwent a TVT sling procedure between January 1998 and June 2000. All patients had a preoperative urodynamic assessment. The objective outcome was assessed at 3 months and 6-monthly thereafter. The subjective assessment was via a self-administered postal questionnaire completed after a median of 2 years. Demographic data, surgical and hospitalization details and complications were recorded.
Results The mean age of the patients was 56 years and the mean follow-up 26 months; 23 patients (66%) had stress incontinence and 12 (34%) had mixed urge/stress incontinence. Nine patients (26%) had undergone previous incontinence surgery. The mean duration of incontinence was 4.47 years. In the objective assessment, 86% of patients were completely dry and 11% improved; one patient showed no improvement. In the subjective assessment, 63% were cured, 17% had a major improvement, 14% were improved, one had no change and one was worse. Two patients reported de novo postoperative urgency. Complications included urinary retention (9%), bladder perforation (3%), UTI (12%) and dyspareunia (6%).
Conclusions The TVT procedure is simple to perform, has minimal postoperative morbidity and a durable success rate at 2 years. Subjective cure rates assessed via a self-administered questionnaire differ from the objective cure rates. Further long-term follow-up is required to assess the durability and allay fears about sling erosion.

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Cadaveric fascia lata sling repair for stress incontinence – initial results at the 2-year follow-up

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Introduction Sling procedures have been reserved for patients with recurrent stress incontinence or for those with intrinsic sphincter deficiency, because of the increased morbidity of the procedure. The use of cadaveric fascia lata has significantly reduced the morbidity of the procedure. We describe our initial results with a minimum of 2 years of follow-up.

Patients and methods The study included 28 patients (age range 36–78 years) who underwent cadaveric fascia lata sling procedures, as a 'sling on a string', using a 10 cm length of fascia lata (Tutoplast®). Fifteen procedures were undertaken for primary stress incontinence and 13 for recurrent stress incontinence. All patients had urodynamically confirmed stress incontinence and five had detrusor instability. All patients underwent voiding trials 36 h after surgery.
Results All patients were assessed by a pad test and quality-of-life questionnaire. The mean (range) follow-up was 24 (22–30 months) and the mean operative duration 44 (26–65) min. Of 15 patients with primary stress incontinence, 14 are dry and the other improved. Of 13 patients with secondary stress incontinence 10 are dry, two improved and one no better. There was no increase in the incidence of instability after surgery. Nineteen patients voided with residuals of < 200 mL at 36 h; seven further patients were voiding with residuals of <200 mL at 2 weeks; one patient used CISC for 5 weeks and one had an indwelling catheter for 8 weeks before voiding spontaneously.
Conclusion Cadaveric fascia lata sling procedures are safe and effective, with low morbidity in the short term. The procedure is quick and comparable with colposuspension or tension-free vaginal tape.

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How effective is re-operative retropubic surgery for recurrent stress incontinence?

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Introduction Re-operative surgery after failed retropubic surgery is hampered by previous scarring in the periurethral and retropubic area, more pronounced sphincter weakness, limited paravaginal tissue mobility, and increased patient apprehension, often exacerbated by failed previous surgery. This is a difficult group of patients, with greater operative morbidity.
Patients and methods Thirty-eight women with significant prolapse and stress incontinence underwent redo colposuspensions between 1992 and 1999; eight underwent a concomitant sling procedure. All were assessed before and after surgery with a standardized history (BFLUTS, Kings QOL Health and SF36 general health questionnaires) and an examination.
Results Of the 38 women, 33 (mean age 44 years, range 33– 72) who had undergone a mean (range) of 1.2 (1–4) previous continence procedures and had a mean follow-up of 45 (3–101) months (67% >36) had evaluable data sets. The preoperative mean pad usage was 4.5/day. After surgery, 27 (84%) patients currently report no symptoms of stress incontinence; 10 women developed de novo urge symptoms and six had persistent urge incontinence. The postoperative mean pad usage was 1.3/day, with 69% using 0–1 pads/day. Seven women (22%) had temporary voiding difficulties and four (13%) are still using CISC. Of the eight patients undergoing both a colposuspension and sling procedure, two remain on long term CISC and six report that their residual urinary symptoms have little or no impact on their lives.
Conclusions Repeat retropubic surgery for recurrent stress incontinence offers a high rate of success and patient satisfaction in the medium term. The concurrent use of a sling procedure and colposuspension is worth considering and will be discussed.

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Preliminary clinical results of a new AUS with conditional occlusion for genuine stress incontinence

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Introduction A new AUS with conditional occlusion has been developed. This prototype device has received full MDA and local ethics approval for Preliminary Clinical Investigation. The new device is in one piece and has a stress-relief balloon which transfers transient abdominal pressures to the bulbar urethral cuff to achieve conditional occlusion. The pressure is adjusted (0–70 cmH_2O) at activation by the percutaneous injection of sterile saline through the self-sealing port in the base of the pump unit.
Patients and methods Patients with genuine stress incontinence GSI after prostatectomy were included in the study. Four weeks after implantation the device was activated and the pressure adjusted for minimal urethral occlusion consistent with optimal continence. Continence was assessed using standardized leak tests in the laboratory and patient voiding diaries at home.
Results The device has been activated in two patients; during tests there was a significant reduction in leakage after both five strong coughs ($P<0.01$) and a Valsalva manoeuvre for 5 s ($P<0.03$) when comparing the device inflated and deflated, with bladder volumes of >400 mL. The results from the voiding diaries of one of the patients showed that there was a significant reduction in the ratio of leaked to voided volumes during the 5 weeks after activation.
Conclusion The new sphincter is simple to implant and provides continence at low regulated pressures, because of the conditional occlusion facility, thereby helping to protect the urethral tissues from pressure-induced atrophy.
Funding: LINK Medical Implants Programme DTI + DoH

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Outcome of the AUS in the female patient

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Introduction To review the outcome of all female patients in our unit in whom an AUS was inserted.
Methods The notes were reviewed for 68 patients and a postal questionnaire was distributed to those with no recent follow-up.
Results The median time since insertion was 12 years; overall, 25 patients had their original AUS *in situ* and were dry, with a median follow-up of 7 years. The sphincter had been replaced for loss of function in 12 patients, of whom 11 were dry with their replaced device, and removed for erosion or infection in 31 patients. Of these, 19 patients had had the device successfully replaced or were continent after removal of the device, giving an overall continence rate of 81%. Patients with neuropathic bladder dysfunction achieved a continence rate of $>90\%$, although half had required removal of the sphincter initially. When the indication for insertion was stress incontinence, 70% had their original or a replaced sphincter *in situ* and 82% were continent. All patients with previous pelvic irradiation had their sphincters removed and had been diverted.
Conclusions The overall continence rates in female patients after insertion of an AUS are satisfactory. Continence in patients with neuropathic bladder dysfunction and intrinsic sphincter deficiency stress incontinence are excellent, and the AUS should be considered first-line treatment in these groups. The risk of revisional surgery is high in the neuropathic group. Pelvic irradiation is a contra-indication to an AUS in female patients.

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The rectus tendon transfer colposuspension (RTTC) – a long-term follow-up

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Introduction The RTTC was developed in our unit 15 years ago. The technique has been presented as a video at BAUS previously. We now present the long-term follow-up of 44 patients who underwent this procedure.

Patients and methods Two surgeons at one centre operated on patients with genuine stress incontinence. Efficacy was assessed by patient interview and completion of the Bristol Female Lower Urinary Tract Symptom questionnaire. Uroflowmetry, frequency/volume charts and standard pad tests were also performed.

Results The mean (range) follow-up was 92.2 (7–161) months and the inpatient stay 8.4 (4–20) days; 16% of patients had a complication but only one was serious; 11% of patients had incomplete bladder emptying after the procedure, requiring self-catheterization. Thirty-three patients underwent the pad test at a mean follow-up of 83.2 months; 20 (61%) had no leak, six (18%) had minor leakage and seven (21%) had significant leakage. Survival curves were constructed to chart continence. At 3 months, 70% were dry, 17% had minor leakage and 13% were wet. At 36 months, 66% were dry, 17% had minor leakage and 17% were wet. At 60 months, 62% were dry, 21% had minor leakage and 17% were wet. At 108 months, 38% were dry, 17% had minor leakage and 45% were wet. At 152 months, 39% were dry and 61% were wet.

Conclusions Prolonged follow-up shows that continence continues to fail up to 13 years after an initial success. Medium-term continence is comparable with that of other established surgical treatments for genuine stress incontinence.

14.30–15.30
Poster Session 3
Prostate cancer 1

P22

Monoclonal antibody scans are not helpful in the preoperative evaluation of prostate cancer

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Introduction The ability to refine the selection of patients with truly localized prostate cancer from those with negative CT or MRI staging is a developing challenge in preoperative assessment. The mAb scans taken in our department were reviewed to assess their usefulness in staging men with prostate cancer before radical therapy, and to determine their influence on patient management.
Patients and methods Twenty-one patients (mean age 63.4 years, range 51–69) were reviewed, 15 with preoperative scans and six scanned after surgery, all of whom were negative on CT and bone scans. The mean (range) PSA level was 10.2 (3.5–19.5) ng/mL and the follow-up 9–33 months.
Results Whilst all 15 preoperative immunoscintigraphy scans showed increased prostatic uptake, half of those reported as localized disease were margin-positive at surgery, whilst a third of those suggesting capsular invasion were organ-confined. Subsequent histology was also negative for a patient with positive bilateral obturator node uptake. In those scanned after surgery four scans showed nodal recurrence (of which three also had prostatic fossa recurrence).
Conclusions In our experience, preoperative mAb scans do not reliably identify capsular invasion or nodal disease. However, they may have a role in guiding the management between local radiotherapy to the prostatic bed or early hormonal therapy for men with PSA relapse, but otherwise negative imaging results.

P23

Clinical evaluation of an optimised RT-PCR for PSA

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Introduction RT-PCR is a sensitive molecular technique that can be used to detect circulating tumour cells in peripheral blood. In previous studies the clinical sensitivity has been disappointing. We describe the use of a simple, reproducible method with increased sensitivity, in a clinical setting.
Patients and methods This is an ongoing study that continues to recruit patients; the initial 60 results are presented. An optimized one-step RT-PCR system (Roche) for PSA mRNA was used to analyse peripheral blood in patients attending a prostate clinic. Patients with both BPH and prostate cancer receiving a variety of treatments were included; samples were analysed in quadruplet.
Results RT-PCR was positive in 84% of patients with metastatic disease (both hormone-manipulated and escaped). Reactions were negative in 10 normal female controls. Patients after radical prostatectomy with an undetectable serum PSA were positive for PSA mRNA in 67% of cases. Patients with a serum PSA of <4 ng/mL and a clinical diagnosis of benign disease were also positive in 36% of cases.
Discussion This simple easily reproducible method of RT-PCR that has a higher sensitivity than those used in previously published studies. This technique may be of use in the diagnosis, staging and monitoring of disease. Patients after radical prostatectomy with a positive assay represent an interesting group and will be monitored, and the correlation with histopathology and outcome assessed.
Funding: Prostate Research Campaign

P24

Have we begun prostate cancer screening in the community? Current concepts of PSA estimation and diagnosis of prostate cancer in an East London general practice

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Introduction Adenocarcinoma of prostate is the second commonest cancer in men in the UK. The measurement of PSA has dramatically changed the way that prostate cancer is managed but there is controversy about the benefits of an early diagnosis. The unrestricted availability of PSA measurement has brought with it the problem of inappropriate usage of the test. We carried out a survey of GPs to assess their concepts of PSA estimation and diagnosis of prostate cancer.
Methods All 395 GPs from three Primary Care Groups in East London were sent questionnaires about their views on PSA testing and prostate cancer. The responses received within 5 weeks were analysed and are presented in this study.
Results Of the 395 questionnaires sent, 302 responses were received (76%); 88.5% of GPs routinely measure PSA in men with bladder outlet symptoms and 14.5% of GPs use PSA as a screening test in asymptomatic men. Although 83% of GPs are aware of increased yield of prostate cancer by a DRE, only 55% use the DRE. The remaining 45% thought that a DRE would affect the PSA estimate; 20% of GPs were not aware of age-adjusted PSA levels; 44.5% of GPs were not aware that prostate cancer could occur in the presence of a normal PSA level, while 38.4% were unaware that a significant proportion of men with a raised PSA do not have prostate cancer.
Conclusions This study indicates the necessity of implementing proper guidelines on PSA estimation and its limitations. There is also a need to educate GPs about prostate cancer and the vagaries of PSA estimation.

P25

Influence of PSA on prostate cancer presentation: demographic changes in an inner city population

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Introduction The widespread use of serum PSA estimation is in part responsible for the increasing incidence of prostate cancer seen over the past decade. Screening and case-finding in the USA have been associated with a shift in the tumour stage and grade at diagnosis. The aim of this study was to determine the change in characteristics of prostate cancer at presentation in a British inner city population.
Patients and methods Using a combination of the pathology, clinical coding and the BAUS oncology databases, patients with prostate cancer diagnosed between 1994 and 2000 were identified. Their

notes were reviewed and details of clinical presentation and initial treatment were extracted. Data were analysed in annual cohorts.
Results During the 7-year period, 510 patients with a new diagnosis of prostate cancer were identified. A mean (range) of 73 (57–86) patients presented per year, with the incidence peaking in 1997. The age at presentation did not change (mean 72.7 years, range 45–92). The median PSA at diagnosis was 23–46 ng/mL with no significant time trend. There was no shift in stage at diagnosis (30–44% of patients with clinically localised disease, 28–41% locally advanced, and 23–30% with metastases). There were more moderately differentiated tumours, whilst both well and poorly differentiated tumours declined with time (1994, well 31%, moderate 29% and poor 39%; 2000, 19%, 64% and 17%, respectively).
Conclusions In a deprived inner city population (27% social class IV and V, 13.4% unemployment) there has been no change in age or clinical stage at presentation of men with prostate cancer despite the increased use of PSA. There has been an unexplained trend towards tumours of moderate differentiation.

P26

Improving specificity in prostate cancer detection: the role of complexed PSA density of the transition zone

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Introduction Complexed PSA (cPSA) accounts for most of the measurable total PSA (tPSA) in serum. With advanced BPH, prostate volume contributes significantly to tPSA levels, leading to unnecessary biopsies in men without cancer. To correct for prostate volume and improve the specificity of PSA in prostate cancer detection, PSA density (PSAD) and PSA density of the transition zone (PSATZ) were developed. In men with suspected prostate cancer who underwent extended core (parasagittal sextant, four lateral peripheral zone, two transition zone) TRUS-guided prostate biopsies, we evaluated the relative usefulness of total and complexed PSAD (tPSAD, cPSAD) and total and complexed PSATZ (tPSATZ, cPSATZ) to distinguish between positive and negative biopsies.
Patients and methods Before extended core prostate biopsies, 424 men with suspected prostate cancer gave blood samples for the measurement of tPSA. In a subset of 224 men, cPSA levels were also determined. Total prostate volume and transition zone (TZ) volume were estimated by ultrasonography, using the prostatic ellipsoid method. ROC curves were then constructed for tPSAD, cPSAD, tPSATZ and cPSATZ.
Results Cancer was detected in 134 (32%) patients; in men with cancer, the median total prostate volume (36 mL) and TZ volume (19.7 mL) were significantly lower than the median total prostate volume (44.6 mL) and TZ volume (24.6 mL) in men with negative biopsies ($P < 0.001$ and 0.0017, respectively). The areas under the curves (AUC) were 0.81 (cPSATZ), 0.8 (cPSAD), 0.77 (tPSATZ) and 0.76 (tPSAD). The best results were obtained with cPSATZ at a threshold of 0.18, giving a sensitivity of 90%, a specificity of 34%, a positive predictive value of 38% and a negative predictive value of 88%. At 90% sensitivity, the specificities of the other derivatives were 5–10% lower than for cPSATZ.
Conclusion At a clinically relevant sensitivity, a cPSATZ threshold of 0.18 can help to avoid 34% of unnecessary prostate biopsies in men without cancer.

P27

Two core biopsy characteristics (percentage involvement and apical positive biopsy) can predict organ-confined prostate cancer

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Introduction Current clinical staging methods used preoperatively in predicting organ-confined prostate cancer are of limited value in an individual patient. The usefulness of some of the prostatic biopsy characteristics has been studied, with conflicting results. We used a multivariate analysis of eight preoperative variables to investigate their usefulness as predictors of extracapsular extension (ECE) and positive surgical margins (PSM).
Patients and methods Seventy men with clinically localized prostate cancer (T1/T2) and undergoing radical prostatectomy (RP) were enrolled in the study. The biopsy procedure (standardised protocol of 12 cores) and RP were performed by the same urologist. The biopsy cores and the RP specimen were analysed by the same team of two uropathologists following a standard protocol. The eight preoperative variables assessed were age, clinical stage, PSA, PSA density (PSAD), Gleason score, number of positive biopsies, percentage core involvement (PCI) and apical positive biopsies (APB).
Results In this series, 21 patients (30%) had ECE with 18 (26%) patients having PSM. A univariate analysis showed that PCI ($P < 0.001$), APB ($P = 0.0013$), PSA ($P = 0.003$) and Gleason score ($P = 0.01$) were significant predictors of ECE. However, in a multivariate analysis, PCI ($P < 0.001$) and APB ($P = 0.001$) were the only significant predictive variables for ECE. For predicting PSM, the APB ($P < 0.001$), PCI ($P = 0.001$) and PSA ($P = 0.01$) were of statistical value on univariate analysis. However, only APB ($P < 0.001$) and PCI ($P = 0.003$) predicted PSM on multivariate analysis.
Conclusion The results of this study clearly show the importance of the two biopsy characteristics PCI and APB, in predicting whether an individual patient has ECE and PSM.

P28

Outcome of an extended-core prostate biopsy protocol in the detection of prostate cancer

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Introduction Studies have suggested that TRUS-guided parasagittal sextant needle biopsies under-sample the prostate gland and therefore, under-detect the presence of cancer. Also, although postmortem studies suggest that as many as 24% of prostate cancers arise in the transition zone (TZ), only 2–4% of men undergoing routine TZ biopsies will have isolated TZ cancer. We investigated whether taking two TZ and four lateral peripheral zone (PZ) biopsies in addition to parasagittal sextant biopsies would improve our diagnostic yield in men with suspected prostate cancer.
Patients and methods The study included 493 men (mean age 68.7 years, SD 8.2) with elevated PSA levels with or without an abnormal DRE who underwent TRUS-guided prostate biopsies. 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 164 of the 493 (33%) men biopsied. Sextant biopsies were positive for cancer in 133 of 164 (81%) men. All three sets of biopsies were positive in 53 (32%) cases. In 77 (47%) men both the sextant and lateral PZ biopsies were positive while in 29 (18%) men, both sextant and TZ biopsies were positive. Thirty-one (19%) tumours were not

detected by sextant biopsies, 10 (6%) confined to the lateral PZ alone, 17 (10%) confined to the TZ alone and four (2.5%) where both the TZ and lateral PZ together were positive. There were no differences in PSA levels, total prostate volume or TZ volume or between men with an isolated TZ cancer and men with cancer elsewhere in the prostate. However, 77% of men with TZ cancer had a PSA level of >10 ng/mL, compared with 60% of men with cancer at other sites within the prostate.
Conclusion An extended core biopsy protocol increases the detection rate for prostate cancer by 19% when compared with the standard sextant biopsy protocol alone. Routine TZ biopsies should be considered for men with serum PSA levels of >10 ng/mL.

P29

The use of agar in processing prostate biopsies

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Introduction We report a technique of processing prostate biopsies in a gel matrix which allows several biopsies to be aligned and orientated on a single slide without creating extra work for the pathology department. Agar has been described for use in temporal artery biopsies [*Ophthalmology* 1999; 106: 2106–8].
Patients and methods Ethical approval was obtained; 0.2 g of low melting-point agarose was dissolved in 20 mL boiling water and allowed to set in a tray at 4°C. Biopsies were laid onto this gel matrix and a second layer of liquid agar poured on top and again allowed to set. The small block containing the biopsies was then cut out and put in formalin. The specimen was then sent to the pathology laboratory for processing.
Results After initial experimentation with chicken thigh tissue, prostate biopsies from six patients were processed. They stained, cut well and were interpretable with no loss of detail. The agar technique preserved the orientation of the prostate biopsy tissue during processing and embedding.
Conclusions We believe that this technique can be used to process prostate biopsies. We are currently refining the technique so that all prostate biopsies can be processed in one gel matrix. The thickness of agarose gel may be crucial in allowing penetration of the fixative. The extra degree of orientation this allows would facilitate the positioning of re-biopsy when histology of the primary biopsy shows an equivocal area.

P30

Reducing the rate of negative prostate biopsy – the role of a second PSA estimate before outpatient consultation

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Introduction The frequency of negative prostate biopsy in the investigation of a raised PSA level remains a problem for patients and urologists. Reference ranges for PSA are largely derived from asymptomatic screened populations atypical of many UK urological practices. A decision for prostate biopsy, based on one elevated PSA value, may be inappropriate in symptomatic patients in whom a high PSA could be transient. A second PSA estimate before consultation would detect a transient PSA elevation and may help prevent unnecessary biopsy.
Patients and methods All men referred to a single consultant urologist, at an outreach clinic, over a 1-year period with a PSA level of <50 ng/mL underwent a repeat PSA estimate before attending the clinic. Management was based on the history, examination, presenting and repeat PSA values.
Results In all, 549 men were referred to the clinic; 58 men (median age 73 years, range 49–84) were referred with a raised PSA of <50 ng/mL. The median (range) PSA level was 10 (4–47) ng/mL; 33 (57%) men presented with LUTS, 11 (19%) with symptoms suggestive of urinary infection, eight (14%) with haematuria and three (5%) as screening. In 35 of the 58 (60%) patients the second PSA level was lower than the first, the median fall being 4 (0.2–37) ng/mL. In 14 (24%) the PSA fell into the age-specific normal range. Seventeen men (29%) underwent TRUS and biopsy; 10 patients were found to have carcinoma and four prostatic intraepithelial neoplasia, giving a biopsy rate of 82%.
Conclusion Repeating the PSA measurement before consultation may be valuable in reducing unnecessary prostatic biopsy.

P31

Does the site of prostate cancer affect the chance of diagnosis?

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Introduction About 20% of prostate carcinomas are predominantly anterior in distribution and may not be readily detected on standard sextant biopsy. This hypothesis was tested by comparing biopsy features in patients with predominantly anterior and posterior tumours, respectively, at surgery.
Methods All tumours with an anterior distribution (at least 75% of tumour anterior to the urethra) on radical prostatectomy whole-mounts, in which the number and results of sextant biopsies were available, were selected from our prostate cancer database (62 cases). Sixty-one posterior tumours (at least 75% of the tumour posterior to the urethra) with sextant biopsies were extracted for comparison. The number of sets of sextants required to make the diagnosis, the number of positive cores and the summed tumour length were recorded, together with gland weight and tumour volume.
Results There was a significant difference between the number of sets of sextant biopsies required to diagnose anterior compared with posterior prostate cancers (anterior, one set 47, >1 set 15; posterior, one set 57, >1 set four; $P=0.007$). Furthermore, there was also a significant difference between the number of positive cores and summed tumour length between anterior and posterior tumours; anterior, mean (SD) number of positive cores 1.8 (1.01), summed tumour length 5.05 (4.10) mm; posterior, 2.50 (1.30) ($P=0.001$) and 9.25 (7.80) mm, ($P<0.001$), respectively. There was no significant difference in respective mean gland weight (43.8 g and 48.3 g, $P=0.3$) or tumour volume (1.85 mL and 1.49 mL, $P=0.11$).
Conclusion Anterior tumours yielded smaller areas of carcinoma on sextant biopsy than did posterior cancers in glands of similar weight and tumour burden. Multiple sets of biopsies were more frequently required in anterior than posterior neoplasms. If a diagnosis of prostate cancer is suspected but biopsies are negative, the anterior gland should be targeted at subsequent biopsy.

P32

You are what you eat: diet and prostate cancer

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Introduction Carcinogens of dietary or environmental origin may play a role in the aetiology of prostate cancer. Potent mutagenic and

carcinogenic heterocyclic amines and polycyclic aromatic hydrocarbons are produced in cooked meat, and after metabolic activation, some of them are strongly associated with prostate carcinogenesis in rodents. Such cooked-meat carcinogens include 2-amino-1-methyl-6-phenylimidazol [4,5-b] pyridine (PhIP) and benzo[a]pyrene (B[a]P). The susceptibility of human prostate epithelial cells (PECs) to PhlP and B[a]P is being examined.

Patients and methods Benign prostate tissue was obtained from TURP, minced in PFMR-4a medium and homogenates seeded onto collagen-coated Petri dishes. The ability of adherent PECs to activate carcinogens was examined using the alkaline single cell-gel electrophoresis (Comet) assay. PECs were treated with PhIP, its metabolite N-OH PhlP or B[a]P for 30 min at 37°C. DNA damage (single-strand breaks) was quantified as 'comet tail' length (CTL). The expression of key cytochrome P450 enzymes was investigated by RT-PCR.

Results Treatment of PECs (from four individuals) with PhIP (2.0, 20.0 and 200.0 μmol), N-OH PhIP (0.01, 0.1 and 1.0 μmol) and B[a]P (0.9, 9.0 and 90.0 μmol) induced comet formation. Control median CTLs ($n=4$) ranged from 13.5–18.0 μmol. After exposure to increasing concentrations of PhIP ($n=4$) or N-OH PhIP ($n=2$) median CTLs were 25.5–40.5, 52.2–78.5, 71.5–126.0, 45.5–71.0, 69.5–134.0 and 96.0–188.5 μmol, respectively. After exposure to increasing concentrations of B[a]P ($n=2$) median CTLs were 22.0–114.0, 28.0–138.0 and 75.0–184.0 μmol, respectively. PECs expressed CYP1A1, CYP1A2 and CYP1B1.

Conclusions Prostate cells are able to activate dietary carcinogens, leading to DNA adduct formation and DNA damage, which are important events in carcinogenesis. This may contribute to the overall risk of prostate cancer development.

14.30–15.30
Poster session 4
Stones

P33

Early renography does not alter the management of acute ureteric obstruction caused by stones

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Objective Acute ureteric obstruction caused by calculi is common and can lead to irreversible damage if left with no intervention for any duration. The objective of this study was to determine whether early renography in patients with ureteric obstruction by stone helps in deciding whether early intervention is required.
Patients and methods Admissions with ureteric colic over a 1-year period were assessed. All patients underwent IVU and those found to be obstructed by stone underwent MAG3 renography within 72 h. The subsequent management was determined by considering the patient's clinical condition, renographic and radiological findings.
Results Of 112 patients with colic who were evaluated, 57 had ureteric stones; 56% (32) had lower ureteric stones while the remainder had mid or upper ureteric calculi. Obstruction was evident in 13 patients and three of them required intervention. In the remaining 10 patients, five had no renographic evidence of obstruction; three of these passed the stone spontaneously. Of four with partial obstruction, two had deterioration in function renographically, but had cortical loss radiologically; the other two required ureteroscopic stone extraction. One patient was completely obstructed renographically, but had a long-standing cortical loss requiring nephrectomy.
Conclusions Early renography detected only one patient in whom renal function was markedly affected by ureteric calculus. In the other nine patients none had deterioration of renal function in the absence of IVU evidence of chronic cortical loss. Early renography does not, therefore, influence the management of patients with acute ureteric obstruction by calculus.

P34

Ureterolithiasis – the patient management journey is long and arduous!

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Introduction Obstructing ureteric calculi cause significant morbidity, including pain, sepsis and loss of renal function. Renographic studies have shown 'silent' loss of function in up to 30% of patients. Urgent management is therefore a priority. This multicentre study aimed to investigate the ureterolithiasis patient 'journey', with emphasis on waiting times for treatment.
Patients and methods The first 76 applicable patients presenting from February 2000, in four large NHS hospitals, were studied. Case notes were reviewed to determine the mode of presentation, initial assessment and treatment plans, subsequent interventions and follow-up to discharge. The intervals between these episodes were recorded.
Results About 60% were emergency admissions from GPs or A&E; outpatient referrals (40%) waited 1–55 days to be seen. Treatment plans depended on presentation, although ESWL was suggested for 70% in one centre, compared with $<10\%$ in another. The use of stents and/or nephrostomies also varied significantly. Waiting times for ureteroscopy were 1– >150 days and for ESWL 1–19 days; 97% of patients had IVU but only 4% had renography. One man needed a nephrectomy because of loss of function whilst waiting.
Conclusions Treatment strategies vary significantly; the delays in initial outpatient assessment can be long. Waiting times for treatment were unacceptable in many cases. Previous studies suggest early intervention (within 7 days) may save function. Measures similar to those now introduced for cancer care are needed if appropriate care is to be offered nationally to patients with ureterolithiasis.

P35

ESWL monotherapy for ureteric calculi: the influence of diuresis on stone fragmentation

A.M. Yousuff and D.J Almond *Princess Royal Hospital, Department of Urology, Kingston Upon Hull, UK*

Introduction An experimental study carried out previously in our department showed that in pig ureters fragmentation time was significantly reduced when fluid was introduced as an interface between the stone and ureteric wall. We believe that this result shows the importance of the cavitation phenomena during ESWL. The aim of the present study was to investigate the importance of the fluid-stone interface in a clinical study.
Patients and methods Patients with upper ureteric stones were selected and a prospective randomized double-blind study undertaken. Patients in group A were fasted for 6 h and given a placebo injection; those in group B were encouraged to take oral fluid and given 20 mg frusemide intravenously at the start of treatment. Both groups received standard ESWL monotherapy using a Comair C3000 lithotripter. Patients were reviewed with a plain radiograph 3 weeks later.
Results The mean duration of treatment in group A was 28.65 min and the mean number of shocks was 914. The mean time to treatment in group B was 23.35 min ($P=0.097$) and the mean number of shocks 742. There was no statistically significant difference between the groups. However, stones were fragmented in all patients in group B and in nine of 13 patients the stones were cleared. In group A the stones were fragmented in seven of nine patients and stones cleared in only three.
Conclusion These early data suggest that enhancement of the fluid-stone interface during *in situ* ESWL improves fragmentation and clearance of ureteric calculi.

P36

Comparison of the efficacy of two shock-wave generators in a prospective randomized study

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Introduction We compared the efficacy of two shock-wave energy sources: electrohydraulic (Dornier MFL-5000 lithotripter) and electromagnetic (Dornier Lithotripter S, DLS) for treating urinary calculi.

Patients and methods A prospective randomized study of 694 patients was conducted over 12 months to compare the efficacy of both machines; X-ray localization was used in both arms. Entry criteria were radio-opaque upper urinary stones of <25 mm, with no previous treatment. Success was defined as no residual stones at the 3-month follow-up. The results were analysed using univariate and multivariate statistics to evaluate variables that may have an effect on success, including the treatment.
Results In the multivariate analysis, the side, site of the stones, renal morphology and type of lithotripter had an independent effect. The mean (SD) treatment time was significantly longer for MFL, at 65.7 (44.7) min, than for the DLS, at 54 (32.9) min ($P<0.001$). The re-treatment rate was higher for the MFL (51.6%) than for the DLS (34%; $P<0.001$). The success rate was 82.4% for the MFL and 88.5% for the DLS ($P=0.03$). There was no significant difference between the lithotripters for ureteric calculi, while the success rate was higher in the DLS group for renal stones ($P<0.05$). The success rate was higher in the DLS group for stones of <10 mm, at 92.8% vs 85.3% for the MFL ($P=0.03$), while it was comparable for stones of >10 mm ($P>0.05$). There was no statistically significant difference in the complication rate for both groups.
Conclusion The electromagnetic lithotripter has clinical advantages over the electrohydraulic lithotripter in terms of treatment time, re-treatment rate and success rate.

P37

A comparison of percutaneous nephrolithotomy tract methods: balloon vs telescopic metal dilators

Z. Hussain, R.D. Inman, A.W.S. Elves, R. Orme and S.W.V. Coppinger *The Royal Shrewsbury Hospital, Shrewsbury, UK*

Introduction Haemorrhage is a worrying complication of percutaneous nephrolithotomy (PCNL); fluid absorption may also be a significant problem. It has been suggested that blood loss and transfusion may be reduced by using balloon dilators but the issue of fluid absorption has not been addressed. We report the results of a prospective randomized study comparing balloon dilatation with telescopic metal dilators for tract formation in patients undergoing percutaneous surgery for upper tract calculi.
Patients and methods The tract was formed by a uro-radiologist to accommodate a 30 F Amplatz sheath. The urologist was unaware of the method of dilatation. Intraoperative blood loss was measured using the HemoCue photometer and fluid absorption calculated using a gravimetric method. Sample size was calculated so as to be able to detect a difference of 100 mL of blood loss with 95% power. The surgical view was graded on a 10-point scale.
Results Fifty-seven consecutive patients were randomized to the two groups; there was no significant difference between the groups in age (mean age 49 and 48 years) or stone location. The total operative (77 vs 88 min), tract formation (5 vs 6 min) and fluoroscopy time (6.9 vs 7.3 min) were not significantly different. One patient in each group required postoperative transfusion. While the mean blood loss was less in the balloon group (43 mL vs 75 mL) this was not statistically significant. Fluid absorption (280 vs 300 mL) and morphine requirements (35 vs 44 mg) were also less in the balloon group, but not significantly so. The surgical view was marginally better using balloon dilators.
Conclusions Blood loss is not reduced by using balloon dilators. This study does not exclude relatively small differences in fluid absorption or analgesic requirements. We feel that the surgical view is probably more dependent on other factors. We have not found sufficient benefit to justify the much greater cost of balloon dilators.

P38

Routine placement of a nephrostomy tube after percutaneous nephrolithotomy is unnecessary

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Introduction In a previous series Bdesha *et al.* [*Br J Urol* 1997; 79: A3) reported the outcome of patients undergoing percutaneous nephrolithotomy (PCNL) where a nephrostomy tube was not routinely placed. We have continued our series and report our experience to date.
Methods A retrospective analysis, from case notes and radiographs, was conducted on a continuous series of patients; 100 PCNLs were performed on 96 patients. Of the stones, 23 were staghorn calculi, 56 were predominantly pelvic, whilst 16 were predominantly calyceal. Thirty-eight patients had undergone previous procedures for renal calculi. Seven patients had earlier PCNL, two had open nephrolithotomy and 29 patients had received lithotripsy (ESWL). In all cases, the track was dilated over a guidewire with a balloon (Cook) to 30 F for 1 min, followed by placement of an Amplatz sheath. Nephrostomy tubes were only left *in situ* if a further procedure was anticipated or if there was significant haemorrhage. When ESWL was required after PCNL, then a JJ stent was inserted antegradely at the time of the operation. Most patients had ureteric drainage, normally in the form of a ureteric catheter for 24-48 h.
Results Eight procedures (8%) required nephrostomy tubes after PCNL; three for planned nephrostograms, three for preservation of the track and in two when significant bleeding had occurred during the operation. Ninety-two patients did not receive nephrostomies at the time of PCNL. Three of these patients (3.3%) had urgent insertion of nephrostomy postoperatively for obstruction and of these, two had ureteric drainage and one did not.
Conclusion This analysis supports the conclusion that routine nephrostomy insertion after PCNL is only necessary if a specific indication exists.

P39

Laparoscopic stone surgery

D. Cahill, M. Perry and C. Eden *Frimley Park Hospital, Surrey, UK*

Introduction The role of open stone surgery has been marginalized by ESWL, ureteroscopy and percutaneous nephrolithotomy (PCNL). This trend has been extended by laparoscopic stone surgery. The indications are failed or contraindicated lesser invasive methods and any patient considered for open surgery.
Patietns and methods Between 1997 and 2000, 23 patients with stone disease were treated laparoscopically (17 ureterolithotomies four pyelolithotomies and one nephrolithotomy). All cases were undertaken using open-access extraperitoneal laparoscopy with balloon dissection. Otherwise the procedures mimic the equivalent open procedure.
Results Seventeen ureterolithotomies were undertaken with no conversion, using a ureteric stent, sutured ureterotomy, a wound drain and urethral catheter. The mean (range) operative duration was 116 (90–180) min and the postoperative stay 2.6 (2–4) nights. Four laparoscopic pyelolithotomies were carried out as part of a dismembered pyeloplasty. The nephrolithotomy was undertaken for a symptomatic calyceal diverticular stone in a patient who was severely allergic to contrast medium and had failed ESWL. The stone was located by intraoperative laparoscopic ultrasonography. The patient was rendered stone- and symptom-free with no complications.
Discussion Laparoscopic stone surgery is a novel and effective option for managing stones which would otherwise require open surgery.

Cases which are difficult laparoscopically are difficult at open surgery, and vice versa, and we no longer regard technical difficulty as a reason for conversion. It is effective, precise, reduces wound morbidity and the consequences thereof, and patients prefer it. Laparoscopy has further reduced the indications for open stone surgery in our department.

P40

Ureteroscopic holmium-laser lithotripsy for ureteric calculi – a prospective study

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Introduction The safety, effectiveness and outcome of ureteroscopic holmium-laser lithotripsy (HOLL) for ureteric stones was evaluated by a prospective study.
Patients and methods In 97 patients a total of 108 stones of 3–20 mm diameter were treated with transurethral ureteroscopic HOLL. Twenty-three stones were in the proximal, 27 in the middle and 58 in the distal third of the ureter, with 66 stones in the left and 42 in the right ureter. HOLL was administered with 7.5 F rigid and 8.5 F flexible ureteroscopes, 220 or 365 nm flexible laser fibres and a holmium:YAG laser (5–15 W, 0.5–1.0 J, 10–15 Hz). Most of the procedures were carried out by residents.
Results Flexible ureteroscopy was possible; all stones were assessed and fragmented, irrespective of their location and metabolic composition. Of 97 patients, 71 (73%) were immediately free of stones; 16 (17%) lost their residual fragments spontaneously and two patients were successfully treated with additional chemolitholysis for uric-acid stone fragments. Thus 90% of patients were stone-free with only one ureteroscopic HOLL. However, 10 patients (10%) still had residual calculi 4 weeks after HOLL; two asymptomatic patients (2%) refused any additional treatment, three patients (3%) were treated by ESWL and five (5%) had a successful second HOLL, thereby raising the success rate of ureteroscopic HOLL to 95%. Two patients showed contrast-medium extravasation on retrograde ureterograms, because of guidewire perforation. One ureteric stricture developed at the site of an encrusted large stone which had to be treated by two sessions of HOLL. The stricture was treated with holmium laser endoureterotomy.
Conclusions Ureteroscopic HOLL is a safe and effective minimally invasive therapy for ureteric calculi. In contrast to ESWL, electrohydraulic, electromechanical and dye-laser lithotripsy, ureteric calculi can be treated successfully, irrespective of their location and metabolic composition.

P41

Ureteric stent symptoms questionnaire (I): development and validation of a new outcome measure

H.B. Joshi, N. Newns, A. Stainthorpe, F.X. Keeley Jr, R. MacDonagh and A. Timoney *Bristol Urological Institute, Southmead Hospital, Bristol, UK*

Introduction We developed the Ureteric Stent Symptoms Questionnaire (USSQ), a self-administered and valid measure to evaluate the effect of stents on patients' quality of life (QoL).
Methods A structured literature search, patient interviews (nine) and prospective studies using existing generic (90) and symptom-specific (60) instruments with stents both *in situ* and after removal were conducted. The results formed the foundation for an initial draft of the USSQ, with 106 questions. After a review by the experts and field-testing (40), a final 38-item draft was produced. Formal validation studies of the new questionnaire were carried out to assess construct validity, internal consistency, sensitivity to change (50) and test-retest reliability (20). Discriminant validation was conducted by administering the questionnaire to 40 patients with renal calculi who did not have stents (stones) and patients with LUTS (40).
Results The final draft addressed various domains of health (five sections) covering urinary symptoms (11 items), pain (eight items with a visual analogue score), general health (six items), work performance (five items) and sexual matters (three items) with additional problems covered in five items. There was a high degree of internal consistency for all sections (Cronbach's $\alpha > 0.8$). A scoring system consisting of simple sum of the individual item scores was derived. The questionnaire has good test-retest reliability (Pearson coefficient >0.8) and construct validity. The USSQ showed significant changes in the score ($P<0.005$) across all domains with the stent *in situ* as against after its removal. All but the pain items (stones group) discriminated well between patients with and without stents.
Conclusions The new USSQ is useful in evaluating the effect of stents on patients' QoL. It is a psychometrically valid and reliable instrument, and is expected to be a useful outcome measure to compare different types of stents.
Funding: Hospital Research Foundation

P42

Ureteric stent symptoms questionnaire (II): evaluation of symptoms, quality of life and utility with indwelling ureteric stents

H.B. Joshi, A. Stainthorpe, F.X. Keeley Jr, R. MacDonagh and A. G. Timoney *Bristol Urological Institute, Southmead Hospital, Bristol, UK*

Introduction Indwelling ureteric stents are associated with various symptoms that affect patients' daily activities and quality of life (QoL). We conducted an in-depth evaluation of the symptoms by developing a new questionnaire, the Ureteric Stent Symptoms Questionnaire (USSQ), and present the evidence from a validation study.
Patients and methods Ninety consecutive adult patients (62 men and 28 women, mean age 54 years, range 19–80) with unilateral indwelling ureteric stents participated during the validation phase. They completed the USSQ and EuroQol, a weighted utility instrument, a month after stent insertion and removal. In addition, 40 patients completed these questionnaires 1 week after stent insertion to assess utility transition ('time trade-off' technique).
Results In all, 68 (76%) patients completed all necessary questionnaires. Urinary symptoms and pain that affected work performance and general health were important problems; 78% of patients reported bothersome storage symptoms, incontinence and haematuria; 80% of patients experienced stent-related pain affecting daily activities; 32% of patients reported sexual dysfunction; 58% of patients reported reduced work capacity (frequent rests, reduced number of hours) and negative economic impact. For a 30-day stent indwelling time, a mean (range) of 4.2 (0–14) days were spent in bed and 12.2 (1–30) half-days worth of activities were lost through stent-related problems. The EuroQol utility values (0 = death and 1 = perfect health) indicating patients' satisfaction were reduced after stent insertion. The mean utility scores (0.749) at week 1 reduced further (0.646) at one month after stent insertion. The scores (0.873) improved after removing the stent.
Conclusions Indwelling ureteric stents are associated with morbidity, resulting in compromised functional capacity and reduced QoL in up to 80% of patients. The utility values deteriorated as the duration of stenting increased. The results have implications in terms of routine clinical practices and better patient counselling.
Funding: Hospital Research Foundation

16.00–17.00
Poster session 5
Bladder Cancer 1

P43

Towards an assessment of EGFR in bladder cancer in routine clinical practice

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Introduction ErbB proto-oncogene expression is becoming increasingly important in the molecular assessment of human tumours and as a therapeutic target (c.f. herceptin). We previously showed a strong correlation between erbB-1 (EGFR) status and clinical outcome in bladder cancer using frozen tumour tissue. Antibodies suitable for use with paraffin-embedded samples have subsequently been developed, potentially facilitating the use of EGFR testing in routine histopathological tumour assessment. This study aimed to evaluate the immunohistochemical (IHC) detection of EGFR in corresponding paraffin tumour sections from our original frozen tumour series, to allow a comparison of the two techniques.
Materials and methods A subgroup of 101 tumours from the original series of 212 was identified. Paraffin sections were stained using NCL-EGFR mAb (Novocastra Labs, UK) and standard IHC. Stained sections were scored on a 4-point scale by two independent observers. Our clinical database was updated and currently we have complete data for 76 patients. The mean (SD) period of follow-up is now 67 (49) months.
Results In the assessment of EGFR, overall concordance between the techniques occurred in 74% (exact correlation in 49%); 8% of cases were EGFR(+) using paraffin sections and EGFr(–) using frozen sections, whereas the converse was true in 18%. Other comparative data for positive EGFR status were:

Group	*Frozen, %*	*Paraffin, %*
Overall	36	32
Ta–T1(42)	16	16
T2–T4 (34)	60	56
G3 (38)	55	50

Conclusion This study shows that techniques for the estimation of EGFR status using paraffin-embedded and frozen tumour tissue have good levels of concordance. The paraffin series needs to be expanded to determine if the same clinical correlations hold true for assessing EGFR in paraffin sections. Providing this is the case, we propose that such a technique could be used for future routine assessment of EGFR expression in bladder cancer.

P44

A haematuria clinic audit: cancer detection and the 2-week wait

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Introduction This is a prospective audit of the process of our haematuria clinic; to assess waiting times, compliance with clinic protocols and compare TCC detection rates with other series.
Patients and methods From October 1999 to September 2000, patients with macroscopic haematuria, or those > 50 years old with microscopic haematuria, were assessed with by a history, examination, urine cytology, ultrasonography and flexible cystoscopy. Data were entered into a database, which was completed after interventions.
Results Data were collected on 475 consecutive patients; malignancy was detected in 74 (16%), of whom 59 had TCC of the bladder. Other definite pathology was identified in 47 patients (10%) and no cause for haematuria was found in 354 (74%). The median time from haematuria to GP referral was 20 days and from referral to the haematuria clinic was 42 days. In those patients with TCC of the bladder, the median time from clinic to intervention was 45 days and from haematuria to intervention was 177 days. Patients with renal carcinomas waited a mean of 98 days from clinic to intervention. Compliance with clinic protocols was good, with 96% having urine cytology, 99.6% having upper tract imaging and 98% having cystoscopy. In those patients with microscopic haematuria 10 of 176 (6%) had a TCC detected, as opposed to 53 of 297 (18%) patients with macroscopic haematuria. Ultrasonography detected two of three ureteric tumours, the other being detected by urine cytology. Initial cystoscopy missed two TCC of the bladder.
Conclusions A clinically significant proportion of cancers was detected (16%), similar to results in other series. Although compliance with the one-stop protocol was very high, capacity problems led to waits much greater than current Government targets. Meeting the present targets for the proposed speed of the patient's journey has major resource implications for urology and will require very significant increases in funding to support the necessary extra activity.

P45

Neoadjuvant chemotherapy in the treatment of invasive transitional bladder cancer: a controlled prospective randomized study

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Introduction The definitive role of neoadjuvant chemotherapy in treating invasive bladder cancer has not yet been settled. This study was designed to address this issue through a controlled prospective randomized study in a single centre.
Patients and methods The study included 196 patients with locally invasive TCC of the bladder. Patients were prospectively randomized into two treatment groups. In group 1 (96 patients) two cycles of neoadjuvant chemotherapy (carboplatin 300 mg/m^2, methotrexate 50 mg/m^2 and vinblastine 4 mg/m^2) were given before radical

surgery. In group 2 (100 patients), radical cystectomy alone was used.
Results Patient and tumour characteristics were comparable in both treatment groups; the median (range) follow-up was 22.5 (0–144) months. The estimated mean (SD) 5-year tumour-free survival was 51 (5.1)% in group 1 and 30 (4.6)% in group 2 ($P = 0.003$, log rank test). Nevertheless, in a multivariate analysis in which several patient and tumour characteristics were included this difference was not sustained.
Conclusions Although neoadjuvant chemotherapy had an apparent therapeutic advantage over cystectomy alone, this benefit is not the result of an independent influence of chemotherapy.

P46

Bladder cancer trends over the last 25 years: incidence, mortality and survival in England and Wales

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Objectives To examine the trends in bladder cancer incidence and mortality in England and Wales in the last 25 years.
Methods The National Cancer Intelligence Centre database was used to calculate the current age-standardized incidence and mortality rates for bladder cancer.
Results Between 1971 and 1997 the total number of cases of bladder cancers increased by 67% from 7245 to 12 080. Over the same period age-standardized incidence increased by 22% in males and by 50.5% in females, whereas mortality fell by 25% in males and by 6.3% in females. The age-standardized relative 5-year survival in adults improved from 44% for patients diagnosed in 1971–75 to >62% for those diagnosed during 1986–90.
Conclusion The incidence of bladder cancer in England and Wales has been steadily rising, particularly in women. However, there has been a steady decline in mortality rates, which is more marked in males. The reasons for some of these trends are unclear.

P47

Morbidity of radical radiotherapy and cystectomy in the treatment of invasive bladder cancer

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Introduction Treatment options for invasive bladder cancers include radiotherapy and cystectomy. While the paramount issue in the choice of treatment should be oncological cure, in the absence of clear superiority, the morbidity and mortality of treatment and subsequent quality of life will determine treatment selection.
Patient and methods The study assessed 398 patients treated between 1993 and 1996 in Yorkshire.
Results Of the 398 patients, 302 received radical radiotherapy and 96 underwent radical cystectomy. Gastrointestinal complications were responsible for most complications soon after radical and salvage cystectomy. Bowel leakage occurred in 3% after radical and in 9.5% after salvage cystectomy. Urinary leakage occurred in 4% after both forms of cystectomy. Recurrent pyelonephritis and intestinal obstruction were responsible for most complications in the follow-up period. The re-operation rate for complications after both forms of cystectomy was 16%. The exacerbation of co-morbid medical conditions was responsible for a proportion of the mortality. Bladder and gastrointestinal complications accounted for most complications after radical radiotherapy. Severe bladder problems, which rendered the bladder nonfunctional or required surgical correction, occurred in 6.3% of patients; 2.3% of patients underwent surgery for bowel obstruction related to radiotherapy-induced bowel strictures. The 30-day and 3-month mortality for radical cystectomy, radiotherapy and salvage cystectomy were 3% and 8.3%, 0.3% and 1.4% and 8.6% and 15.5%, respectively.
Conclusions Gastrointestinal complications were responsible for most complications. The treatment-associated mortality at 3 months was two- or three-fold higher than the 30-day mortality, emphasizing its importance as an indicator of the true risks of cystectomy.

P48

Radiotherapy or cystectomy for invasive bladder cancer?

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Introduction Primary treatment options for invasive bladder cancers include radical radiotherapy and radical cystectomy. However, no satisfactory prospective studies have been carried out which provide clinicians with evidence on which to base management decisions. This study aims to compare survival after radical cystectomy and radical radiotherapy in patients with carcinoma of the bladder.
Patient and methods The study assessed 398 patients treated between 1993 to 1996 in Yorkshire.
Results Of 398 patients studied, 302 received radical radiotherapy and 96 underwent radical cystectomy. The patients undergoing radiotherapy were significantly older, but there was no difference in the distribution of ASA grades in the two treatment groups. The stage distribution of cases in the treatment groups was not significantly different. The 30-day and 3-month treatment-associated mortality for radical cystectomy, radiotherapy and salvage cystectomy were 3% and 8.3%, 0.3% and 1.4%, and 8.6% and 15.5%, respectively. Gastrointestinal complications were the major source of early mortality. Local recurrence in the pelvis was seen in 23.9%, 12.8% and 19.2%, respectively. The 5-year survival after radiotherapy (with or without salvage cystectomy) was 37.4%, while 36.5% of patients were alive 5 years after radical cystectomy. There was no statistically significant difference in the cancer-specific and overall 5-year survival values, stage for stage, between the primary treatments. Tumour stage, ASA grade and sex were the only independent predictors of survival on multivariate analysis.
Conclusions This retrospective regional study shows that there is no significant difference in the 5-year survival of patients with invasive bladder cancer treated with radiotherapy or radical cystectomy.

P49

Early radical cystectomy for T1G3 bladder cancer

S.Masood, M.S. Naseem, K. Subramonian, J.H. Palmer and G.R. Mufti *Department of Urology, Medway Maritime Hospital, Gillingham, Kent, UK*

Introduction More than half of patients with high-grade non-muscle invasive (T1G3) TCC of the bladder treated conservatively can develop muscle-invasive disease. These patients are also at life-long risk of dying from bladder cancer [*Br J Urol* 1997; 80: 762–5]. Our policy has been to offer these patients early radical cystectomy. This study is a retrospective analysis of our 9-year experience.
Patients and methods The records of 30 patients (24 men and six women) who underwent radical cystectomy for T1G3 tumours from 1991 to 2000 were reviewed. The preoperative histology was compared with that of the cystectomy specimen. Kaplan–Meier

estimates were used to determine survival and freedom from recurrence after cystectomy.
Results Seventeen patients presented with a single tumour with no CIS; in seven of these, the pathological tumour stage of the cystectomy matched the preoperative stage. In one the tumour was upstaged and in nine there was no tumour present in the cystectomy specimen (T0). Thirteen patients had multiple tumours or a single tumour with CIS at the time of cystectomy. In six of these, the pathological tumour stage of the cystectomy matched the preoperative stage and in seven the disease was upstaged. One patient died within 60 days of surgery. The 5-year survival and recurrence free rates were 92% and 82%, respectively.
Conclusions These results suggest that in patients with a single T1G3 tumour with no CIS the risk of muscle invasion is small (6%) and the likelihood of the bladder becoming tumour-free after TUR is 52%. Therefore, it is probably safe to persevere with conservative measures in this group. However, in patients with multiple tumours or those with a single tumour with associated CIS, the risk of the disease already being muscle invasive is 54%. Delaying radical surgery can jeopardise the chances of a cure in this group.

P50

Radical cystectomy vs radical radiotherapy for invasive bladder cancer: a comparative analysis from a single institute

S.F. Mishhriki, N.P. Cohen, A. Mawas, A. Golash and R. Mason *Department of Urology, Aberdeen Royal Infirmary, UK*

Introduction Evidence for the superiority of radical cystectomy over radical radiotherapy for the treatment of invasive bladder cancer is lacking. There have been no comparative studies or control trials.
Patients and methods In all, 157 patients treated for invasive bladder cancer between 1993 and 1999 were identified from the Grampian bladder cancer database; of these, 99 received radiotherapy (mean age 74 years, range 53–89) and 58 underwent primary radical surgery (mean age 69 years, range 52–85). The mean follow-up was 865 days, with minimum follow up of 12 months.
Results The tumour stage was comparable in both groups: T1, 13 (34%) and 15 (26%); T2/T3, 58 (58%) and 39 (67%); T4, seven (6%) and four (7%), respectively, for radiotherapy and cystectomy. Fifty-six (57%) and 27 (46%) patients died, and 43 (43%) and 31 (54%) are alive after radiotherapy and cystectomy, respectively. The median (95% CI) survival was 2.96 (1.91–4.00) and 1.85 (1.10–2.57) for radiotherapy and cystectomy, respectively. This was not statistically significant.
Conclusion In this study of the treatment of invasive bladder cancer neither cystectomy nor radiotherapy was found to confer superior survival. However, with longer follow-up, a trend in favour of cystectomy is now just starting to appear.

P51

The impact of treatment delays on survival for patients with invasive bladder cancer

R. Chahal, S.K. Sundaram, P.M.T. Weston, R. Iddenden and S.C.W. Harrison *Department of Urology, Pinderfields and Pontefract NHS Trust, Wakefield, West Yorkshire, and NYCRIS, Arthington House, Leeds, UK*

Introduction Intuitively, the detection and treatment of cancer at an early stage should improve the overall prospect for cure. Based on this, major efforts are being made to drastically decrease the time from referral to definitive treatment of all cancers. Thus we assessed the time delays encountered in the 'patient journey' of patients with invasive bladder cancer and evaluated the effect of these delays on survival.
Patient and methods The study assessed 398 patients treated between 1993 to 1996 in Yorkshire.
Results Of 398 patients studied, 302 received radical radiotherapy and 96 underwent radical cystectomy. Only 35.5% of patients had reported within 1 month of the onset of haematuria. The median delay from the GP referral to clinic review was 3.7 weeks, with a median 4.3 weeks then elapsing until transurethral tumour resection and a further 11.5 weeks until radical treatment was started. The overall median delay from GP referral to radical treatment was 19.5 weeks. Factors associated with longer delays included male sex, age >70 years, a presentation with irritative symptoms, a lower T stage and treatment with radiotherapy. Kaplan–Meir survival curves for patients with short (<12 weeks) and long overall delays (>12 weeks) to definitive treatment revealed no statistical difference in the survival at 5 years of follow-up. Although univariate analysis showed that patients with longer delays fared better at 5 years, multivariate analysis showed that only clinical stage, ASA grade and the sex of the patient were independent variables.
Conclusions Published reports provide conflicting evidence about the effect of treatment delays on the survival of patients with invasive bladder cancer. This study was unable to show any influence of treatment delays on survival.

16.00–17.00
Poster session 6
BPH TURP

P52

Finasteride given for 2 weeks before surgery reduces bleeding in patients undergoing TURP

J.F. Donohue, H. Sharma, R. Abraham, S. Natalwala, D.R. Thomas and M.C. Foster *Good Hope Hospital, Birmingham, UK*

Introduction Bleeding associated with TURP can often be significant and lead to increased morbidity and occasionally mortality. Finasteride reduces bleeding in patients with haematuria of prostatic origin. We hypothesized that bleeding in patients undergoing TURP could be reduced by giving them finasteride for 2 weeks before surgery, by reducing prostate vascularity via a reduction in dihydrotesterone.
Patients and methods Seventy patients due to undergo elective TURP were randomized to receive either 5 mg of finasteride daily or placebo for 2 weeks before surgery. Exclusions included those already on finasteride, hormonal treatment for prostate cancer or renal failure. Serum haemoglobin (Hb) was measured before and after surgery, and on the following day. The volume of irrigation fluid used and its Hb concentration, along with the weight of resected prostate, was recorded.
Results In all, 68 patients underwent TURP; two withdrew before surgery; 32 received finasteride and 36 placebo. There was no difference between the groups in age (mean 70 years), weight of prostate resected (mean 18.3 g), preoperative catheterization, aspirin usage or those diagnosed with prostate cancer. There was significantly less blood loss in irrigation fluid in the finasteride group than in the control group; 43.6 g Hb vs 69.3g Hb ($P=0.011$). The difference was more significant when expressed as blood loss per gram of prostate resected, i.e. 2.65 vs 4.65 ($P<0.001$). There was a difference in serum Hb loss between the groups but it was not significant.
Conclusion This study shows that finasteride given for 2 weeks before surgery reduces bleeding in patients undergoing TURP.

P53

Haematuria – a long-term complication of TURP?

E. Bowden and S.J. Foley *Royal Bournemouth Hospital, Bournemouth, Dorset, and Battle Hospital, Reading, Berkshire, UK*

Introduction Haematuria after TURP is well recognized but the incidence is unknown. It was considered that bleeding from the prostate remnant was the most common cause of haematuria after TURP; this study aimed to clarify this hypothesis.
Patients and methods A prospective study was conducted on 100 consecutive patients (mean age 74.5 years) presenting to the haematuria clinic, to identify the cause of bleeding in patients who had previously undergone TURP (mean time since TURP, 8.5 years) for histologically confirmed BPH.
Results The cause of haematuria was prostatic regrowth in 63%, bladder cancer in 12% and prostate cancer in 10%.
Conclusion This study supports our hypothesis that haematuria in patients who have previously undergone TURP is most likely to be caused by prostatic bed bleeding. If necessary this could be treated with finasteride, which has previously been shown be effective. However, all patients need a full investigation, as the incidence of malignancy in this age group is very high.

P54

Ten-year trends in TURP for BPH in Scotland – are we doing it better?

M. Hehir, M. F. Smith, A.C.N. Rogers, S. Pandian, C. Lynch and the Stirling Prostate (Natural History) Study Group *Stirling Royal Infirmary, Stirling, Scotland*

Introduction TURP remains the standard surgical approach for BPH despite the popularity of medical therapies and the introduction of laser therapy and other novel techniques. The methods for patient selection have developed considerably and most urologists are undertaking fewer TURPs.
Methods Data supplied by the Information and Statistics Division of the Scottish Health Service were assessed to determine if outcomes and complications were changing, and to establish benchmarks for current practice.
Results The number of TURPs for BPH has decreased by 44% in 10 years, the decrease from 1994 to 1999 being steep (47%), from 3843 to 2019. In the same time from 1990 the number of urologists has increased by 33%, giving a change in TURPs per urologist from 100 per year to 42. Of the total number of TURPs, ≈ 1000 per year are undertaken after an episode of urinary retention. This has remained constant over 10 years, suggesting that episodes of urinary retention have remained common and now account for nearly half of patients undergoing TURP. The 30-day mortality has remained constant during the 10 years and is age related, with $<0.5\%$ mortality in those aged <65 years, $<1\%$ mortality for 65–75 years and 1.5% in those >75 years. The mortality for those >85 years old is 3–4%. The length of hospital stay has decreased dramatically; total bed nights have decreased from 43 000 to 17 000 for all TURPs in Scotland. The mean stay has declined from 8.12 days to 5.49; this has a major effect on NHS resources.
Discussion The changes in the management of BPH have implications for both urological practice and urological training. A reduction of 60% in the number of TURPs per consultant will have a significant implication for trainees. The mortality rate has not changed over 10 years, so efforts need to be directed towards improving this, particularly in the very elderly. Local departments and individual urologists can use national data to audit their practice and outcomes.

P55

A review of transrectal intraprostatic vasopressin

D.P. Sharma and A.B. Harvey *Woodlands Hospital, Georgetown, Guyana, South America*

Introduction The Third World urologist needs to be concerned about bleeding and water absorption during TURP, because there are financial and technical constraints with this procedure. We proposed the use of intraprostatic vasopressin (IPVP) to vasoconstrict prostatic vessels and so reduce blood loss during TURP. We predicted that narrowed, vasoconstricted vessels would allow less fluid to enter the circulation. We tested these hypotheses in two separate studies.
Patients and methods In the first study, 38 patients were randomized to two groups; group 1 received IPVP and group 2 did not. The prostates of both groups were $\leqslant 20$ g. The IPVP group received a single transrectal bolus of 10 U of vasopressin in 0.5 mL,

diluted with 9.5 mL isotonic saline. No special equipment was required. The second study consisted of 36 consecutive patients presenting for TURP with prostates of $\geqslant 40$ g. Alcohol was added to the water irrigant and blood loss measured using Nesbit's technique. The free haemoglobin was measured using Ames reagent strips before and after TURP; serum sodium concentration was measured using a spectrophotometer. Patients were breathalysed during TURP using a Lion alcolmeter.
Results IPVP halved the blood loss; minimal irrigant entry was detected in the second study, except in one patient who had early capsular damage.
Conclusion We conclude that IPVP reduces both blood loss and irrigant entry. Can IPVP reduce glycine absorption and prevent cardiotoxicity?

P56

What do men expect to happen to their symptoms after TURP?

R.J. Frymann, P. Abrams and J. Donovan *Bristol Urological Institute, Southmead Hospital, Westbury-on-Trym, Bristol, UK*

Introduction Realistic expectations of the potential benefits of any treatment are important considerations when counselling patients during informed consent. Patients with unrealistic expectations are at risk of dissatisfaction and, therefore, expectations may be crucial in determining satisfaction after surgery. As expectations have never been measured before in men awaiting TURP, we attempted to measure the range of expectations of a group of men before TURP, and to assess whether expectations are influenced by current symptom severity.
Methods A new, validated, self-completed questionnaire, based on the ICSmale questionnaire, was given to 91 men before TURP. The questionnaire was designed to measure current symptomatology, and expected future symptomatology, and was completed by 65 men with LUTS, and 26 men with a catheter. All men under 80 years old, awaiting surgery for clinical BPO, were approached.
Results The mean (range) age of the patients was 70.1 (52.7–80.8) years. The data were analysed as five separate scores: daytime frequency, nocturia, filling and voiding scores, and impact on quality of life (QoL). All patients expected to have a significant reduction in their overall symptoms scores after surgery ($P<0.01$). Although the catheterized patients expect to have higher mean symptom scores than the symptomatic group after surgery, the difference was not significant.
Conclusions Most patients have high expectations of TURP, with 33% expecting to be completely symptom-free after surgery, and 65% expecting to have a score of $\leqslant 2$ out of 40. Expectations are unaffected by baseline symptom severity or catheter status.
Funding: Glaxo Wellcome

P57

Sub-group analysis of IPSS values predicts a better outcome from TURP

H. Toussi, N. Athmanathan and S.G. Vesey *Department of Urology, Southport & Ormskirk Hospitals, Southport, UK*

Introduction The validity of sub-grouping IPSS values into separate filling and voiding scores has been confirmed. However, such sub-grouping is not predictive of the outcome of medical therapy for BPH. We examined whether symptom sub-grouping could better predict the outcome for the surgical treatment of BPH.
Patients and methods The IPSS and quality of life (QoL) score of 179 patients undergoing TURP were examined. Filling and voiding score ratios were calculated for each patient. A 'void minus fill' (V-F) score variable was calculated for each patient by subtracting the filling from voiding score ratios. Patients were divided into 'good outcome' (154) and 'poor outcome' (25) groups based on their postoperative QoL score and/or IPSS changes. The above variables were then assessed for their ability to predict the outcome of surgery.
Results The mean age of the patients in the poor-outcome group was higher (71.9 vs 68.1 years) but this was not statistically significant. The preoperative IPSS and voiding symptom ratios were significantly lower in the poor outcome group ($P=0.034$ and 0.014, respectively). Patients with poor outcomes had significantly higher filling and voiding symptom ratios after TURP ($P<0.001$ and 0.001). Poor outcome patients had a more negative V-F score (i.e. higher filling symptoms), both before and after TURP, but these differences were not statistically significant. The preoperative QoL and filling symptom scores were similar in both outcome groups.
Conclusion Sub-grouping the IPSS values into filling and voiding sub-groups is useful in predicting the outcome of TURP. Patients with higher preoperative obstructive scores have better outcomes.

P58

LUTS bother partners too

S.F. Mishhriki, N.P. Cohen, A. Mawas, G. Banerjee, A. Golash, R. Mason and A. Sutherland *Department of Urology, Aberdeen Royal Infirmary, UK*

Introduction Symptom scores are important in assessing men with LUTS suggestive of BOO. Men sometimes make light of their symptoms, causing delay in seeking medical advice. Wives or partners are occasionally a better judge of symptom severity.
Patients and methods In all, 458 men with LUTS were referred for consideration for TURP. Objective assessments, before and after TURP included measurement of flow rates and bladder residual volumes, and AUA symptom scores, quality-of-life and bother scores were completed by patients before and at 3 and 6 months after TURP, and after 6 years of follow-up. Similar questionnaires were completed by the partners accompanying the patients, at home, or posted back.
Results

Variable	*Before TURP*	*6/12 months*	*6 years*
AUA score	18	6.3	10.3
Bother:			
patient	15.39	4.65	8.16
partner	19.61	3.49	6.75
QoL			
patient	7.92	2.38	3.45
partner	9.9	1.68	3.43
Q_{max}, mL/s	10.2	18.51	17.17

Generally, partners scored preoperative symptoms more severely than their husbands, but symptom improvement after TURP was greater with lower postoperative scores. Although the mean scores increased for both patients and partners at the 6-year follow-up, the 6-month follow-up trend was maintained.
Conclusion Patients' perception of voiding symptoms varies. This prospective long-term follow-up study showed that partners regard their husband's preoperative symptoms as being more severe, but report a greater improvement in their postoperative symptoms. This adjustment persisted long-term. Partners are able to provide useful additional information about the symptoms suffered by their male partners.

P59

Is the complication rate after TURP influenced by the histological diagnosis?

P. Crow and A.W.S. Ritchie *Urology Department, Gloucestershire Royal Hospital, Gloucester, UK*

Introduction During an SAC visit, an 'inspector' commented that he normally tried to avoid TURP for patients with malignant prostates, because the complication rate was 'high'. A literature search failed to substantiate this assertion and we thus examined our database.
Patients and methods A prospective, computer database was used to collect operative and outcome data. 'In hospital' complications, recorded at the time of the discharge summary, were classified as 'none', 'major' or 'minor' and validated at monthly audit meetings. Histology results were classified as benign, malignant or microscopic malignancy.
Results Between May 1991 and September 2000, 3036 discharges after TURP were identified. There was no significant difference in the major (2.1% vs 2.6%, chi squared 0.63, $P<0.5$) or minor complication rate between patients with benign or malignant histology. The length of stay was not significantly longer for patients having malignant vs benign histology, but was significantly longer for patients who had complications, irrespective of histology ($P<0.001$).
Conclusions These data do not confirm that the complication rate or length of stay is related to the histological diagnosis.

P60

TURP can improve your sex life

N.P. Cohen, S.F. Mishhriki, A. Mawas, B. Gibbons, G. Bannerjee, A. Golash R. Mason and A. Sutherland *Department of Urology, Aberdeen Royal Infirmary, UK*

Introduction Several studies have claimed a significant risk of adverse effects from TURP on potency. We studied sexual activity before and after TURP as part of an overall assessment of patients referred electively for the treatment of LUTS. We have now followed up these patients for at least 6 years after TURP.
Patients and methods After a full assessment, 280 patients referred with symptomatic BPH underwent TURP (mean age 68 years, range 49–88). Sexual questionnaires about the patients' interest in sex and engagement in sexual activity were completed before TURP, at 6 months afterward and at the 6-year follow-up. Patients, wives or partners completed similar questionnaires independently. Of the 280 men, 120 (43%) were still sexually active before TURP; 160 (57%) were either sexually inactive or reported significant dysfunction before TURP. This was supported by the wives' questionnaires.
Results Of the 120 sexually active men, 73 completed the full follow-up at 6 months. All of these men were still sexually active after TURP; 17% of men with pre-existing sexual dysfunction reported improved sexual activity and erection quality at the 6-month follow-up visit. Of the 73 patients, 45 (mean age 70 years) have completed the 6-year follow-up to date. Of these, 29 (64%) are still sexually active.
Conclusion Historical reports suggest that TURP carries a significant risk of sexual dysfunction. In contrast, this long-term follow-up prospective study showed that erectile difficulties frequently precede surgery. By using partner questionnaires independently of the men, we showed that TURP has no adverse effects on sexual function. Moreover, preoperative sexual dysfunction can be improved by TURP.

P61

Does TURP affect long-term survival?

G. Banerjee, R. Mason, N.P. Cohen, A. Mawas, M. Nicol and S.F. Mishhriki *Department of Urology, Aberdeen Royal Infirmary, UK*

Introduction One of the commonest surgical modalities for the treatment of BOO is TURP. However, several studies reported an increase in short- and long-term mortality.
Patients and methods Between 1993 and 1995, 458 patients with BOO were entered into a prospective study; 280 underwent TURP and 178 chose medical therapy or watchful waiting. The follow-up was conducted for 6–7 years and the mortality of the two groups compared. The mortality of the TURP group was also compared with an age-matched group from a background population.
Results The mean (range) age for the TURP and conservatively treated groups was 68 (49–88) and 65 (42–84), respectively. Of those who had TURP, 61 (22%) died from unrelated causes, vs 34 (19%) who did not. The relative risk of death for those having TURP was 1.18 (95% CI 0.738–1.886) when compared with men on medical therapy or watchful waiting (not statistically significant). Moreover, the TURP group had a lower mortality than the background population.

Age category	*Total no.*	*No. deaths expected*	*Observed*	*Standardized mortality rate*
55–59	6	0.7	0	0
60–64	20	3	3	100
65–69	52	15	4	27
70–74	70	25	13	52
75–79	71	36	21	58
80–84	43	29	17	58
>84	18	15	5	33

Conclusion The mortality of the TURP group was not significantly different from those who had medical or no treatment. The mortality for the men who had TURP was less than the expected. Medical treatment is widely used in BOO. Where TURP is indicated it should be regarded as a safe operation; it does not affect long-term survival.

P62

Long-term satisfaction after TURP

R. Mason, F. Mishriki, A. Mawas, A. Golash, N.P. Cohen and A. Sutherland *Department of Urology, Aberdeen Royal Infirmary, Aberdeen, UK*

Introduction TURP remains the commonest surgical treatment for BOO. However, up to 25% of patients may have residual symptoms afterward. It has been widely assumed that persistence of symptoms is the cause for dissatisfaction. We have studied patients' satisfaction and perceived success of surgery in an attempt to identify indicators of outcome.
Patients and methods In all, 280 consecutive men with BOO and undergoing TURP were prospectively studied. Objective assessments included pre- and postoperative flow rates, AUA symptom scores, quality-of-life and bother scores. These were completed by the all patients before TURP, at 3 and 6 months and after 6 years of follow-up. Patients' partners completed similar questionnaires independently.

Results In all, 166 and 114 patients were followed up after 6 months and 6 years, respectively. At 6 months only 15 (9%) patients and at 6 years 19 (17%) were truly dissatisfied with the outcome of surgery. Although some patients had residual symptoms most had marked improvements in flow rates and symptom scores, which persisted up to 6-year follow-up (see Table in abstract P58). The patients' mean bother and quality-of-life scores decreased; the partners recorded similar improvements in their husbands' symptoms.

Conclusion TURP remains the gold standard treatment for BOO. The vast majority of patients experienced long-term successful and satisfactory results. In the minority who do not improve, a variety of factors appear to be involved. Residual symptoms are one factor, despite marked improvements in objective and subjective measures. Inadequate preoperative explanation or inappropriate expectations may be involved.

Wednesday 27 June
10.30–11.30
Poster session 7
Basic Science - Oncology 1

P63

Caspases: mediators of prostate cancer cell apoptosis

R.N.T. Coffey, R.W.G. Watson and J.M. Fitzpatrick
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Introduction The caspases comprise a family of death proteases that play an central role in the signalling and execution phases of apoptosis. Expressed in almost all cell types, they exist as inactive pro-forms. Their role in the aetiology of prostate cancer is currently a major area of research. Caspase activation is essential during the process of glandular regression after androgen withdrawal and their inability to be cleaved to an active state has been associated with hormone-insensitive prostate cancer. The aims of this study were: (i) to identify a potential means of sensitizing prostate cancer cells to apoptosis by targeting the expression of the caspases; and (ii) to assess the effects of androgen on LNCaP caspase expression, and determine how this effects apoptotic sensitivity.
Materials and methods Apoptosis in primary and secondary (PC-3, DU145, LNCaP and LNCaP-Bcl-2) prostate cancer epithelial cells was assessed by flow cytometry using propidium iodide incorporation. RNA protection assays and Western blotting were used to assess caspase gene and protein expression.
Results Increased caspase protein expression by treatment with sub-toxic doses of diethylmaleate was effective in sensitizing all cell types to chemical- (Fas, VP16, cycloheximide) and radiation- (5 Gy) induced apoptosis. Androgen supplementation in the LNCaP cell line had a protective effect against apoptosis, a process that was dependent upon altered caspase gene expression.
Conclusion Targeting the caspases could be a useful adjuvant-based strategy for treating prostate cancer. Our data suggest a protective role of androgen against apoptosis, thus supporting the rationale for androgen ablation before radiotherapy.
Funding: Irish Cancer Society

P64

CD40 expression in prostate cancer

P.W. Cooke, R. Ganesan, N.D. James, S. Hussain, P. Atherton, D.M.A. Wallace and L.S.Young *Department of Urology, Queen Elizabeth Hospital, Department of Pathology, City Hospital, and CRC Institute for Cancer Studies, University of Birmingham, UK*

Introduction CD40 is a member of the TNFR superfamily which plays a critical role in normal humoral and T cell-mediated immunity, and is implicated in the regulation of normal epithelial differentiation. It is expressed by most tumours, and may be of great significance in the development and treatment of cancer.
Materials and methods Archived paraffin-embedded TURP/trans-rectal needle biopsy specimens from 64 patients with prostate cancer (stages T1–T4 NxM0/M1) were stained immunohistochemically using an APAAP technique and the anti-CD40 antibody G28.5. The immunostaining was assessed under light microscopy by a pathologist.
Results Normal prostatic epithelium was present in all of the specimens examined, but in seven cases no tumour was seen. CD40 was expressed by normal epithelium in all of the specimens, and was restricted to the basal (stem) cell layer. Conversely, expression was completely absent in all tumour cells where present (57 cases).
Conclusion The development of prostate cancer is associated with the loss of CD40 expression, which is in contrast to virtually all other tumours. This suggests differences in the mechanism of normal cellular differentiation, and its relationship to CD40, between the prostate and other epithelia. The absence of CD40 expression seen in prostate tumour cells may result in reduced presentation of tumour antigens, by down-regulation of MHC Class II, TAP 1 and 2, and co-stimulatory molecules such as B7.1 and B7.2, ICAM1 and LFA1. It also has implications for the future development of novel CD40/CD154-based immunotherapy. Further studies are warranted.
Funding: Zeneca, CRC

P65

Alteration in protein kinase C expression is associated with hormone independence

P.A. Cornford, A.D. Desmond, M.V.P. Fordham, K.F. Parsons, K.A. Woolfenden, J.P. Neoptolemos and C.S. Foster *Department of Urology, The Royal Liverpool University Hospital, and Departments of Surgery and Pathology, The University of Liverpool, Liverpool, UK*

Introduction Protein kinase C (PKC) isoenzymes are a family of second messengers important in the control of cell proliferation, differentiation and apoptosis. They are particularly important in transmitting the effects of growth factors which modulate the effects of androgens. Their expression is altered in prostate cancer. In addition, the effect of modulating PKC differs between androgen-responsive and -independent cell lines. This study evaluated the expression of individual PKC isoenzymes in human prostate cancer tissue and compared it with the degree of apoptosis, proliferation and the hormone status of the tumour.
Materials and methods Prostate tissue from 85 patients with advanced prostatic adenocarcinoma, previously treated with BSCO, was included. Patients were classified as hormone-sensitive (54) or -escaped (31). The expression of PKC-α, -β, -ε, -λ and -ζ was assayed by immunohistochemistry. The immunohistochemical expression of Ki67 was used to assess proliferation, whilst apoptosis was quantified using the TdT-FragEL DNA Fragmentation Detection Kit. Specimens were scored by two investigators. The data were analysed using the chi-square test and Kruskal–Wallis analysis.
Results There was no significant difference in the expression of PKC-α, -λ or -ζ between the hormone-sensitive and -insensitive cancers. Tissue from patients with hormone-escaped prostate cancer showed increased expression of PKC-β ($P<0.001$) and PKC-ε ($P=0.007$). Expression of PKC-β correlated with the apoptotic index ($P=0.003$) but not the proliferative index, whilst PKC-ε expression correlated with the proliferative index ($P=0.05$), but not the apoptotic index.
Conclusions A decrease in the rate of apoptosis is known to be an important part of the mechanism by which androgen independence develops. We propose that alterations in PKC isoenzyme expression are involved in allowing prostate cancer cells to survive in a low-androgen environment.
Funding: Helen Tomkinson Award

P66

The role of adenoviral vectors in genetic prodrug activation therapy in prostate cancer

J.D. Eaton, I.D. Clarke, H. Pandha, A.G. Dalgleish and R.S. Kirby *St George's Hospital Medical School, Tooting, London, UK*

Introduction Genetic prodrug activation therapy (GPAT) is an innovative approach that can kill tumour cells by inserting suicide genes into cancer cells. The cancer cells then use their cellular machinery to convert an otherwise benign exogenous substance (prodrug) into an agent that is cytotoxic to the cell. Current gene transfer technologies do not allow all cells to be transfected. Therefore, critical to the success is the 'bystander effect', which confers cytotoxicity on neighbouring untransfected cells. Adenoviral vectors using the herpes simplex virus thymidine kinase/ganciclovir (HSVtk-GCV) system are being used increasingly. To establish the susceptibility of prostate cell lines to adenoviral transfection, we used an adenoviral vector containing green fluorescent protein (GFP) to transfect nine human prostate cell lines (benign and malignant) and two rat prostate cancer cell lines.
Materials and methods The cell lines were exposed to the replication-deficient adenoviral vector (CMV) containing GFP (Ad5-CMV-GFP) at PFU:cell ratios of 0–100. The cells were exposed to the virus for 4 h, and then virus was removed and replaced with normal medium. GFP expression was assessed after 24, 48 and 72 h using FACScan analysis. Cell viability, using a standard MTT assay, was also assessed to ensure the virus had no toxic effects, even at the higher PFU:cell ratios.
Results All the cell lines showed a dose-dependent increase in GFP expression with increasing PFU:cell ratio. The cell lines showed variability in susceptibility to transfection. LNCaP was the most susceptible line to transfection, with 99% of cells GFP positive at 100 PFU/cell, and even at 1 PFU/cell, 60% of cells expressed GFP. The virus appeared to have no toxic effects on the cells even at the ratio of 100 PFU/cell.
Conclusions This preliminary work shows that adenoviral vectors are acceptable for transfection of prostate cells. However, the level of transfectability is highly variable among cell lines and therefore the mechanism of transfection and the bystander effect needs to be explored in these cell lines. We are currently working on these areas and have also commenced work using Ad-CMV-HSVtk in these cell lines.

P67

Androgen-inducible fibroblast growth factor 8 in prostate cancer

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Introduction Fibroblast growth factor 8 (FGF8) was first identified as an androgen-inducible gene in mouse mammary carcinoma cells. In human prostate cancer we showed FGF8 transcript over-expression and an association with poor survival. In this study we investigated the interaction of FGF8 with steroid hormones.
Materials and methods The FGF8 proximal promoter was sub-cloned into a luciferase expression vector and used to study its response to steroid hormones. Using a FGF8b antibody we investigated expression of FGF8 protein in a range of prostate cancer cell lines. LNCaP cells were then treated with androgens and assayed for FGF8 protein levels. Finally, we studied FGF8 protein expression in 30 cases of clinical prostate cancer (TUR biopsies) by immunohistochemistry.
Results In the prostate cancer cell lines LNCaP, DU145 and PC3, the FGF8 gene promoter was induced 2.5-fold by exogenous androgens. Furthermore, oestrogens, via the oestrogen receptor, had a similar inductive effect in prostate cancer cells and a breast cancer cell line (MCF 7). FGF8 protein was expressed in androgen receptor (AR)-positive LNCaP cells line and in DU 145 cells (AR-negative) but not PC3 cells (AR-negative). LNCaP cells treated with androgens had a dose- and time-dependent enhancement of FGF8 protein expression. In clinical prostate cancer high levels of FGF8 protein expression correlated significantly with high-grade ($P < 0.001$) and late-stage disease ($P = 0.02$).
Conclusion FGF8 is an androgen- and oestrogen-regulated growth factor that is expressed in both androgen-dependent and -independent prostate cancer. In clinical cancers, FGF8 protein expression is associated with more advanced disease.
Funding: Cancer Research Campaign

P68

NF-κB manipulation of the inhibitors of apoptosis alters apoptotic responses in LNCaP cells

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Introduction NF-κB is a transcription factor involved in pro-inflammatory and anti-apoptotic pathways, and is inhibited by IκB. When activated, NF-κB upregulates the expression of various anti-apoptotic genes, including cIAP-2. We hypothesized that the apoptotic resistance seen in prostate cancer cells may be altered by manipulating NF-κB activation. Our aims were: (i) to detect enhanced apoptotic susceptibility and reduced IAP expression in an IκB over-expressing cell line; (ii) to show that NF-κB activation results in reduced apoptotic susceptibility.
Materials and methods Apoptosis was induced in LNCaP, LNCaP IκB over-expressing cells (L-IκB) and LNCaP cells treated with RANK ligand, an activator of NF-κB (L-RANKL, 10 ng/mL), using etoposide (62.5 μmol/L). The percentage of apoptosis was assessed after 24 h by propidium iodide DNA incorporation using flow cytometry. RNA was isolated, hybridised with a probe set to the IAP family and resolved as an RNA protection assay. Total protein extracts were used for Western blot analysis of IAPs.
Results The mean (SD) percentage of apoptosis in the various cell lines was:

Cell line	*Control*	*Etoposide*
LNCaP	15.1 (2.0)	33.2 (8.3)*
L-IκB	18.5 (3.0)	72.2 (8.4)*
L-RANKL	7.7 (2.2)	10.4 (3.7)

*$P < 0.05$ vs control, Student's *t*-test.

L-IκB cells were more susceptible to etoposide-induced apoptosis; L-RANKL reduced etoposide-induced apoptosis. IκB transfection resulted in reduced expression of cIAP-2 and XIAP at both the mRNA and protein level. RANKL treatment increased protein expression of cIAP-2.
Conclusion NF-κB activation represents a novel site of therapeutic manipulation in the treatment of prostate cancer.
Funding: BUF

P69

Basal Akt signalling in androgen-resistant prostate cancer cells

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Introduction Androgen-insensitivity remains a significant limiting factor in the treatment of advanced prostate cancer. This study investigates the contribution of PI3-kinase/Akt survival pathways to apoptotic resistance. The aims of this study were: (i) to determine the basal phosphorylation status of Akt and its target Bad in different prostate cancer and HL60 cell lines and correlate this with apoptotic susceptibility to etoposide; (ii) using a specific PI3-kinase inhibitor, to investigate whether it was possible to sensitise prostate cancer cells to etoposide.
Materials and methods Total cellular protein was extracted from DU145, PC3, LNCaP and human leukaemic (HL60) cell lines to determine basal Akt and Bad phosphorylation using Western blotting. Cells were pre-incubated with the specific PI3-kinase inhibitor, LY294002 (LY) and apoptosis induced with etoposide. Apoptosis was assessed by propidium iodide DNA staining using flow cytometry.
Results The expression of phospho-Akt/Bad was increased from DU145 = PC3 > LNCaP > HL60. This correlated with resistance to etoposide-induced apoptosis. Pre-incubation with LY had no significant effect on basal apoptosis. LY increased sensitivity to etoposide-induced apoptosis in LNCaP and HL60, but not in DU145 and PC3.
Discussion These results show altered basal expression of phosphorylated Akt in different prostate cell lines. Increased activation of Akt is associated with increased phosphorylation of Bad. PI3K/Akt inhibition only increases sensitivity to apoptosis in cells expressing high basal Akt. Manipulation of the PI3-kinase/Akt pathway alone may have limited therapeutic benefit in prostate cancer and additional pathways need to be identified.

P70

Characterization of tumours from human prostate cancer cell lines in an *in vivo* model

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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. We have been able to induce tumour growth *in vivo*, in nude mice, using several routes of inoculation and a variety of human prostate cancer cell lines, with a view to characterizing the tumours obtained.
Materials and methods MF-1 male nude mice were injected with one of the following cell lines: LNCaP, LNCaP-LN3, PC-3M, PC-3M-LN4 and PC-3M-Pro4. Each cell line was injected by three routes, using a different animal for each route, i.e. (i) intracardiac, (ii) intratibial and (iii) intraprostatic. The animals were then monitored over a 3-month period at the end of which they were humanely killed, or sooner if morbidity became a problem.
Results To date, 30 animals have been injected, two for each cell line via each route. Of these, seven of 25 animals (28%) developed large tumours; three from the intratibial group and two in each of the other groups. Analysis of these tumours is currently underway in the form of histological examination, and investigation of gene and protein expression for candidate factors involved in the mechanisms of osteoblastic metastasis, i.e. bone morphogenetic protein-6, parathyroid hormone-related protein, osteoprotegerin, and the Smad proteins.
Conclusion This model represents an invaluable tool in the investigation and modulation of various factors involved in the cascade of events responsible for tumour growth and metastasis in prostate cancer. The techniques will be discussed in full, including their advantages and limitations. Characterization of the tumours will be described and discussed.
Funding: BUF, RCS(Eng)

P71

1,25-dihydroxyvitamin-D3 and its analogues as therapeutic agents in three animal models of prostate adenocarcinoma

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Introduction The major risk factors for prostate adenocarcinoma (age, race and geography) can be explained by low serum levels of 1,25-dihydroxyvitamin-D3 (1,25-D3). 1,25-D3 has also been shown to induce differentiation and inhibit cell proliferation of several malignant cell types. Its clinical uses are limited by hypercalcaemic side-effects and analogues have therefore been developed. We investigate the *in vitro* and *in vivo* role of 1,25-D3 and two analogues (EB1089 and CB1093) in three models of prostate cancer.
Materials and methods The Dunning and Pollard rat models, and a human xenograft nude mouse model, were used for the *in vivo* studies. *In vitro* expression of the vitamin D receptor and effects on cell growth were studied.
Results MLL, PA3 and LNCaP cells expressed the vitamin D receptor. 1,25-D3 and analogues inhibited the growth *in vitro* of MLL and LNCaP cells. PA3 cells were not inhibited at 100 nmol/L. Similar results were seen *in vivo*, as 1,25-D3 and its analogues inhibited tumour growth and prolonged survival in Dunning rats with MLL tumours and LNCaP xenografts in nude mice, but not in Lobund-Wistar rats with PA3 tumours. Serum calcium levels were significantly higher in animals treated with 1,25-D3 than with analogues.
Conclusion The antiproliferative properties shown here suggest EB1089 and CB1093 may represent new therapeutic agents for treating prostate cancer. Potentiation of the effects of these agents in the more resistant model is an ongoing area of research.
Funding: AstraZeneca Fellowship

P72

A gene therapy/targeted radiotherapy strategy for treating prostate cancer

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Introduction Targeted radiotherapy is the selective irradiation of tumour cells by radionuclides conjugated to tumour-seeking molecules. One promising agent is radiolabelled meta-iodobenzyl-guanidine (MIBG) which is actively taken up via the noradrenaline transporter (NAT). At present this therapy is restricted to neuroendocrine tumours which naturally express the NAT gene. Introducing the NAT gene into prostate cells would enable MIBG to

be used to treat prostate cancer. Experimental work with LNCaP cell lines is presented.
Materials and methods The NAT cDNA was cloned into an IRES plasmid (IRES/NAT) under the control of the CMV promoter. Stable transfectants were derived and were endowed with the capacity for active uptake of [^{131}I]-MIBG at levels 15 times greater than inhibited controls.
Results After administering [^{131}I]-MIBG, a dose-dependent cell kill was shown in monolayers via clonogenic assays. The added advantage of radiation cross-fire conferred to this system was investigated in three-dimensional multicellular tumour spheroids. Growth delay assays indicated that this degree of [^{131}I]-MIBG uptake was sufficient to inhibit growth at radioactive concentrations of 4 MBq/mL. A virulence-attenuated herpes simplex virus (HSV1716) expressing the NAT transgene is being investigated as a potential *in vivo* delivery vehicle. This has shown tropism for the prostate carcinoma cells, and cells were killed with administration of increasing titres of virus alone. The enhanced cell kill by concurrent administration of [^{131}I]-MIBG is being evaluated. It is hoped this work will be the basis of a clinical trial to assess this treatment as an adjuvant therapy for prostate cancer.
Funding: BUF and RCPS, Glasgow

P73

Expression of the membrane-type metalloproteinases in prostate carcinoma cell lines using real time Taqman RT-PCR

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Introduction The membrane-type metalloproteinases are a group of six furin-activated transmembrane metalloproteinases (MT-MMP 1-6). Apart from MT-MMP 4, they activate *in vitro* the latent form of MMP-2, which is one of the key proteinases in the invasion and metastasis of various cancers. We examined the mRNA expression of MT-1, -2, -3 and -4 MMPs in three human prostate carcinoma cell lines (PC-3, DU-145 and LNCaP) and MT-5 and -6 MMPs in PC-3 cell lines using quantitative real time RT-PCR.
Materials and methods The prostate carcinoma cell lines were cultured in RPMI-1640 medium supplemented with 10% heat inactivated fetal calf serum and penicillin/streptomycin. Total RNA was extracted from the cell lines when they had reached confluency. After RT, real-time PCR was used to determine the expression of the MT-MMPs.
Results MT-MMP-2 mRNA was expressed in each of the three cell lines. MT-MMP-3 mRNA was found in the PC-3 and LNCaP lines, and MT-MMP-1 and -4 mRNA only in the PC-3 lines. MT-MMP-5 and -6 were only assessed in PC-3 lines, with MT-MMP-6 mRNA being detectable.
Conclusion The detection of the expression of this group of MMPs indicates their potential role in prostate cancer invasion and metastases. Further studies are required to determine the expression of the membrane-type metalloproteinases in clinical tissue specimens.
Funding: Big C Cancer Charity

P74

Soluble fibroblast growth factor receptor as a novel therapy for prostate cancer

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Introduction Prostate cancer remains a major clinical problem worldwide. Peptide growth factors, e.g. fibroblast growth factors (FGFs) and their high-affinity membrane tyrosine kinase receptors (FGFRs), play key roles in prostate carcinogenesis and progression. There is evidence to suggest that inhibition or down-regulation of the growth factors and/or their receptors has beneficial effects against human malignancies. Furthermore, the expression of a soluble form of the FGFR (sFGFR) in a transgenic mouse model confirms its ability to abolish FGF-mediated organogenesis [*EMBO J* 1998; 17: 1642–55]. We hypothesized that the expression of such sFGFR inhibits prostate cancer cell growth.
Materials and methods The extracellular domain encoding the IIIc isoform of human FGFR1 was generated by PCR and subcloned into a selectable green fluorescent protein-tagged adenoviral expression system [*PNAS* 1998; 95: 2509–14]. Human prostate cancer DU145 cells were successfully infected with the generated recombinant adenovirus, treated with exogenous FGF-1 and analysed by western blotting for expression of the activated MAP kinase, pERK1.
Results We successfully engineered a recombinant adenovirus expressing the soluble FGFR1-IIIc construct (Ad-IIIcR1). Expression of pERK1 induced by exogenous FGF-1 was almost completely abolished in Ad-IIIcR1-infected DU145 cells, in contrast with Ad-IIIcR1-negative DU145 cells.
Conclusions We show for the first time that expression of sFGFR in prostate cancer cells may have a potential therapeutic role. Future work will be directed to develop this model for *in vivo* assessment as well as to study FGFR-mediated cellular activities.

10.30–11.30
Poster session 8
BPH Lasers

P75

The utility of PSA in predicting BOO in patients presenting with LUTS

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Introduction Recent studies have indicated that serum PSA may be used to infer the volume of the prostate gland, the risk of acute urinary retention, and the potential need for surgery because of LUTS. This study evaluated whether PSA could also predict the presence of BOO.
Patients and methods Consecutive patients referred from the community for LUTS were evaluated by a PSA assay (Immulite supersensitive PSA, Diagnostics Products Corporation), pressure-flow urodynamic studies and TRUS of the prostate, as part of their routine investigations. Prostate biopsies were taken when prostate cancer was suspected and, if found, patients were excluded. A linear regression was used to predict prostate volume and the BOO index (BOOI; formerly known as the Abrams-Griffiths number) from the PSA level; a multiple linear regression was constructed to predict BOOI from free flow rates and PSA level. Log transformations were used where appropriate.
Results As expected, PSA level was able to predict much of the variation (49%) in prostate volume ($P<0.001$, $n=209$), but PSA level explained only 10% ($P<0.001$) of the variation in BOOI; the prediction interval for BOOI at any given PSA level was too wide to be useful in many patients. Free flow rates were a much better predictor of BOOI and, in a multiple linear regression, the combination of flow rate and PSA level was marginally better than flow rate alone.
Conclusions Although PSA level can be used to predict prostate volume, it does not usefully predict the presence of BOO, as determined by urodynamics.

P76

Serum total PSA has a stronger correlation with benign prostate volume than complexed PSA

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Introduction Serum total PSA (tPSA) correlates closely with benign prostate volume. We studied the correlations between complexed PSA (cPSA) levels, age, total prostate volume (PV) and transitional zone volume (TV) in men with benign prostates, comparing the tPSA values.
Patients and methods A series of 209 men presenting with LUTS were assessed. All men with a tPSA of $\geqslant$ 4 ng/mL and or an abnormal DRE had undergone TRUS and prostate biopsies, and men with prostate cancer excluded. All these men had blood samples taken before any manipulation and serum tPSA (Elecsys immunoassay) and cPSA (Bayer immunoassay) were measured. PV and TV were measured with a 7.5 MHz TRUS transducer using a standardized protocol, which has been shown to be reproducible. The Pearson correlation coefficient (r) was calculated for age, PV, TV, tPSA and cPSA.
Results The mean (range) for age, PV, TV, tPSA and cPSA were 67.4 (44–84) years, 65.9 (15.4–224.0) mL, 35.0 (4.1–134.0) mL, 6.4 (0.1–14.7) ng/mL and 5.1 (0.03–12.6) ng/mL, respectively. The tPSA correlated strongly with PV ($r=0.53$, $P<0.01$) and TV ($r=0.50$, $P<0.01$), although less with age ($r=0.01$, $P>0.05$). The cPSA correlated similarly although more weakly with PV ($r=0.45$, $P<0.01$), TV ($r=0.42$, $P<0.01$) and age ($r=0.01$, $P>0.05$).
Conclusion Correlations between tPSA and age, PV and TV were better than those for cPSA, possibly because free PSA forms a larger proportion of the tPSA in men with benign prostates.

P77

Interstitial laser ablation of the prostate – a randomized prospective study with 3-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 $\leqslant$ 60 g against standard TURP.
Patients and methods From January 1997 to June 2000, 125 patients with BPH entered the study (mean age 69 years, range 52–85; prostatic weights 35.3 g, range 20–60). They were randomized 2:1; thus 83 patients were treated by interstitial laser coagulation (ILC) using the Indigo 830e™ laser-optic system and 42 underwent standard TURP. Variables assessed were the IPSS, QoL, uroflow, postvoid residual volume and TRUS findings; biochemical variables were PSA and creatinine levels.
Results

Group/ variable (n)	*Mean (SD)*				
	Before	*6 weeks*	*1 year*	*2 years*	*3 years*
ILC (83)					
IPSS	20.0 (5)	10.0 (6)	6.9 (6)	6.2 (5)	6.6 (4)
QoL	4.1 (1)	2.6 (1)	1.6 (1)	1.5 (1)	1.5 (1)
Q_{max}	8.4 (2)	16.6 (6)	18.1 (6)	18.2 (7)	17.4 (6)
TURP (42)					
IPSS	20.0 (4)	7.6 (6)	5.8 (4)	6.8 (5)	7.0 (4)
QoL	3.8 (1)	1.6 (1)	1.2 (1)	1.1 (1)	1.6 (1)
Q_{max}	8.4 (2)	21.0 (7)	18.9 (6)	17.3 (8)	15.8 (6)

All values after 1 year were significantly different from baseline values, $P<0.001$.

Retrograde ejaculation was recorded 44% after ILC, compared with 74% after TURP. No blood transfusion was recorded during ILC, compared with 9% in TURP. Irritative symptoms lasted for 6 weeks after ILC in 11% and after TURP in 2.4%. The catheter-free trial at 48 h after ILC failed in 9.6% (two patients required endoscopic desloughing) and after TURP in 2.4%. In the ILC group 2.4% (one at 6 months, one at 2 years) required TURP. The mean hospital stay was 1.5 days with ILC and 3.5 days with TURP.
Conclusions At the 3-year follow-up both ILC and TURP produced equivalent improvements in IPSS, QoL, flow rate and postvoid residual volume. ILC produced irritative symptoms in nine (11%) and failed in two patients (2.4%). TURP produced a longer hospital stay, a strictured urethra in one (2.4%) and bladder neck stenosis in one patient (2.4%).

P78

Transurethral holmium laser enucleation vs open suprapubic transvesical enucleation of prostates >100 g: preliminary results of a randomized prospective trial

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Introduction Transurethral holmium laser enucleation (HoLEP) seems to be an effective alternative to TURP for small and medium-sized prostates. A randomized prospective trial should evaluate whether HoLEP could be an endourological alternative to open suprapubic transvesical prostatectomy (Open P). Preliminary results of this ongoing study are presented.
Patients and methods To date, 107 urodynamically obstructed patients were randomly appointed to HoLEP or Open P; 52 patients were treated with HoLEP (holmium:YAG laser 2.0 J, 40 Hz, 80 W, 550 nm bare laser fibres) and 55 were treated by Open P. All patients were assessed before and at 1, 3, 6 and 12 months after treatment with the AUA symptom score, peak urinary flow rate and postvoid residual urine volume. All complications were noted; 10 patients were lost to follow-up (incidental prostate carcinoma, death, etc.).
Results The results were:

Variable	*HoLEP*	*Open P*
Mean patient age, years	68.3	71
Prostate volume, mL	114.4 (100–230)	112.6 (100–200)
Resection weight, g	91.9 (60–200)	96.6 (61–220)
Operation time, min	136.7	90*
Haemoglobin loss, mg/L	19	29*
Median:		
Catheter time, h	24	144*
Hospital stay, h	48	240*
Complications, n		
Arterial bleeding	2	3
Blood transfusions	0	8
Secondary resection	2	0
Bladder neck contracture	0	1

*$P<0.001$; Mann-Whitney *U*-test.

Both HoLEP and Open P resulted in significant improvements in AUA symptom scores, peak urinary flow rates and postvoid residual volumes. There were no statistically significant differences in any of the variables at any time of the study between the HoLEP and the Open P group.
Conclusions Transurethral HoLEP appears to offer an endourological open surgical enucleation of the prostate, with equally good functional results, a longer operative duration, but significantly less blood loss and a much shorter catheter time and hospital stay.

P79

Longer resection times using holmium laser resection of the prostate are associated with good results without the complications of TURP

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Introduction Holmium laser resection of the prostate (HoLRP) differs from standard TURP in that saline is used as the irrigating fluid. It has also previously been shown to be associated with less blood loss. This study examined the effect of resection time on the results of HoLRP.
Patients and methods Patients were selected as for standard TURP and resections undertaken using the standard HoLRP technique. A specially designed tissue morcellator was used to remove large prostatic fragments. Patients were divided into three groups according to the resection time. All were assessed before and after HoLRP using the AUA symptom score (SS) and maximum flow rate (Q_{max}).
Results In all, 239 patients were assessed and results are summarized in the table. There were no perioperative deaths, cases of major haemorrhage or of TUR syndrome. Two patients in the >60 min group required blood transfusion after HoLRP; one bled after restarting warfarin and the other had idiopathic thrombocytopaenic purpura.

Mean (SD or range) variable	*Resection time, min*		
	0–30	*31–60*	*>60*
Tissue weight, g	3.5 (3.6)	12.3 (8.2)	22.3 (11.6)*
Energy, kJ	41.7 (24.7)	115.7 (34.5)	187.3 (59.1)*
Catheter time, days	1 (1–9)	1 (1–5)	2 (1–7)*
Before			
SS	22.3 (6.6)	21.0 (7.2)	20.5 (6.6)
Q_{max}	10.6 (4.7)	10.2 (4.5)	10.8 (6.6)
6 weeks			
SS	8.4 (5.2)	8.9 (6.0)	6.9 (4.8)
Q_{max}	21.9 (13.2)	19.5 (11.3)	23.6 (12.6)
6 months			
SS	8.9 (7.7)	6.4 (6.0)	5.3 (5.6)
Q_{max}	20.2 (8.1)	22.4 (10.3)	24.1 (11.7)

* $P<0.01$.

Conclusions With traditional electrosurgery, resection times of >1 h have been associated with significant complications such as bleeding and TUR syndrome. This does not appear to be the case for HoLRP, suggesting it is an ideal method for transurethral resection of larger prostates.

P80

Transurethral electrovaporization of the prostate after 5 years: is it effective and durable?

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Introduction To update our prospective randomized trial comparing the safety, efficacy and durability of prostate vaporization using the VaporTrode™ with standard TURP.
Patients and methods The study included 104 patients, admitted from the waiting list for surgery for BPH, who were randomized to TUVP (52 patients, mean age 67.5 years) or TURP (52 patients, mean age 70.2 years). Fifty-one, 47 and 40 patients in each arm, and 27 in the TURP and 26 in the TUVP groups, completed 1, 2, 3, and 5 years of follow-up, respectively.
Results Both groups had a comparable IPSS, quality-of-life score (QoL), maximum flow rate (Q_{max}) and postvoid residual volume (PVR) before surgery. Follow-up data at 5 years showed a significant and maintained improvement in mean (SD) in the TUVP and TURP groups, respectively, for the IPSS, at 5.9 (6.3) and 8.6 (7.1) ($P=0.16$); for QoL, at 1.1 (1.2) and 1.7 (1.4) ($P=0.09$); and for Q_{max}, at 21 (9) and 17.9 (13.1) mL/s ($P=0.17$), with decreases in PVR, at 27.3 (44.3) and 10.7 (13.1) mL ($P=0.08$). Two patients in

each group (4%) developed urethral strictures. Two TURP patients (4%) had bladder neck strictures, compared with one TUVP patient (2%). In each arm, seven patients (13%) had a re-operation over a period of 5 years. Postoperatively and at up to 3 years of follow-up, impotence was reported in 17% of the TUVP group and 11% of the TURP group ($P = 0.49$) and retrograde ejaculation in 72% and 89%, respectively ($P = 0.47$).
Conclusion These 5-year follow-up results confirm that TUVP is as effective as standard TURP in treating moderate-sized BPH. The re-operation rate and long-term complications are comparable, and the initial improvement was maintained over 5-years in most patients in both groups.

P81

Holmium laser enucleation of the prostate vs TURP for large prostates (40–200 g)

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Introduction Holmium laser enucleation of the prostate (HoLEP) combined with transurethral tissue morcellation was compared with TURP in a randomized trial in larger prostates.
Patients and methods The study included 61 urodynamically obstructed patients with TRUS-estimated prostate volumes of 40–200 g, randomized to HoLEP (31) or TURP (30); enrolment is complete. Routine variables were assessed during and after surgery, with follow-up assessments at 1, 3, 6 and 12 months after surgery.
Results The values before surgery were similar in each group. The mean operative duration was 63.8 min in the HoLEP group and 41.1 g of tissue was retrieved (0.64 g/min); respective values in the TURP group were 33.7 min and 24.1 g of tissue (0.71 g/min). The duration of catheterization was 17.9 h (HoLEP) and 46.2 h (TURP). The hospital time was also correspondingly shorter in the HoLEP than in the TURP group (25.3 vs 55.6 h); these two differences were significant ($P < 0.01$). There was one transfusion in the TURP group (4%). Four patients in the TURP group required re-catheterization compared with four in the HoLEP group. The postoperative AUA scores, Q_{max} values and QoL scores were similar at 1, 3, 6 and 12 months after surgery.
Conclusions HoLEP is a safe effective procedure with a shorter catheter time and hospital stay than TURP in larger prostate glands. The efficiency of tissue removal was similar.
Funding: NZ Lotteries Board

P82

Transurethral needle ablation of the prostate: a prospective study with 6-year follow-up

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Introduction Transurethral needle ablation (TUNA) is a method used to deliver low-level radiofrequency through a catheter device fitted with adjustable needles and placed in selected prostatic tissue areas. TUNA ablation produces necrosis by attaining a tissue temperature up to 110°C. Our objectives were to study the clinical efficacy of TUNA for treating symptomatic BPH and to compare this with TURP.
Patients and methods From April 1994 to October 1998, 152 patients (mean age 67.5 years, range 47–87; mean prostatic weight 43.3, range 20–88) with symptomatic BPH were entered into the trial. Seventy-six patients were treated with TUNA and 76 underwent TURP. Variables assessed were the IPSS, QoL, uroflow, postvoid residual volume and TRUS findings. Biochemical variables assessed were the PSA and creatinine levels.
Results The mean (SD) values were:

	TUNA			*TURP*		
Follow-up (years)	*IPSS*	*QoL*	Q_{max}	*IPSS*	*QoL*	Q_{max}
Before	19.1 (5)	4.1 (1)	7.5 (2)	20.5 (5)	3.8 (1)	8.3 (2)
0.5	7.8 (5)	1.7 (1)	15.7 (5)	6.0 (8)	1.2 (1)	19.3 (8)
1	7.8 (5)	1.6 (1)	15.0 (5)	5.1 (4)	1.2 (1)	19.6 (7)
2	8.1 (5)	1.8 (1)	14.2 (6)	5.1 (4)	1.2 (1)	19.3 (7)
3	7.9 (5)	1.5 (1)	14.1 (5)	5.7 (5)	1.0 (1)	19.2 (7)
4	8.9 (6)	1.6 (1)	12.5 (5)	–	–	–
5	8.6 (5)	1.6 (1)	13.1 (6)	–	–	–
6	5.3 (4)	2.1 (1)	11.1 (2)	–	–	–

–Not meaningful because attendance was low.

No ejaculatory dysfunction was recorded after TUNA, compared with 76% after TURP. No blood transfusion was required after TUNA compared with 10.5% after TURP. In the TURP group, there was a urethral stricture in 2.6% and bladder neck obstruction in 2.6%; in the TUNA group 1.3% had stricture of the urethra, At the catheter-free trial at 48 h the retention rate was 13.2% after TUNA and 2.9% after TURP. The mean hospital stay was 1.2 days after TUNA and 3.5 days after TURP. The failure rate with TUNA was three (4%) in the first year, two (2.6%) in the second year, one (1.3 %) in the third year, two in the fourth year, two in the fifth year and none at 6 years. In TURP one patient required re-resection in the second year.
Conclusions TUNA produces minimal morbidity and is tolerated well. The failure rate in after TUNA over 6 years was 13%. This treatment is highly recommended where ejaculatory dysfunction is a major concern.

P83

Plasmakinetic vaporization of the prostate: a safe and effective technique for removing prostatic tissue in men with BPH

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Introduction Plasmakinetic technology uses a radiofrequency energy-delivery system that allows prostatic tissue removal equivalent to TURP, using 0.9% sodium chloride as the irrigant fluid.
Patients and methods Twenty-five patients with moderate to severe LUTS and benign disease underwent plasmakinetic vaporization of the prostate (PKVP). Their mean age (range) age was 68 (56–84) years, IPSS 20.4 (11–31), QoL score 4.4 (2–6), PSA level 2.35 (0.1–6) ng/mL, Q_{max} 8.1 (2.6–16.4) mL/s, and postvoid residual volume (PVR) 195.5 (0–685) mL; 60% of them were ASA score III. Simultaneously the depth of thermal injury was assessed in another four patients who underwent open prostatectomy (two) and prostate enucleation (two). Safety variables were monitored during and after surgery. In addition, a 3-month follow-up was completed.
Results There were no major complications during or after surgery. The mean (range) fluid absorption was 0.86 (−2.5 to 6) L; one patient developed intraoperative congestive cardiac failure (6 L absorption), which resolved with no sequelae with diuretic treatment. No blood transfusion was required at any stage. The mean (range) operative duration was 40 (16–87) min and the hospital stay 3.04 (1–7) days. The depth of thermal injury was 0.4–1 mm, compared with TURP at 1–3 mm in the same patients. At 3 months there was a significant improvement, with the mean

Q_{max} of 21.1 (4.8–44.6) mL/s, PVR 65.7 (0–391) mL, IPSS 6.15 (1–21) and QoL 1.67 (1–6).

Conclusions PKVP is a safe and efficient technique for prostatic tissue removal, making it a valid alternative to TURP. Although TURP syndrome is impossible with this technique, the surgeon must be aware of possible fluid overload-related problems. In addition, the lesser thermal injury may result in decreased postoperative irritative symptoms.

Funding: Gyrus Medical Ltd

10.30–11.45
Testis Cancer

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A 15-year follow-up of the Anglian Germ Cell Cancer Group adjuvant studies of carboplatin as an alternative to radiation or surveillance for stage 1 seminoma

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Background Prompted by increasing recognition of the risks of late second malignancy after radiation, and problems of late relapse with paraplegia after surveillance alone for stage 1 seminoma, in 1985 this group began to explore adjuvant single-agent carboplatin as an alternative.
Methods This paper updates our previous report and presents results from a randomized phase II study of carboplatin vs radiotherapy, devised to justify the current ongoing phase III trial. The table summarizes the sequential phase II studies in stage 1 seminoma. Sixty-two patients were entered into the randomized phase II toxicity study. After 30 Gy in 20 fractions in para-aortic and ipsilateral pelvic lymph nodes, the mean cumulative combined SHO haematology, WHO toxicity and Rotterdam Symptom score per patient at 8 weeks was 22.51, vs 8.51 in patients treated with carboplatin. Chemotherapy patients had more anaemia, thrombocytopenia and altered taste, while irradiated patients had more vomiting, diarrhoea and tiredness. At 12 months, six of nine patients have persistent abdominal symptoms after radiation, compared with one of seven treated with carboplatin.
Conclusion With no relapses after 2 years, adjuvant carboplatin is clearly a viable alternative to radiation; the apparent reduction in tumours in the contralateral testis provides support for further work on using this treatment for testis conservation.

Outcome	*Surveillance*	*RT before 1997*	*RT after 1997*	*Carbo ×2**	*Carbo ×1**
No. cases: Total/FU	110/98	178/208	57/128	146/52	187/95
% with GCT relapse	19	6.4	2.7	1.75	0.7
2nd GCT primary	4.5	2.6	3	0	0.7
2nd primary other	0	16.7	0.5	3.5	0
Deaths GCT	0	5	1	0	0
Deaths other	2.7	29.5	3.2	3.5	0
Alive and disease-free	98.3	65	95.7	96.5	100

RT = 30 Gy; *AUC7.

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Chronic ileo-femoral arterial disease after EBRT for testicular seminoma

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Introduction Adjuvant radiotherapy is commonly used in the treatment of stage I, IIA and stage IIB testicular seminoma. The risk of radiation-induced vascular occlusive disease in men after radiotherapy for testicular seminoma has not been regarded as a major factor in their long-term care. Several animal studies have shown the importance of established vascular risk factors, e.g. hypercholesterolaemia and hypertension, in the pathogenesis of radiation-induced atherogenesis.
Patients and methods We present three cases of chronic ileo-femoral arterial disease presenting 5, 13 and 16 years after exposure to therapeutic levels of irradiation for the treatment of testicular seminoma. The patients were aged 40–45 years and all had associated known atherosclerotic risk factors. The patients had received radiation therapy of 3500–4000 rads in a standard 'dog-leg' fashion to the ipsilateral aorto-ileal lymph node chain.
Results Two of the three patients presented acutely with lower-limb ischaemia and all were treated successfully with by-pass procedures. The operative findings were uniformly consistent with overlying radiation dermatitis, scarred tissue planes, perivascular fibrosis and diseased vessels. The findings were apparently limited to the field of irradiation. There was no evidence of recurrent tumour.
Conclusion Men treated with 'dog-leg' radiotherapy for testicular cancer should be targeted from the outset for atherosclerotic risk-factor reduction, to lessen the chance of developing radiation-induced atherogenesis.

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Measurement of immunoreactive PLAP in the management of germ cell tumours of the testis

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Introduction The PLAP assay has previously been dependent on enzymic activity; as this can alter through aberrant ectopic expression and changes in sample storage conditions, levels are inconsistent among assays and patients. We describe the use of a novel two-site immunometric assay in patients with testicular tumours.
Patients and methods Serum levels of immunoreactive PLAP (iPLAP) and enzymic PLAP (ePLAP) were measured by specific immunoreactive mAb and IAEA in 15 age-matched, disease-free control patients. Levels of iPLAP, ePLAP, βhCG and AFP were measured before and after orchidectomy in 15 patients presenting with suspected testicular tumours (nine seminomas, six nonseminomatous germ cell tumours, NSGCTs) and two patients with benign testicular masses.
Results In the control group, the median (range) level of iPLAP was 0.3 (0.3–0.8) mg/L and of ePLAP was 3 (3–5) IU. Of the 17 incident cases, two had benign lesions, nine presented with seminomas and six with NSGCT. Elevated iPLAP was detected in the serum of 13 of 15 patients with GCTs (eight of nine seminoma and five of six NSGCT). Conventional serum markers (AFP and βhCG) were

elevated in only six of the 15 GCTs. One patient has persistently elevated iPLAP after orchidectomy with no other evidence of disease, and is under review.
Conclusions Using an immunoassay technique for serum measurements, iPLAP appears to be a useful marker of both seminomatous and NSGCTs, unlike currently available tumour markers for testicular malignancy.

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Measurement of tumour marker levels within cystic residual masses of metastatic testis cancer can confirm the diagnosis

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Introduction Cystic retroperitoneal masses of metastatic testicular teratoma are usually shown to be differentiated teratoma (TD) after post-chemotherapy retroperitoneal lymph node dissection (PC-RPLND). However, in some cases there is doubt and recurrent cystic masses can be confused with postoperative lymphoceles. Needle biopsy and cytological aspirates are unreliable. We evaluated the measurement of tumour markers in aspirated fluid to confirm the diagnosis of TD.
Patients and methods Between 1999 and 2000, a consecutive series of 15 men underwent PC-RPLND for testicular teratoma and cystic masses. The masses were excised intact and the fluid within them sent immediately for assay of AF) and hCG. Serum AFP and hCG had also been assayed before and after chemotherapy. In one man with a pelvic cystic mass 15 years after PC-RPLND, fluid was aspirated under TRUS guidance.
Results Histology showed TD in all patients; serum tumour marker levels were normal at the time of PC-RPLND in all patients and had never been elevated in two. Within the cystic mass fluid, AFP was above normal serum levels in eight men (range 1–187 kU/L) and hCG was elevated in all 15 (range 11–242 085 IU/L). The one patient who underwent TRUS-guided aspiration had elevated hCG in the fluid and TD was confirmed on later excision.
Conclusions After chemotherapy for metastatic testicular teratoma, cystic masses contain TD alone in this series of 15 patients. The cyst fluid had high hCG levels in all and AFP in eight, even when serum marker levels had never been elevated. Aspiration of cystic masses, particularly after previous PC-RPLND, is a potential method for confirming the diagnosis of TD.

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Congenital anomalies encountered in men undergoing retroperitoneal lymph node dissection for metastatic testis cancer: possible predisposing factors for testis cancer

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Introduction Cryptorchidism and infant inguinal hernia are well known factors that predispose to a higher incidence of testicular cancer. We prospectively collected anatomical data from men with metastatic testicular cancer undergoing retroperitoneal lymph node dissection (RPLND), to determine if there are any other congenital anomalies that might predispose to the disease.
Patients and methods A consecutive series of 150 men with metastatic testis cancer underwent RPLND by one surgeon and any previous corrected anatomical anomalies or those encountered during surgery carefully noted. The incidence of anatomical anomalies was compared with those published previously, using the chi-squared test.
Results In all, 21 men (14%) had an anatomical anomaly; 10 had previously undergone orchidopexy (unilateral in six, bilateral in four). There was a history of inguinal hernia in three, a solitary kidney in two and a horseshoe kidney in one patient. One patient had intersex with an ovary, testis and uterus. Vascular anomalies included four left-sided inferior vena cavae (IVC) and two retro-aortic renal veins. Compared with previous data there was a significantly greater incidence of horseshoe kidney ($P=0.01$), cryptorchidism ($P=0.03$), solitary kidney ($P=0.05$) and left-sided IVC ($P=0.05$) in this series.
Conclusions Cryptorchidism is a well-known risk factor for testis cancer. Other anomalies, e.g. horseshoe or solitary kidney and left-sided IVC, made apparent at RPLND appear to increase the risk of developing testis cancer. It is tempting to postulate that such anomalies might increase the risk of testicular cancer by altering the blood supply to or from the testis.

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Malignant cells in cord blood of testicular tumours

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Introduction The Chevassu manoeuvre involves applying a soft clamp to the cord of a potentially malignant testicle before it is mobilised and examined, whether it is bivalved for frozen-section examination or not. However, there is no direct evidence that metastases spread via testicular vessels in the cord.
Patients and methods Patients undergoing orchidectomy for testicular cancer also underwent the standard Chevassu manoeuvre. Where malignancy was confirmed a Mayo crushing clamp was applied to the cord proximal to the soft clamp and a standard radical orchidectomy undertaken. When the operation was over a second crushing clamp was applied to the cord on the specimen, just above the testis, and the original clamp was removed, enabling collection of the cord blood in a potassium-EDTA haematology bottle. The blood was spun through a filter to remove the red cells and the supernatant used to prepare cytological slides with Papanicolaou stain, and where malignant cells were identified, testicular tumour panel immunological staining.
Results Five patients have been assessed to date; one patient had a seminoma with vascular invasion and multiple malignant cells detectable in his cord blood. Another patient had a seminoma with vascular invasion and a few multinuclear cells, suspicious but not definitely diagnostic of malignancy in cord blood. Three patients had tumours that were not invasive and showed no malignancy in cord blood.
Conclusions Manipulating malignant testicular tumours can produce malignant vascular dissemination. This appears most likely in vascularly invasive tumours. The cord should be clamped before testicular manipulation.

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Patient satisfaction with testicular prostheses

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Introduction The only indication for a testicular implant is patient choice, but compared with breast implantation, little has been published on the results of this procedure. The aim of this study was to assess satisfaction with and reasons for accepting or declining a prosthesis, with the aim of improving future outcome.

Patients and methods In all, 424 men who had undergone radical orchidectomy and were part of the testicular cancer follow-up programme were sent a questionnaire; overall, 55% (234) responded. The questionnaire covered issues about satisfaction with and reasons for accepting/declining a prosthesis.
Results About a third (71) accepted an implant, a third declined and a third were not offered the choice. About 90% of all the men who replied felt that it was extremely important to be offered an implant at the time of surgery and were angry if they had not been offered one. Of the 71 who accepted an implant, 27% were dissatisfied and felt that they had an average or poor result. The reasons for this dissatisfaction are presented and discussed, as well as the men's feelings about scrotal cosmetics.
Conclusions All men undergoing orchidectomy should be offered an implant, irrespective of age. Patients should be shown the implants and be involved in the choice of size during counselling. The small and some of the medium implants are often too round, and lead to dissatisfaction among recipients.

14.00–15.15
Prostate cancer 2

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The use of conjoint analysis to assess patients' preferences in the treatment of organ-confined and locally advanced prostate cancer

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Introduction There are several therapeutic options for men with organ-confined or locally advanced prostate cancer, associated with various complex compromises. We report the use conjoint analysis to elicit patients' preferences for these options.
Methods Men with nonmetastatic prostate cancer were invited to participate in a structured interview. Patients were presented with short vignettes about the possible adverse effects of treatments. Patients ranked the attributes associated with each vignette. Conjoint measurement was then used to elicit patients' preferences for attributes and to assess how they compromised between them. A random effects probit model was used to analyse preference data.
Results Of 195 men invited to enter the study, 129 agreed to participate (mean age 71 years, median PSA level 1.3 ng/mL); 41% were staged as T1, 29% as T2, 29% as T3 and only one patient as T4. The ranking exercise showed that life expectancy was the most important attribute to patients (mean rank, of 8 = 2.6) followed by physical energy (3.4) and avoiding diarrhoea (3.6); avoiding out-of-pocket costs was least important (6.5). Men were willing to trade 3.01 months of life expectancy to avoid lack of energy, 1.80 to improve from moderate to mild diarrhoea, but only 0.53 months to avoid hot flushes.
Conclusions The attribute most important to men was life expectancy, but men were willing to trade some life expectancy to reduce certain adverse effects. The conjoint approach to measuring preference has an important role in the clinical and economic evaluation of alternative therapies for prostate cancer, especially when the adverse effects of those treatments vary substantially.
Funding: AstraZeneca

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Ten-year experience with salvage radical prostatectomy after radiotherapy

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Introduction The past decade has seen a marked stage shift towards the earlier diagnosis of prostate cancer and recurrence after primary treatment; this is a growing and important clinical problem. We present our experience with salvage radical prostatectomy for recurrence after primary EBRT, and attempt to define the indications and selection criteria for this procedure.
Patients and methods Twenty patients were selected for salvage radical prostatectomy. The following criteria were used in selection and analysis: (i) biopsy-confirmed local recurrence; (ii) no extra-prostatic extension or distant spread on imaging; (iii) a life expectancy of $\geqslant 10$ years; (iv) peak PSA levels measured before and after EBRT; and a Gleason score after EBRT.
Results There was no operative or perioperative mortality; in three patients the procedure was terminated without completing the radical prostatectomy because of gross nodal disease (not apparent on imaging), and in one because of initial blood loss on dissection of the retropubic space. One patient had prolonged urine leakage and required temporary nephrostomy drainage. There were two rectal injuries in 17 patients. Postoperative continence was good and only one patient required an AUS. Of the 17 patients 15 were alive up to 11 years after surgery.
Conclusion Our results from this technically challenging operation are encouraging and indicate that morbidity is lower than reported earlier. We believe that there is a role for this procedure in selected patients.

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Laparoscopic radical prostatectomy: the initial UK experience

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Introduction Our large and complex laparoscopic and open radical prostatectomy practice persuaded us to investigate this technique, to determine whether the published results for it are reproducible.
Patients and methods Thirty consecutive patients diagnosed with clinical stage T2N0M0 prostate cancer (or less) underwent laparoscopic radical prostatectomy.
Results One patient was converted to open surgery. The mean operative duration was 280 min, the mean (range) blood loss 362 (50–1300) mL, the postoperative parenteral opiate requirement 30 (0–160) mg morphine sulphate and the hospital stay 4.2 (3–13) nights. There were five complications: an ulnar nerve palsy; a rectal injury recognized immediately and repaired laparoscopically with no sequelae; postoperative bleeding from the right neurovascular bundle requiring re-operation and premature removal of a drain, requiring open drain insertion; and a bladder neck stenosis. All but the last of these occurred in the first 15 patients. Six patients (21%) had positive margins. The PSA level of all patients at 3 months was 0.1 mg/L. The mean (range) follow-up was 3.6 (0.5–9) months. One patient was immediately continent upon removal of his catheter. The overall pad-free rates were 65% at 3 months and 86% at 6 months. Five (17%) patients have regained potency.
Conclusion Once the steep learning curve has been overcome this technique offers the patient an effective radical prostatectomy, a faster convalescence with reduced morbidity and a lower likelihood of blood transfusion. Continence rates thus far appear satisfactory. No comment is possible at this stage about potency or long-term oncological efficacy.

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Are lymphadenectomy or frozen-section examination of lymph nodes necessary in patients undergoing radical retropubic prostatectomy?

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Introduction A pelvic lymphadenectomy is commonly used as a staging procedure in men undergoing radical retropubic

prostatectomy (RRP) for clinically localized prostate cancer. If there is a suspicion that the nodes may contain metastases they can be submitted for frozen-section examination. The benefit of this procedure has recently been challenged in the USA. The aim of this study was to evaluate the risks and benefits of bilateral iliac-obturator lymphadenectomy (BIOL) in men undergoing RRP.
Patients and methods A consecutive series of 285 men (median age 61.2 years, range 43–73) with clinically localized prostate cancer underwent RRP between 1992 and 2000. Their median (range) preoperative PSA level was 11.6 (0.1–59) ng/mL. All 285 patients underwent total bilateral anatomical excision of the lymph nodes lying in the space bordered by the external iliac vein, internal iliac artery, obturator nerve and the obturator internus muscle. When the nodes appeared suspicious they were sent for frozen-section analysis before proceeding to RRP. All subsequently had a paraffin-section histological examination.
Results Frozen-section analysis showed no nodal metastases in any of the patients; however, microscopic nodal metastases were detected within paraffin sections in four of the 285 men (1.4%), one of whom had a negative frozen-section examination. The preoperative PSA levels in these men were 15.1, 16.9, 24.2 and 44.6 ng/mL and the biopsy total Gleason scores were 6 or 7. There were no apparent side effects attributable to BIOL.
Conclusion In men with clinically localized prostate cancer frozen-section examination of lymph nodes appears not to be useful before RRP and may fail to detect micro-metastases. The incidence of nodal metastases is very low and, although the morbidity of BIOL in our hands is insignificant, in our opinion it is unnecessary in men undergoing RRP and with a PSA level of <8 ng/mL.

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Impact of radical prostatectomy on LUTS and quality of life

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Introduction In the absence of a screening programme, men with localized prostate cancer are primarily referred for treatment of their LUTS. Researchers investigating treatment options for prostate cancer commonly focus on cancer control and the complications of therapy. However, there are little data on the impact of radical prostatectomy on LUTS and associated quality of life (QoL).
Patients and methods We carried out a prospective study between January 1999 and September 2000 on 50 consecutive men, initially assessed in the nurse-led prostate assessment clinic for their LUTS, and subsequently diagnosed to have localized prostate cancer. The assessment carried out before and 3 months after surgery included the self-administered IPSS and QoL questionnaire, uroflowmetry and measurement of postvoid residual urine volume (PVR). Finally, each patient completed a self-administered continence questionnaire 6 weeks and 3 months after surgery.
Results The mean (SD) values of the IPSS, QoL, peak flow rate and PVR before and 3 months after radical prostatectomy were 17.6 (6) and 5.3 (5), 3.7 (1) and 1.4 (0.6), 11.3 (4) and 27.3 (5) mL/s. and 63 (42) and 12 (20) mL, respectively. At 3 months after surgery, 38 patients reported complete continence, nine had infrequent stress leaks only on heavy physical activity and the remainder (three men) used <2 pads/day for protection before heavy physical activity.
Conclusions Radical prostatectomy provides major benefits to men with LUTS, besides cancer control. These data are important in counselling patients about the treatment options, especially in view of the current enthusiasm for brachytherapy and conformal radiotherapy, which may worsen LUTS.

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The outcome of radical prostatectomy in patients with a preoperative PSA level of >15 ng/mL

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Introduction Radical retropubic prostatectomy (RRP) is a therapeutic option indicated for organ-confined prostate cancer. In the USA this operation is generally limited to patients with a PSA level of <10 ng/mL. We assessed the outcome of patients with a PSA level of >15 ng/mL who underwent RRP in our institution.
Patients and methods Thirty-two patients (mean age 61.3 years, range 52–70) who had a preoperative PSA level of >15 ng/mL and who underwent RRP between 1990 and 1998 were assessed. The mean (range) PSA level was 25.46 (15.03–76.6) ng/mL and the Gleason score 6.1 (3–8).
Results Histology showed bilateral malignancy in 30 men (94%), extracapsular extension in 27 (86%), positive margins in 30 (94%) and positive pelvic lymph nodes in five (16%). To date, 10 (31%) are alive with no evidence of disease recurrence with a mean follow-up of 46 (18–88) months; their PSA level before surgery was 18.5 (18.0–25.8) ng/mL and the Gleason score 6, with a clinical stage of T1 in seven. No patient had seminal vesicle or lymph node involvement. Fourteen (44%) had biochemical evidence of disease recurrence at a mean follow-up of 60 (33.6–114) months; their PSA level before surgery was 25.4 (15.3–54.7) ng/mL and the Gleason score 6, with a clinical stage of T1 in only five. Eight patients had seminal vesicle involvement and four had positive lymph nodes. Three patients died, two from recurrent prostate cancer, and five patients were lost to follow-up.
Conclusion RRP may be considered in patients with a PSA level of >15 ng/mL if they have a negative seminal vesicle biopsy at the time of TRUS-biopsy and negative lymph nodes on frozen-section analysis.

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Prostate brachytherapy: patient assessment and symptomatic response

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Introduction In a study of the first 60 patients treated with brachytherapy for prostate cancer the role of urodynamics in patient selection was explored; this has not been addressed previously.
Patients and methods Data are presented for the first 70 patients (mean age 66 years, range 58–77) with up to 24 months of follow-up. Their mean (range) presenting PSA level was 9.3 (8.5–16.4) ng/mL and the Gleason score 6 (3–8); most presented with T2 tumours. Patients underwent urodynamics and the IPSS, and were followed up with IPSS questionnaires from 1 week and with PSA assays from 3 months.
Results One patient failed to void after treatment and three had mild rectal symptoms that resolved with medical therapy. Seven patients required a period of CISC after the procedure, of whom one required a TURP at 10 months. Patients requiring CISC had either equivocal or overt urodynamic obstruction. The IPSS deteriorated markedly initially, were much improved by 3 months and normal at 9 months. Urodynamics suggested detrusor instability to be an adverse predictor of most acute urinary symptoms. Regardless of detrusor instability, prostate size, urodynamic obstruction, presenting IPSS or dosimetric variables the symptoms returned to baseline at 9 months. The mean PSA level at 6 months was 0.5 ng/mL and at 12 months was 0.3 ng/mL.

Conclusions Urodynamics may be useful in assessing patients for brachytherapy.

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Immediate vs deferred hormone treatment for prostate cancer: updated trial data

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Objectives To compare immediate vs deferred hormone treatment in advanced prostate cancer, reviewing the data with a follow-up for up to 15 years.
Patients and methods In all, 938 men with advanced prostate cancer were randomized to immediate or deferred hormone treatment from 1985 to 1993. A further year of follow-up data will be available before the presentation.
Results Of the 938 men, 838 (89%, 408 immediate, 420 deferred) have died. The improvement in disease-specific survival remains highly significant after immediate treatment ($2P=0.007$), but the difference in overall survival is now much reduced ($2P=0.052$). Differences in rates of TURP and the incidence of complications continue to favour immediate treatment. The manifestations of local progression have tended to increase with time in the immediate-treatment group (TURP, 74 vs 149 for immediate vs deferred, ureteric obstruction, 43 vs 59). Differences in metastatic complications are largely unchanged, with spinal cord compression occurring in 10 vs 24 (immediate vs deferred), pathological fracture in 15 vs 23, and extraskeletal metastases in 44 vs 59, respectively. There are more deaths from cancer other than in the prostate in the immediate treatment group (29 vs 15) but not from cardiovascular deaths (83 vs 93).
Conclusions Immediate hormone treatment has an impact on advanced prostate cancer, improving disease-specific survival. The incidence of serious complications is reduced, not simply delayed. However, the reduction in an overall survival difference seen on long-term follow-up suggests an adverse effect of prolonged hormone treatment in increasing mortality from other causes. An excess of cardiovascular disease is not apparent in patients treated immediately, but more died from cancer other than of the prostate.

15.30–16.30
Reconstruction

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The effect of anastomotic urethroplasty upon erection of the glans penis

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Objective To test the hypothesis that anastomotic urethroplasty might impair erection of the glans penis. The spongiosus-glans complex has a dual blood supply, the arteries to the bulb entering proximally and the terminal branches of the deep dorsal artery of the penis penetrating the glans. There are a few very small arteries that communicate between the corpora cavernosa and the spongiosus in the mid and distal penile area. During anastomotic urethroplasty, when the bulbar urethra is transected, it is invariably noted that there is very brisk bleeding from the proximal segment and only a trickle from the distal end. It was postulated that the glans-spongiosus blood supply that remained might be inadequate for erection of the glans.
Patients and methods A questionnaire designed to indicate the quality of erection of the glans was administered to 22 patients who had undergone anastomotic urethroplasty.
Results Of those who were potent, none indicated that erection of the glans was different from what it had been before surgery. Only two of the patients were >50 years old and none had evidence of vascular disease.
Conclusion While this pilot study showed that anastomotic urethroplasty does not appear to adversely effect erection of the glans in the mainly young patients studied, further studies are needed in older patients and patients having had anastomotic urethroplasty many years ago.

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The long-term results of urethroplasty

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Introduction There are no published 10- or 15-year values for the results of urethroplasty.
Patients and methods In all, 166 patients were followed for up to 15 years after anastomotic (82) or substitution urethroplasty (84).
Results The 10- and 15-year stricture-free survival rates after anastomotic repair were 11 of 82 (87%) and six of 43 (86%), respectively, and the complication rate was 7%. For substitution urethroplasty the values were 26 of 84 (69%) and 27 of 42 (58%), respectively, and the complication rate was 33%.
Conclusions The results of anastomotic repair are sustained in the long-term, whereas after substitution urethroplasty there is a steady annual attrition rate. Nevertheless, when most of these urethroplasties were carried out (before 1990) most patients had impassable or otherwise complicated strictures, and generally worse than those presenting for urethroplasty in the last 10 years. It is therefore possible that better long-term results are achievable now, with less severe stricture disease.

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Should a labial fat pad be used in all female urethral reconstructions?

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Introduction The repair of urethral diverticulae or urethrovaginal fistulae is associated with a significant recurrence rate. The use of a labial fat pad (Martius flap) may reduce this problem. This paper reviews a group of patients who underwent urethral reconstruction including using a labial fat pad. The treatment advantages and problems of this technique were documented to identify whether all such patients would benefit from this procedure.
Patients and methods Twenty patients (urethrovaginal fistula in seven, urethral diverticulum in 12, vesicovaginal fistula in one) underwent urethral reconstruction using a labial fat pad. Eight had undergone previous attempts at repair without a fat pad, with subsequent recurrence. In all cases the fat pad was mobilized via a longitudinal incision on the most prominent aspect of the labia majora and transferred to the vaginal incision below the labia minora, to buttress the repair.
Results After interposing the fat pad 19 patients had complete resolution of the fistula or diverticulum (seven of eight secondary repairs, all 12 primary repairs). Postoperative problems included recurrent fistula in one, labial wound dehiscence in one and labial incisional pain in three patients. No other complications related to the fat pad were encountered.
Conclusion The inclusion of a labial fat pad in urethral reconstruction appears to improve the primary success rate considerably. The procedure is simple and has minimal complications. These results strongly support the use of this technique in the primary repair of all cases of urethral diverticulum or fistula.

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Functional results of an orthotopic ileal neobladder with serous-lined extramural ureteric reimplantation: experience with 450 patients

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Introduction We report the functional results of an orthotopic ileal neobladder constructed using the serous-lined extramural tunnel as an antireflux procedure.
Patients and methods A one-stage radical cystectomy and orthotopic ileal W neobladder construction was undertaken in 450 patients (353 males and 97 females) for invasive bladder cancer. The ureters were reimplanted using a serous-lined extramural tunnel to prevent reflux; 344 patients were evaluable, with a mean (SD) follow-up of 38 (25) months. The evaluation included clinical and radiographic studies to determine the functional and oncological outcome.
Results Four patients died in the hospital (0.8%); early complications occurred in 42 patients (9%). All were treated conservatively except for three females who underwent vaginal repair of a pouch-vaginal fistula. During the observation period there were 90 oncological failures; of these, three patients developed an isolated urethral recurrence. Late complications included pouch stones (10), outlet obstruction (11), mucus retention (two), adhesive bowel obstruction (three) and overcontinence in nine females. The incidence of day

and night continence was 93% and 80%, respectively. The upper tracts remained unchanged or improved in 96% of the reimplanted renal units; reflux occurred in 3%.
Conclusions The serous-lined extramural tunnel has proved its efficiency and durability as an antireflux technique.

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Can conduit diversion be avoided in the devastated, irradiated female urinary tract?

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Introduction Radiation therapy for cervical cancer is often curative, but causes significant urinary tract morbidity, prompting management by conduit diversion in many cases. This paper reviews the surgical strategies required to rehabilitate the urinary tract in a group of patients with severe radiation damage, avoiding conduit diversion.
Patients and methods Sixteen patients underwent surgical reconstruction for urinary tract complications related to radiation. The interval between this therapy and the onset of complication was 1–15 years; the mean (range) age of the patients at reconstruction was 53 (30–75) years. Nine patients presented with vesicovaginal fistulae, further complicated by enterovaginal fistula in four, and ureteric stricture in two. A contracted bladder was the primary problem in five, plus ureteric stenosis in one, VUR in one, intrinsic sphincter deficiency in three and urethral stenosis in one. Two presented with bilateral ureteric strictures only.
Results The bladder was rehabilitated in 13 patients, with seven requiring cystoplasty, four a primary fistula closure, one an ileal interposition and one bilateral Boari flaps. Additional procedures at this stage included ureteric reimplantation in four, a pubovaginal sling in four, and a continent stoma, nephrectomy and closure of an enterovesical fistula in one each. In the remaining three patients the bladder was deemed unreconstructable and a continent pouch was constructed. Over a mean (range) follow-up of 4 (1–10) years, six patients required revisional surgery. At the time of this review 15 of 16 had functional reconstructions.
Conclusion With careful intraoperative selection, the irradiated female may be reconstructed successfully, avoiding conduit diversion.

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The long-term results of clam cystoplasty

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Introduction The clam ileocystoplasty was first described for the treatment of adult enuresis and urge incontinence by Bramble in 1982. There have subsequently been several reports describing the short-term results of this procedure. In this study, the long-term results in patients who underwent clam cystoplasty >10 years previously are examined.
Patients and methods The study comprised a retrospective note review and telephone questionnaire in 45 patients undergoing clam cystoplasty between May 1985 and February 1990 at one centre. Preoperative symptoms and urodynamics were evaluated, as well as previous additional treatments and relevant comorbidity. Short- and long-term patient satisfaction was evaluated by a standardized questionnaire, and any complications and further treatments noted.
Results In all, 17 patients were lost to follow-up; thus 28 patients were assessed (22 men, overall mean age at operation 45 years). The mean (range) follow-up was 149.6 (122–180) months. The main urodynamic indication for the clam procedure was primary instability; all patients had undergone at least one other treatment which had failed before surgery. Ileal segments were used in 24 procedures and sigmoid colon in four. After 10 years, five patients had no complications or further treatment and were highly satisfied. Six had undergone an ileal conduit formation. Eleven of 22 patients still voided spontaneously and 11 used CISC; 24 of the 28 patients had regular UTIs. No bladder malignancies were reported in the study group.
Conclusion It is difficult to predict from a preoperative evaluation which patients will fare well in the long term, although patients with no preoperative comorbidity tend to do better. There is still a place for this procedure in the long-term treatment of primary bladder instability.

14.30–15.30
Poster Session 9
Bladder Cancer 2

P84

Virtual bladder biopsy: the use of electrical impedance spectroscopy measurements in the diagnosis of human bladder pathology – a pilot study

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Introduction Erythematous areas are seen frequently at cystoscopy, representing a variety of pathologies, ranging from simple inflammation through to interstitial cystitis and flat carcinoma *in situ* (CIS). A definitive diagnosis can be made only by biopsy. Biological tissues have an electrical impedance which is a function of frequency, because tissues contain components which have both resistive and charge storage (capacitive) properties, giving rise to a complex electrical impedance. This impedance is known to differ according to cell morphology, and has been used to detect pre-cancerous changes in the cervix. We conducted an *ex vivo* study on human cystectomy specimens to correlate electrical impedance spectroscopy measurements with histopathological findings in various pathological conditions.
Materials and methods In all, 67 measurements were made on 11 cystectomy specimens. Impedance was measured immediately after resection, with a custom-designed probe. Several areas were assessed in each bladder specimen. A punch biopsy was then taken at each measurement point.
Results Of the 67 points, histopathology showed that 10 had invasive carcinoma, nine showed CIS, 32 had various degrees of inflammation and 16 were benign with no inflammation. Correlation with histopathological findings showed separation between benign and malignant changes.
Conclusions In a preliminary set of *ex vivo* measurements we established patterns of electrical impedance in the human bladder. Early results suggest that this simple and minimally invasive technique has the potential to differentiate between benign and malignant bladder pathology.
Funding: BUF/MSD fellowship, RCSEd.

P85

Advancing the molecular diagnosis of bladder cancer: the role of tumour-specific exon-assembly during CD44 expression

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Introduction Numerous recent studies have proposed that the analysis of disorderly CD44 gene expression in urothelia is a useful tool for the early detection and diagnosis of bladder cancer. Whilst the current data are encouraging, sensitivity and specificity need to be improved, particularly for detecting non-invasive papillary tumours. This study represents part of an ongoing programme investigating the biology of CD44 splicing and exon assembly, and investigates the role of CD44 exon 12 expression and preferential linkage to CD44 exon 5 in malignant bladder cells and tissues.
Materials and methods CD44 exon 12-specific expression was determined in mRNA extracted from 10 samples each of normal and malignant bladder tissues, exfoliated urothelial cells from normal volunteers and consented patients with histologically confirmed bladder tumours, using RT-PCR ELISA technology. The preferential linkage of CD44 exon 12 with exon 5 was investigated in RT112 and T24 human bladder cell lines, and in normal bladder urothelium via RT-PCR, where products were only generated when the 3' of exon 5 was directly spliced next to the 5' end of exon 12.
Results CD44 exon 12 expression was significantly greater ($P<0.005$) in malignant bladder tissue than in normal tissue, the mean (SD) absorbance values/μg of RNA being 0.883 (0.125) and 0.122 (0.012), respectively. Analysis of exfoliated urothelial cells showed similar significant differences ($P<0.005$) with malignant cases at 1.586 (0.234) and normal volunteers at 0.238 (0.098). Exon-linkage analysis revealed that the elevation of CD44 exon 12 expression was directly related to a preferential physical link with CD44 exon 5, i.e. CD44 exon 5 mRNA is joined directly to CD44 exon 12 mRNA in malignant bladder cells.
Conclusions That CD44 exon 12 over-expression in malignant bladder urothelia is associated with a physical link to CD44 exon 5 expression may potentially provide a highly sensitive and specific marker for bladder cancer.
Funding: NGH R&D fund

P86

A study comparing various noninvasive methods of detecting bladder cancer in urine

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Introduction To determine the detection rate of TCC from exfoliated cells in urine using the bladder tumour antigen (BTA)*stat* test, nuclear membrane protein-22 (NMP22), the telomeric repeat amplification protocol (TRAP), urine cytology and a haemoglobin dipstick test.
Patients and methods Urine samples were collected from 81 urological patients (69 men and 12 women, mean age 68.5 years, SD 11.1) including 27 with histologically confirmed TCC. BTA*stat*, NMP22 and TRAP assays were used according to the manufacturers' guidelines. All samples were assessed by cytology and haemoglobin dipstick tests and the results compared with histology.
Result The overall sensitivities for BTA*stat*, NMP22, TRAP assay, cytology and haemoglobin dipstick were 56%, 74%, 88%, 52% and 52%, respectively, and their overall specificities were 89%, 91%, 89%, 94% and 61%, respectively. Combining the NMP22 and TRAP assay increased the overall sensitivity and specificity of diagnosing TCC to 94% and 98%, respectively.

Grade/ stage (n)	*BTA*stat	*NMP22*	*TRAP*	*Cytology*	*Hb*
G1 (8)	25	63	50	25	38
G2(11)	55	73	100	36	46
G3 (7)	86	100	100	85	57
PTa (12)	42	50	78	25	50
PT1 (11)	55	91	75	64	57
PT2 (3)	100	100	100	100	100
PTis (3)	100	100	100	100	68

Conclusion There was a significant improvement in TCC diagnosis using NMP22 and TRAP assays over urine cytology, especially for low-grade ($P=0.038$ for NMP22 and <0.001 for TRAP) and low-stage TCC ($P=0.0035$ for NMP22 and <0.001 for TRAP; chi-squared test). Combining NMP22 and TRAP further increased the diagnostic accuracy. Contrary to this was the poor detection rate of TCC (especially for low-grade and -stage tumours) with BTA*stat and* haemoglobin dipstick.

P87

Tumour progression and survival of patients with pTaG3 bladder cancer

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Introduction High-grade pTa tumours occur infrequently, but are thought to have a significant risk of progression. We evaluated 56 patients to determine the risk of progression and survival.
Patients and methods Between 1990 and 1998, 48 patients with primary pTaG3 and eight with low-grade Ta bladder tumours who progressed to G3pTa were identified (median age 67 years, range 38–91). The median (range) follow-up was 64 (5–130) months. TUR was undertaken in all patients; 39 (70%) received instillations of mitomycin C and 16 (29%) received BCG.
Results The 5-year disease-specific survival was 82%; of the 56 patients, 50 (89%) had one or more recurrences in the bladder. The stage progressed in 23 patients (41%) at a median of 33 (2–98) months. The 5-year progression-free survival rate was 65%. Stage progression in 23 patients was associated with carcinoma *in situ* (CIS) in 14 (61%). Thirteen patients (23%) died from bladder cancer, with a median time to death of 58 (5–107) months. Eight of these patients had associated CIS. Ten patients underwent radical cystectomy, with a median time to cystectomy of 56 months; four survived. Eight patients received EBRT, with a median time to treatment of 46 months; one survived.
Conclusion pTaG3 tumours have a high risk of recurrence and progression. Associated CIS is a significant risk factor for progression and mortality. Immunotherapy and early cystectomy for treatment failure should result in better long-term outcomes.

P88

pTa bladder cancer: is early discharge safe?

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Introduction The optimum follow-up for superficial TCC is unknown. Abel (1997) suggested that patients with solitary pTa tumours not recurring after 12 months should be discharged; Leblanc (1999) stated that G1pTa tumours required a 5-year follow-up. The aim of the present study was to examine the natural history of pTa tumours in patients treated at our institution.
Patients and methods Clinicopathological and follow-up data for all patients undergoing initial resection of superficial TCC in 1994 and 1995 were collated.
Results There were 151 pTa bladder cancers; 86 (57%) recurred and 13 (9%) progressed (to pT1 in eight, 5%, and to muscle invasion in five, 3%). Thirty-one (21%) first recurred after 1 year, 18 (12%) after 2 years and 10 (7%) after 3 years. Of the 122 solitary pTa tumours, 65 (53%) recurred; 26 (21%) first recurred after 1 year, 18 (15%) after 2 years and 10 (8%) after 3 years. Of the 68 G1pTa tumours, 34 (50%) recurred and three (4%) progressed; 13 (19%) first recurred after 1 year, nine (13%) after 2 years and five (9%) after 3 years. There were 57 cases of solitary G1pTa tumours, and 28 (49%) recurred and two (4%) progressed; 12 (21%) first recurred after 1 year, nine (16%) after 2 years and five (9%) after 3 years. In one case the first recurrence was at 42 months. Two solitary pTa tumours progressed at first recurrence at 37 (pT1) months and 49 (pT2) months. No G1pTa tumours progressed after 1 year.
Conclusion Even solitary superficial bladder cancers with low histological grade recur after 3 years of tumour-free follow-up, suggesting that the minimum follow-up should be 3 years.

P89

The biological characteristics of pT1G3 bladder tumours are the same as invasive cancers: a study of cell proliferation and molecular markers of aggressiveness

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Introduction pT1G3 TCC of the bladder has at least a 40% progression rate. Tumour progression occurs through several different mechanisms and hence an evaluation of multiple markers representing differing events in tumorigenesis for an individual tumour may provide more information than using a single marker. The aim of this study was to assess the biological nature of pT1G3 bladder tumour by studying cell proliferation and other immunohistochemical variables, and the survival pattern, comparing the same variables in superficial and invasive bladder tumours.
Patients and methods Fifty-seven patients with TCC who had substantial follow-up (mean 4.1 years) were studied with the following immunohistochemical stains on paraffin sections: p53, pRb, Ki67, EGFR, VEGF and E-cadherin. The microvessel density (MVD) was determined using CD34 immunostaining and the mitotic index (MI) also counted. The study group (pT1G3) included 21 patients; superficial bladder TCC (pTaG1, 18) and invasive tumour (pT2G3, 18) were studied as negative and positive controls. The sections were scored by two observers independently.
Results The MI in pTa tumours was lower than in pT1 and pT2 ($P<0.001$) but was no different between pT1 and pT2 ($P=0.16$) tumours. The same was true for Ki 67 (pTa vs pT1, $P=0.03$; pTa vs pT2, $P=0.03$; pT1 vs pT2, $P=0.40$). Expression of p53 and EGFR increased with grade and stage; pRb and E-cadherin showed an inverse trend. These values were not statistically significant. Kaplan–Meier estimates of progression-free survival comparing pTa and pT1G3 groups were significant ($P=0.004$), but that between pT1G3 and pT2 groups was not ($P=0.101$).
Conclusion pT1G3 tumours have the same clinical and molecular characteristics as muscle-invasive cancers.

P90

Progesterone, a potentially useful adjunct to intravesical chemotherapy?

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Introduction Bladder cancer can be treated with intravesical chemotherapeutics, including epirubicin. Their effectiveness is often limited because of multidrug resistance (MDR) related to increased activity of the drug efflux pump P-gp. Progesterone is a known inhibitor of P-gp function and may potentially reverse MDR. Sensitive (MGH-U1S) and MDR (MGH-U1R) urothelial cell lines were used to investigate the MDR-reversing ability of progesterone in an *in vitro* model.
Materials and methods Sensitive and resistant cell lines were cultured as monolayers and their P-gp status confirmed by immunohistochemistry. The intrinsic cytotoxicity of progesterone

was determined, and from the results a dose of 20 μg/mL selected. The cells were exposed to progesterone or medium for 24 h before treatment with a range of epirubicin doses for 1 h. At control-well confluence, viable biomass was assessed using the MTT assay and nuclear resistance patterns by *in situ* confocal microscopy.
Results Progesterone was cytotoxic in a dose-dependent manner when >20 μg/mL, below which it had no significant effect. When combined with epirubicin, progesterone had no additional effect on sensitive cells. Resistant cells exposed to epirubicin alone produced up to 100% more biomass than those exposed to combination therapy. The addition of progesterone reverted a resistant nuclear fluorescence pattern to a sensitive one.
Conclusion Progesterone and epirubicin therapy can overcome MDR and may kill tumours more successfully *in vivo*. Its additional effects on cell differentiation and apoptosis, as well as its tolerability, make it a potentially very useful adjunct to intravesical chemotherapy.

P91

A randomized trial showing improved efficacy of intravesical epirubicin at alkaline pH for superficial bladder cancer

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Introduction The anthracyclines doxorubicin and epirubicin are established intravesical chemotherapeutic agents, but their efficacy is limited, partly because they are instilled at a suboptimal (acid) pH in aqueous solution. Epirubicin is a weak acid with a pKa of 7.7, making it predominantly neutrally charged and lipophilic at alkaline pH, and positively charged at acid pH. In monolayer cell cultures of both parenteral and resistant bladder cancer cell lines, epirubicin uptake and cytotoxicity is enhanced considerably by alkalinisation of the drug solution to pH 8.0 (unpublished work).
Patients and methods Fifty patients with 2–7 superficial bladder cancer lesions were randomized in a marker-lesion protocol to receive epirubicin buffered with HEPES to pH 8, or prepared conventionally in distilled water, as a single instillation within 24 h of TURBT. The main endpoint was the survival or abrogation of the marker lesion 3 months after treatment.
Results In the group receiving conventional epirubicin (the control arm) the marker lesions in two of 21 patients responded, compared with marker lesions in 11 of 25 patients receiving epirubicin instilled in an alkaline environment.
Conclusion Epirubicin is more effective when buffered to an alkaline pH close to its pKa of 7.7. These findings open the possibility of combining epirubicin with other intravesical agents with a high intrinsic pH, e.g. the novel intravesical agent meglumine γ-linolenic acid; this will enhance the efficacy of epirubicin.
Funding: Scotia Pharmaceuticals

P92

A phase I study of combined mitomycin C and 5-aminolaevulinic acid-mediated photodynamic therapy in superficial bladder cancer

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Introduction 5-Aminolaevulinic acid-mediated photodynamic therapy (ALA-PDT) combined with mitomycin C (MMC) both *in vitro* and *in vivo* has an additive effect on cell death compared with either agent alone. The primary objectives of this study were to assess the safety and tolerability of combined therapy.
Patients and methods Twenty-four patients with recurrent tumour suitable for intravesical chemotherapy were recruited. The trial was stratified into seven levels of increasing light exposure and ALA concentration with prior MMC instillation. All patients received a standard six-dose MMC course as part of the study.
Results There were no episodes of skin photosensitivity nor increases in plasma porphyrin levels perioperatively. Sixteen of the 24 patients had transient increases in irritative score but the scores returned to baseline by day 7 in all cases. All were discharged within 24 h. There were no reductions in functional bladder capacity. Two tumours were detected subsequently.
Conclusions All patients found ALA-PDT an easily tolerable procedure; most experienced mild to moderate dysuria and frequency for 12–24 h, which settled in all. Although not primarily assessing recurrence rates, the early results are encouraging. On this basis, we propose that 40 mg of mitomycin C combined with ALA-PDT (6% ALA and 20 J/cm^2 light) is safe and tolerable. We intend to use these results for an efficacy study of combined therapy in patients with difficult recurrent disease.
Funding: CRC

P93

Recombinant mycobacteria produce durable responses in a murine bladder tumour model

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Introduction The treatment of bladder cancer with BCG represents the most successful form of immunotherapy for any solid human malignancy. BCG stimulates an immune response which is co-ordinated by cytokines. We investigated the potential to use alternative mycobacteria, i.e. *Mycobacterium smegmatis*, for immunotherapy in a murine tumour model. In addition we genetically engineered these mycobacteria to secrete cytokines, to investigate the potential to modify the immune response elicited.
Materials and methods An MB.49 murine tumour was established subcutaneously in C57BL6 mice. These tumours were then treated locally with either saline (PBS), BCG, wild-type *M. smegmatis*, or recombinant *M. smegmatis* engineered to secrete interleukin-15 or TNF-α. Treatment injections were administered on days 0, 2, 6, 9 and 13, and the mice were killed when the tumours reached 1.44 cm^2.
Results The effect of wild-type *M. smegmatis* was similar to that seen with BCG, i.e. it significantly prolonged survival compared with PBS ($P = 0.0023$). TNF recombinants yielded a 70% tumour-free rate. Mice treated with recombinant *M. smegmatis* engineered to secrete interleukin developed palpable nodules at a similar time to other groups, but this group had all survived tumour-free at 100 days. Overall survival in this group was therefore significantly prolonged compared with wild-type *M. smegmatis* ($P < 0.001$).
Conclusion *M. smegmatis* has a potent anti-tumour effect *in vivo* which is significantly increased by genetically engineering it to secrete cytokines. The response seen is durable and not associated with significant toxicity. This approach may increase the role of mycobacteria in the treatment of human malignancy.
Funding: BUF, AICR & ICRF

P94

A phase I study of photodynamic therapy for superficial bladder cancer under local anaesthetic

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Introduction Photodynamic therapy (PDT) using 5-aminolaevulinic acid (ALA) has been used to treat superficial TCC under a general anaesthetic via a rigid cystoscope. We report the technique and results of ALA-PDT administered under local anaesthetic (LA) via a flexible cystoscope.

Patients and methods Eighteen patients with recurrent TCC stage Ta/CIS (grades 1–3) were treated using escalating doses of ALA (3–6%) and light (25–50 J/cm^2). The following intravesical LA techniques were used: (i) no LA; (ii) passive diffusion of 40 mL 2% lignocaine; and (iii) electromotive drug administration (EMDA) of salt-free 2% lignocaine. Pain was assessed using a linear analogue score on a scale of 0–10.

Results Two patients undergoing 3% ALA PDT with no LA experienced pain/spasm and the procedure was abandoned. Using lignocaine all eight patients tolerated the procedure well, with a median (range) pain score of 1 (0–2). On increasing the ALA dose to 6%, six patients reported pain, with a median pain score of 8 (5–10), with three failing to tolerate the intended light dose. Using EMDA of lignocaine with maximum light and ALA dose, two patients were treated successfully (pain score 2). As with PDT under a general anaesthetic, all patients had bladder irritation after the procedure, although this was substantially reduced with intravesical dexamethasone. There was no subjective/objective effect on long-term bladder function. Of the 12 patients tolerating the procedure, nine had significant tumour response, with 6% ALA being the most effective.

Conclusion PDT under LA is safe and well-tolerated; it is effective in a proportion of patients and with further refinement it may be possible for use on an outpatient basis under LA.

14.30–15.30
Poster Session 10
Basic Science - Oncology 2

P95

An *in-situ* hybridization study of three secretory proteins (prostatic secretory protein psp94, probasin and seminal vesicle secretion II) in dysplastic and neoplastic rat prostates

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Introduction A prostatic secretory protein of 94 amino acids (PSP94), probasin and seminal vesicle secretion II (SVII) are the three major proteins synthesized specifically in the lateral lobe of the rat prostate gland [*Prostate* 2000; 42: 219–29]. These secretory proteins are regulated differentially in the castrated rat prostate by androgen, glucocorticoid and progestin [*Endocrinology* 2000; 141: 4543–51].
Materials and methods In the present study, we examined and compared the mRNA expression of these three prostatic proteins in premalignant dysplasia (prostatic intraepithelial neoplasia, PIN) induced in the Noble rat lateral prostate by sex steroids, and in two rat prostatic tumours (an androgendependent Dunning tumour, R3327-H, and an androgen-independent Noble rat prostate tumour, AIT) by *in situ* hybridization. The Dunning tumour was grown in intact male nude mice supplemented with testosterone, whereas the AIT was grown in castrated Noble rats. Sections were hybridized with digoxigenin-labelled RNA probes for PSP94, probasin and SVSII [*Prostate* 2000; 42: 219–29].
Results These three secretory proteins were intensely and specifically expressed in the lateral prostate of the intact rat. Their hybridization signals became reduced in the epithelial cells in the low-grade PIN and became lost or significantly weakened in the high-grade PIN in the hormone-treated lateral prostate. No hybridization signals were detected in both Dunning R3327-H and AIT tumours.
Conclusion The mRNA expression of the three androgen-regulated secretory proteins was less in the low- and high-grade PINs and lost in the two rat prostate tumours, suggesting that these proteins were down-regulated during the malignant transformation of the prostate gland.
Funding: RGC Earmarked Research Grant CUHK 4131-00M, Hong Kong

P96

The expression of filamin in human prostate cancer and a specific role for filamin in the cytosolic-to-nuclear shuttling of the human androgen receptor

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Introduction The androgen receptor (AR) is thought to have a pivotal role in the development and progression of prostate cancer. We identified filamin, an actin-binding protein, as a novel AR-interacting protein. We recently showed that in a filamin-deficient cell line (M2) plus ligand, the AR remains cytosolic. In a filamin-positive cell line (A7), under the same conditions, the AR becomes exclusively nuclear. In this study, we extended this analysis to include the glucocorticoid (GR), oestrogen (ER) and vitamin D receptors (VDR). The filamin gene resides in a region associated with susceptibility to prostate cancer, Xq27-28. Thus we also examined the expression of filamin in a series of prostate cancer specimens.
Materials and methods Cell lines M2 and A7 were transfected with GFP-AR, GR, ER or VDR fusion proteins, then treated with ligand or vehicle. The cellular location of the receptor proteins was assessed via fluorescence microscopy. Filamin expression in human prostate cancer was analysed via immunohistochemistry on sections from 23 patients.
Results The absence of filamin had no effect on the cellular location of the GR, ER or VDR, but had a striking effect upon the AR. Immunohistochemical analysis revealed that in BPH, filamin is expressed in epithelial and stromal cells. However, in high-grade tumours, filamin expression is markedly reduced or absent in epithelial cells.
Conclusion Filamin specifically influences the cytosolic-to-nuclear shuttling of the AR, but not the GR, VDR or ER. Expression of filamin in prostatic epithelial cells appears to be markedly reduced in high-grade tumours. Taken together, filamin appears worthy of further investigation.
Funding: Harker Foundation

P97

Interaction of PSA with α2-macroglobulin

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Introduction PSA is a serine protease with chymotrypsin-like enzymatic activity. α2-Macroglobulin (A2M) binds many proteases, including PSA, but does not bind inactive proteases. Once bound the enzyme is accessible to substrates and inhibitors of small molecular size, but not to those of relatively large molecular size. PSA forms a complex with A2M *in vitro* and *in vivo*. In this form it is undetectable by conventional immunoassays for PSA. The aims of this study were to investigate the binding of PSA to A2M and to determine the enzymatic activity of PSA complexed with A2M.
Materials and methods The binding of PSA to A2M was evaluated by PAGE methods and immunoassay, using the Wallac ProStatus PSA Free/Total method. Complexed PSA enzyme activity was also determined by monitoring the hydrolysis of a synthetic substrate, MeO-Suc-Arg-Pro-Tyr-NH-Np(S-2586).
Results Protein electrophoresis, isoelectric focusing and western-blot analysis showed that PSA binds readily to A2M *in vitro*. Incubation of PSA and A2M resulted in a significant decrease (40–60%) in immunodetectable PSA. PSA bound to A2M was enzymatically active, as shown by the use of the small molecular size synthetic substrate. Treatment of serum with amines resulted in an average six-fold increase in measured free PSA.
Conclusion The PSA 'hidden' by complexing with A2M must be considered a significant component of the total PSA. Measurement of total serum PSA, as carried out routinely for the diagnosis and management of prostate diseases, does not represent the actual PSA present.

P98

A novel method for isolating and evaluating prostatic stem cells

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Introduction Prostate cancer cells are believed to have a stem-cell-like phenotype but research has been limited because there are no definitive stem cell markers. Primitive cells are able to efflux Hoechst 33342 stain, defining a population of Hoechst 'low' cells, termed side-population (SP cells). Such cells from murine skeletal muscle can repopulate the haemopoietic lineages in the mouse [*PNAS* 1999; 96: 14482–6]. We optimized this method and isolated an SP population from human prostatic epithelial cells (PECs).
Materials and methods PECs from 16 men were identified using the Ber-EP4 epithelial marker and SP cells isolated using dual-wavelength flow cytometry after staining with Hoechst 33342. The cells were characterized immunohistochemically with basal integrins, prostate-specific membrane antigen and pp32 found in stem cells. They were also inoculated subcutaneously into athymic nude mice to examine their capacity to reconstitute prostatic glandular tissue.
Results Isolation curves for PECs had similar characteristics to those from haematopoietic lines known to yield stem cells. These SP cells comprise 8.12 (1.2)% of the PEC population and are enriched for the integrin $\alpha 2$ compared with the whole fraction.
Conclusion It is possible to isolate SP cells from prostatic tissue which are similar to stem cells previously identified from haemopoietic, liver, lung, muscle and brain tissue. This technique will enable further study and characterization of human prostatic stem cells.
Funding: BUF, RCS (E)

P99

In vivo analysis of prostate cancer-induced angiogenesis using the dorsal microcirculatory chamber

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Introduction Angiogenesis is important in the development and metastasis of prostate cancer. Androgen ablation and inhibition of angiogenic growth factor expression are both known to suppress prostate cancer-induced angiogenesis, but the detailed mechanisms of this response remain unclear. Therefore, the aim of the present study was to establish the dorsal microcirculatory chamber in mice with implanted prostate cancer cells and quantify angiogenesis using fluorescent *in vivo* microscopy.
Materials and methods Dorsal microcirculatory chambers were implanted by removing an area of skin from the dorsum. The remaining layer of striated muscle and skin was extended between symmetrical frames. Fluorescently labelled prostate cancer (LNCaP-LN3) cells were placed over the exposed tissue and sealed. Tumour growth and angiogenesis were visualized in conscious mice using *in vivo* microscopy every 3–4 days over a 20-day period.
Results Preliminary observations (two control and two tumour) indicated that a solid tumour mass began to form within 3–5 days. Within 7–9 days the tumour cells had induced a microvascular network with blood perfusion which extensively developed over the observation period. Tumour growth was closely associated with the establishment of the tumour-associated microvasculature.
Discussion The current pilot study shows that *in vivo* microscopy combined with the dorsal microcirculatory chamber with implanted cells is a useful technique to assess the complex relationship between prostate growth and the microcirculation. Further research using this model will investigate the effects of androgen ablation as well as anti-angiogenic agents on prostate cancer-induced angiogenesis.
Funding: AICR

P100

GSTP1 polymorphism influences response to hormone therapy in prostate cancer

C.J. Luscombe, A.A. Fryer, M.E. French, S. Liu, M.F. Saxby and R.C. Strange *Department of Urology & Centre for Cell & Molecular Medicine, North Staffordshire Hospital, Stoke-on-Trent, Staffordshire, UK*

Introduction Glutathione S-transferases (GSTs) catalyse the detoxification of a wide variety of electrophiles. One GST gene, *GSTP1*, may have particular relevance in prostate cancer, as it shows near universal methylation of its promoter in cancer and no methylation in BPH. This gene is polymorphic with an Ile105Val substitution effecting catalytic activity. However, polymorphism is not reported to affect susceptibility to prostate cancer and its effects on outcome are unclear. We studied this polymorphism in respect to susceptibility, metastasis and response to hormone therapy in prostate cancer.
Patients and methods In all, 210 patients with prostate cancer and 155 controls with BPH were recruited; the patients were genotyped using PCR techniques. Logistic regression analysis, including age, was used to determine differences between groups.
Results *GSTP1* Ile105Val polymorphism did not affect susceptibility (with reference to the I/I genotype, I/V; $P=0.789$, odds ratio, OR 1.06 and V/V; $P=0.644$, OR 1.17) or metastatic state at diagnosis (with reference to I/I genotype, I/V; $P=0.544$, OR 1.23 and V/V; $P=0.950$, OR 0.97). However, in 118 patients requiring hormone therapy, the genotype did predict the response based on a PSA nadir of $>$ or <4 ng/mL. Compared with I/I, both I/V ($P=0.029$, OR 2.86, 95% CI 1.12–7.35) and V/V ($P=0.137$, OR 2.56, 95% CI 0.74–8.84) were associated with a poor response. A combined group of I/V and V/V predicted poor response in comparison with I/I ($P=0.026$, OR 2.78, 95% CI 1.13–6.38).
Conclusion *GSTP1* polymorphism affects the PSA response to hormone therapy, which is recognized to affect prognosis.
Funding: Staff of Wedgewood plc

P101

Comparison of allelic loss in familial and sporadic prostate cancer

R. Singh, P. Osin, S.M Edwards, S. Clinton, A. Ardern-Jones, A. Murkin, D. Teare, D. Dearnaley, D. Easton, R.J Shearer, the CRC/BPG/UK FPC Study Collaborators and R.A Eeles *Institute of Cancer Research, and The Royal Marsden NHS Trust, Surrey, and CRC Genetic Epidemiology Unit, Cambridge, UK*

Introduction There is a genetic predisposition to prostate cancer in 5–10% of cases. Prostate cancer susceptibility genes are thought to act as tumour-suppressor genes (TSGs) and can be identified by loss of heterozygosity (LOH) in tumour tissue. LOH in sporadic prostate cancer has been extensively studied but little has been reported on LOH in familial prostate cancer. The aims of this study were to compare allelic loss in prostate tumours taken from individuals with familial or early-onset prostate cancer with that seen in sporadic disease.
Materials and methods Prostate tumours (101) from patients with familial prostate cancer were analysed. Microsatellite markers at 24 candidate loci across the genome were investigated.

Results In this family set there were similar rates of LOH at 6p, 8p, 10q and 16q to those previously reported in sporadic prostate cancer. However, there were also significant rates of LOH at three other regions; 37% LOH at *BRCA2*, 28–35% LOH at two markers on chromosome 1, and 28% LOH at 12p13. LOH rates for these markers in a set of matched controls (sporadic prostate cancer) will also be presented.
Discussion Our results show significant LOH on chromosome 1 and further support the possibility of a prostate-cancer susceptibility gene on this chromosome. The high rates of loss seen at *BRCA2* suggest that this gene may play a significant role in the pathogenesis of prostate cancer. The 12p13 region may also harbour a TSG involved in early onset disease, and warrants further detailed analysis.
Funding: Royal Marsden Hospital

P102

TNFα polymorphisms are associated with the risk of bladder cancer and grade of tumour at presentation

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Introduction TNF is known to be important in angiogenesis and has been implicated in the development and progression of tumours. We assessed the role of TNF polymorphisms in the risk of bladder cancer and in subsequent tumour behaviour.
Materials and methods Using a PCR-SSP genotyping technique we examined seven single-nucleotide polymorphisms in TNFα, assessing 208 controls and 198 patients.
Results At locus +488, an A was found in 14.9% of controls compared with 28.2% of patients ($P=0.006$ corrected). At −859 a T was found in 14.9% of the controls compared with 26% of patients ($P=0.027$ corrected). In addition the two loci were in tight linkage disequilibrium, i.e. almost all the individuals having the rare allele at +488 also had the rare allele at −859. Finally, those patients who had the rare allele at +488 or −859 were significantly more likely to present with a moderately differentiated tumour than were those patients who did not.
Conclusions We show for the first time a significant association between TNF polymorphisms at both +488 and −859 and the risk of bladder cancer. There was marked linkage disequilibrium between +488 and −859T which we hypothesise will have functional significance. Finally, we showed that the polymorphisms are associated with the grade of tumour at presentation, in addition to the risk of bladder cancer.
Funding: ICRF

P103

Reduced adhesion of T lymphocytes to E-cadherin-deficient bladder cancer cells

J. Cresswell, W.K. Wong, J.A. Kirby and D.E. Neal *Department of Surgery, University of Newcastle, Newcastle upon Tyne, UK*

Introduction The CD103 integrin is expressed by 90% of intraepithelial lymphocytes (IEL) but only 2% of peripheral blood lymphocytes (PBL). Our group has previously shown the presence of IEL-expressing CD103 in normal urothelium and bladder TCC. The only known ligand for CD103, the cell adhesion molecule E-cadherin, is down-regulated in invasive bladder cancers. Our hypothesis is that loss of E-cadherin may be a mechanism for immune evasion in bladder cancer. This study examined adhesive interactions between CD103-positive lymphocytes and E-cadherin-expressing bladder cancer cells.
Materials and methods CD103 expression was induced on PBL by *in vitro* activation and culture in the presence of TGF-β. A flow cytometric adhesion assay was used to assess adhesion between these lymphocytes and bladder cancer cell lines. Adhesion blockade using mAbs to CD103 was used to confirm the importance of this interaction.
Results Compared with CD103-negative controls, CD103-expressing lymphocytes showed significantly greater adhesion (2.5-fold) to E-cadherin-positive bladder cancer cells ($P<0.001$). This increased adhesion could be abrogated using anti-CD103 adhesion blockade ($P=0.0068$). In the absence of E-cadherin expression, there was no difference in lymphocyte adhesion.
Conclusion The interaction between the CD103 integrin and E-cadherin plays an important role in the targeting of bladder cancer cells by T lymphocytes. Loss of E-cadherin may be a strategy for immune evasion in bladder cancer. Further work is underway to assess the role of CD103 and E-cadherin in the cytotoxicity of bladder cancer cells.
Funding: NHS R&D Executive

P104

Disruption of the regulation of angiogenesis by hypoxia: evaluation of the chemotherapeutic drug geldanamycin

K.J. Turner, D. Cranston and A.L. Harris *Department of Urology, Churchill Hospital, Headington, Oxford, UK*

Introduction Tumour hypoxia is a potent stimulus to angiogenesis, an effect mediated largely by the induction of the angiogenic factor vascular endothelial growth factor (VEGF) by hypoxia-inducible transcription factors (HIFs). Disruption of this pathway is a major research goal. HIFs bind to the molecular chaperone heat-shock protein 90 (Hsp90) and this binding is likely to be functionally relevant. Geldanamycin (GA) is a drug which disrupts the interaction of Hsp90 with client proteins. Here we evaluate GA in the inhibition of the HIF-VEGF pathway.
Materials and methods Using von Hippel Lindau (VHL) wild-type and mutant renal cancer cells, the effect of GA on expression of HIFs (immunoblotting) and VEGF (ELISA) was determined. A specific effect of GA on the HIF response element (HREs) of hypoxia-inducible promoters was investigated by transfection of HRE plasmids, using a luciferase-reporter system.
Results Exposure to GA inhibited VEGF expression in VHL wild-type cells under normoxia and hypoxia. VHL mutant cells were not affected. A specific effect on HIF-mediated transcription was confirmed by the luciferase experiments although there was also a general inhibition of transcription. Contrary to expectations, HIF protein expression was upregulated on exposure to GA.
Conclusions Interaction with Hsp90 probably determines HIF activity but not absolute levels. Disruption of this interaction by GA is effective at inhibiting expression of VEGF in VHL wild-type cells. These early data suggest that GA (which is in clinical trials) may have some role in inhibiting the expression of angiogenic mediators in renal cancer.
Funding: The Royal College of Surgeons of England.

P105

The use of radiolabelled monoclonal antibody specific for the extracellular domain of prostate-specific membrane antigen in the management of prostate cancer

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St Bartholomew's Hospital, West Smithfield, London, UK

Introduction A newly developed radiolabelled antibody to the extracellular domain of the prostate-specific membrane antigen (PSMA), unlike CYT351 which has to penetrate the cell, has been evaluated.
Methods and materials The murine mAb MUJ591, radiolabelled with ^{99m}Tc (600 MBq), was injected intravenously with serial planar and SPECT imaging undertaken at specific intervals after injection. Twenty-eight patients being considered for radical surgery or with suspected recurrence after radical therapy (and giving informed consent) underwent imaging.
Results There was a high sensitivity for detecting prostate cancer (all 28) and the absence of lymph node involvement (13 of 14) when compared with histology. Fourteen patients subsequently underwent radical prostatectomy with lymph node dissection; the disease progressed in three of these 14, two having suspected extraprostatic disease on imaging. Microscopic capsular extension was poorly determined by this imaging technique. Nine patients have undergone radical radiotherapy combined with neoadjuvant LHRH therapy. Four patients underwent imaging for suspected progression, of which three had disease not detected by conventional techniques.
Conclusion This new antibody should be more sensitive than existing antibodies that bind to the intracellular component of PSMA, as it does not require entry into the prostate cancer cells. This study reveals a high sensitivity for detecting prostate cancer and metastatic disease. Its current role in determining capsular breach needs further evaluation. New technology combining data from radiolabelled imaging overlaid onto conventional MRI or CT images may improve the accuracy of localization.

P106

Reduced immunohistochemical staining of thrombospondin-1 is related to progression in superficial bladder cancer

J.C. Goddard, C.D. Sutton, J.L. Jones, K.J. O'Byrne and R.C. Kockelbergh *University of Leicester Hospitals NHS Trust, Leicester, UK*

Introduction Thrombospondin (TSP) is a 450 kDa multifuctional glycoprotein which has anti-angiogenic functions; decreased expression has been associated with a poor outcome in invasive bladder cancer. The purpose of this study was to investigate the relationship of TSP-1 expression in a series of superficial bladder cancers.
Materials and methods A series of samples from 225 cases of superficial bladder cancer were stained with antibody against TSP-1. The location and percentage of TSP-1 staining was assessed, and a scoring system developed and applied to all cases.
Results Of the 255 cases, 60 progressed to muscle-invasive disease and 165 did not. Immunostaining of TSP-1 was discrete and confined to four distinct areas, i.e. the epithelial-stromal junction, perivascular, tumour cell and stromal. There was epithelial-stromal staining in 42% of cases that did not progress, compared with 23% that did, perivascular staining in 51% and 20%, respectively, 2% with tumour-cell staining in both groups, and stromal staining in 9% and 7% of cases, respectively. There was less overall TSP-1 staining in those cases which progressed to muscle-invasive disease. There was a significant difference in the reduction of staining in the epithelial-stromal junction ($P = 0.040$), perivascular staining ($P < 0.001$) and in the total staining score ($P < 0.001$).
Conclusion In this series of superficial bladder cancers, a reduction in the immunohistochemical expression of TSP-1 was significantly associated with disease progression.

16.00–17.00
Poster Session 11
Prostate Cancer 2

P107

Prostate biopsy strategies in the UK

G. Oades, R. Greenhalgh, C. Cutting, R. Kirby and C. Anderson *St George's Hospital, Tooting, London, UK*

Introduction The BAUS Working Party stated that there is a need to develop standard protocols for TRUS and biopsy. The results of a national questionnaire to describe current prostate biopsy strategies are presented here to help formulate such guidelines.
Method In all, 193 hospitals were surveyed using a postal questionnaire to urologists, radiologists and histopathologists.
Results The overall response rate was 59%; in most hospitals radiologists took biopsies and in 17% both radiologists and urologists did so. A systematic biopsy approach was adopted by 90% of urologists who would take or request sextant biopsies, with additional separate biopsies of any focal abnormalities. Of operators, 70% claimed to target the peripheral zone. When taking repeat biopsies, 47% of urologists would take or request more than six biopsies and 30% would target the central zone. Only 28% of all specialists send cores separately to histopathology. Reporting of various prognostic histological features is suboptimal (e.g. Gleason score 82%, high-grade PIN 82%).
Discussion The results of this survey show wide variation in the practice of prostate biopsy strategies in the UK. In general, a systematic biopsy system has been adopted. It appears that about half of clinicians do not regard the refinement of intraprostatic staging as being useful in guiding management decisions. This makes comparisons with subsequent pathological stage and studies of comparative outcome difficult. If biopsies are to be taken by urologists, radiologists and perhaps nurse practitioners, then the devising of national guidelines is essential. A multidisciplinary approach and a close liaison between operator and histopathologist is very important.

P108

A cost- and time-effective biopsy cassette for site-specific biopsies of the prostate

M.E. Laniado, L. McMullen, M.M. Walker and A. Patel *St Mary's Hospital, London, UK*

Introduction Information from site-specific biopsies may be useful in predicting where nerve sparing during radical prostatectomy may result in a positive margin, and the site for repeat biopsy after a suspicious prostate biopsy. Site-specific biopsies of the prostate have traditionally required transport and processing in separate containers, making this a costly and labour intensive procedure
Patients and methods We describe a new multicompartment microcassette that facilitates the carriage and initial processing of site-specific biopsies of the prostate.
Results Time is saved at various steps (72% reduction): booking in the specimen, because there is only one container; no need to transfer the core into a pre-numbered biopsy cassette; embedding only one cassette rather than six separate cassettes; cutting sections; and placing all six biopsies on one slide rather than six, which also avoids having to change the slide six times on the microscope. Cost savings (83% reduction) were considerable because fewer specimen containers and slides were used.
Conclusion A simple cassette allows easy identification and processing of site-specific biopsies, making their use easier and facilitating histological processing. These may prove useful clinically and be cost-effective.

P109

High-dose intravenous fosfestrol in hormone-relapsed prostate cancer – does it have a role?

A.M. Davies and J.J.F. Somerville *Royal Halifax Infirmary, Halifax, West Yorks, UK*

Introduction Patients with symptomatic hormone-relapsed prostate cancer are a difficult group to treat effectively. High-dose intravenous fosfestrol (Honvan™, a synthetic oestrogen) is known to give good symptomatic relief in this group. In this study we investigated whether a symptomatic response to Honvan was associated with any survival benefit.
Patients and methods The study included 19 patients; treatment with Honvan was given for symptomatic disease progression, at a variable interval from biochemical relapse. The response was measured by the relief of symptoms and any decrease in PSA level. Patients were divided into responders (with an improvement in symptoms and decrease in PSA) and non-responders (no improvement in symptoms and PSA static or rising). There was no difference in the initial PSA level, grade of tumour or response to initial treatment between the groups.
Results Fifteen patients responded, with a mean (range) reduction in PSA of 43 (16–95)%. The mean length of symptomatic response was 7.25 (2–24) months. The mean survival after Honvan treatment in the responders was 14.6 (3–43) months, and was 5 (2–7) months in the nonresponders ($P = 0.09$, Mann-Whitney *U*-test).
Conclusions High-dose Honvan has a useful role in the management of patients with symptomatic hormone-escaped prostate cancer, and carries minimal morbidity. In the small group studied it would appear to offer responders a survival benefit. On the basis of these early results we are continuing the study in a larger patient group.

P110

Potential of intermittent hormone therapy for patients with M+ and M0 prostate cancer

F. Chinegwundoh, T. Oliver, A. Lee, D. Farrugia and W. Ansell *St Barts and The Royal London School of Medicine, London, UK*

Introduction Increasingly, animal and clinical studies suggest that intermittent therapy may improve the duration of hormone-dependence in patients with prostate cancer. However, there remains uncertainty as to the optimal duration of treatment, the level of PSA before treatment is restarted and whether it is safe to use this strategy in patients with M0 disease. This study compared outcomes in patients with M+ and M0 prostate cancer receiving intermittent hormone therapy.
Patients and methods Any patients who had achieved complete PSA remission after hormone therapy for metastatic or locally advanced prostate cancer were included in the study. Patients restarted

treatment when symptoms developed or if the PSA rose above pretreatment levels.
Results Fifty patients (17 M+ and 33 M0) entered intermittent hormone therapy after achieving a complete PSA remission. Overall, 57% remained off treatment at 12 months and the median time for restarting further hormone therapy was 14 months; 95% of patients re-treated were progression free at 1 year and 92% were alive at 3 years. Sixteen patients completed a second cycle, 12 a third cycle and three have begun a fourth cycle. There was a slower progression to requiring treatment in M0 vs M+ patients (70% vs 37% continuing off hormones at 1 year). Furthermore, in a subset of M0 patients with a short cycle-time off treatment and having radiation consolidation during their second cycle, there was evidence that radiation could prolong time off treatment (four, median off treatment alone, 7.3 months, median after radiotherapy, 20 months off treatment (testis=? $P<0.001$). Despite the small subgroup overall, 53% of M0 patients treated without radiation remained off hormones at 3 years.
Conclusion It is clearly safe to consider patients with M0 prostate cancer to have radiation therapy or consolidation for intermittent hormone therapy studies. Furthermore, there is a suggestion that it may be safe to give radiation only to consolidate the response of the minority having a short duration off therapy in the first cycle. A randomized trial which has recruited 30 patients in the first year has been initiated to investigate this issue and the initial results from the patients treated will be presented.

P111

Does hormone manipulation significantly raise the risk of osteoporosis in men with non-metastatic prostate cancer

J.S. Royle, G. Krishna and R.A. Blades *Royal Preston Hospital, Preston, Lancashire, UK*

Introduction There is evidence that hormone manipulation may cause significant osteoporosis in men with prostate cancer. Previous studies have included men with metastatic prostate cancer, which in itself has an effect on bone turnover and may predispose them to both osteoporotic and pathological fractures. Our study examined only men with non-metastatic disease.
Patients and methods Thirty-nine men with bone scan-negative prostate cancer and a minimum 5-year follow-up were recruited, and who were able to attend for bone densitometry (DEXA scanning). Twenty-nine men had been treated with hormone manipulation. Ten patients on surveillance-only formed the control group, to assess whether prostate cancer alone can affect the skeleton.
Results Only 10% of men in the watchful-waiting group were osteoporotic, whilst >31% of men in the hormone-manipulated group showed significant levels of osteoporosis. When those patients with osteopaenia were included there was even more evidence that hormone manipulation had a significant effect on long-term bone loss in men with non-metastatic prostate cancer.
Conclusions Early results suggest that there are increased rates of osteoporosis in the hormone-manipulated group. Although the outcomes in terms of morbidity and mortality are not fully established yet, this will have implications for men on long-term hormone manipulation. This may become particularly important for patients who are hormone manipulated after biochemical failure of radical treatment, who potentially have a long life expectancy.
Funding: RPH Research Fund

P112

The fate of patients with PSA recurrence after radical prostatectomy for clinically localized carcinoma of the prostate

M. Winkler, M. Sugiano, R. Persad and D.A. Gillatt *Bristol Urological Institute, Southmead Hospital, Bristol, UK*

Introduction Radical prostatectomy is increasingly used to treat clinically confined carcinoma of the prostate in the UK. Little is known about the natural history of clinical progression after PSA recurrence. Thus the aim was to investigate the clinical recurrence pattern in men with PSA recurrence after radical prostatectomy.
Patients and methods Of 320 patients operated on between 1988 and 1999, 85 had a PSA recurrence of >0.2 ng/mL on at least two separate occasions (median age 63 years, median follow-up 60 months). Clinical recurrence was diagnosed by radioisotope bone scan, a DRE with or without a transrectal biopsy, and was treated with pelvic radiotherapy or hormone ablation, as appropriate.
Results The median time to PSA recurrence was 8 months and 88% recurred within 3 years. Of 85 patients with PSA recurrence 38 (44%) recurred either locally or distally with a median time to recurrence of 43 months. The median time to metastasis was 54 months for the 22 patients with distant metastasis, from the date of PSA recurrence. Only four patients died from prostate cancer and another seven died from other causes but with evidence of recurrent disease. The Kaplan–Meier estimated combined local and distant recurrence-free survival from the time of PSA recurrence was 50% at 5 years.
Conclusion Patients with PSA recurrence after radical prostatectomy have a long time to definite clinical recurrence and the use of early adjuvant treatment with its adverse effects does not seem to be justified.
Funding: Southmead Research Foundation

P113

A 5-year follow-up of men with a PSA level of >20 ng/mL or a Gleason score of >7 after radical prostatectomy

O. Niall, G. Beese and W.G. Bowsher *Department of Urology, Royal Gwent Hospital, Newport, Gwent*

Introduction Men with a PSA level of >20 ng/mL and/or a Gleason score of >7 are often excluded from radical prostatectomy because there is a high likelihood that the prostate cancer is not organ-confined. We present a 5-year follow-up of such a group who underwent radical prostatectomy.
Patients and methods From a database of all 160 radical prostatectomies undertaken at one institution between 1993 and 2000, we assessed all men with a preoperative PSA level of >20 ng/mL or a Gleason score of >7 in the prostatectomy specimen.
Results In all, 25 men had a PSA of >20 ng/mL; their mean (range) follow-up was 60 (5–90) months and their mean PSA level was 41.4 (20.2–155) ng/mL. Twelve patients (48%) had an undetectable PSA level and two a PSA of <1.0 ng/mL at 36 months after radiotherapy. Four men had radiotherapy and then hormone treatment (PSA 0.1–3.1 ng/mL), three had hormone treatment alone (PSA 0.1–0.2 ng/mL) and four men with a PSA of 0.6–1.6 ng/mL are being observed. Thirteen men with Gleason 8–10 tumours were followed for a mean of 57 months; their mean PSA level was 31.1 (1–155) ng/mL, but eight had a PSA of <15 ng/mL and five an undetectable PSA level. Seven had PSA progression and one died.
Conclusion A high PSA level does not exclude a potential PSA progression-free survival at 5 years after radical prostatectomy for clinically localised prostate cancer, but a high-grade tumour has a significantly worse prognosis. These results will help to guide the patient towards appropriate treatment.

P114

Quality-of-life comparison of radical prostatectomy and after-loading (brachytherapy and external beam) in the treatment of clinically localized prostate cancer

F. Sommer, S. Wolter, K. Esdevs, H-P Caspers, A. Digon, T. Klotz, P. Derakhshani and U. Englemann *Department of Urology, University of Cologne, Cologne, Germany*

Introduction To date, no studies have directly compared the quality of life and symptoms of patients with localized prostate cancer treated with curative intent by radical prostatectomy (RP) with those treated by brachytherapy combined with EBRT (after-loading).
Patients and methods Men with clinically localized stage T1c to T3 adenocarcinoma of the prostate, treated with curative intent by after-loading between June 1998 and December 2000, received a questionnaire before treatment and were mailed a questionnaire 1, 3 and 6 months afterward. Patients treated with RP underwent the same procedure. The primary outcome measures were the IPSS and EORTC QLQC30 quality-of-life questionnaire; the rate of potency of each man was evaluated by a German questionnaire of erectile dysfunction (KEED).
Results Data from 62 patients were included in the analysis; 29 underwent RP and 33 after-loading. Patients with after-loading had more voiding symptoms immediately after treatment than those undergoing RP. Patients undergoing RP had an improvement in their quality of life, but the after-loading group had no significant change. The RP group had a decline in sexual function but there was no change in sexual function in the after-loading group.
Conclusions Patients undergoing RP reported fewer irritative or obstructive voiding complaints; they had an overall higher quality-of-life improvement than those treated by after-loading. There were no changes in sexual function in the after-loading group whereas the RP group had a decline in sexual function. The study is continuing, with follow-up planned at 12 and 24 months after treatment. The consistency and magnitude of these trends require further study.

P115

The hazards of case selection for nerve-sparing radical prostatectomy

S. Connolly, K. O'Malley, D. Kelly, A. O'Brien*, D. Mulvin and D. Quinlan *Departments of Urology and *Pathology, St Vincent's University Hospital, Dublin, Ireland*

Introduction Nerve-sparing radical prostatectomy (NSRP) is considered a suitable treatment for adenocarcinoma of the prostate confined to one lobe, based on a DRE and TRUS-biopsy findings. We evaluated whether a nerve-sparing dissection can safely be recommended on the 'benign' side, based solely on these staging criteria.
Patients and methods Between 1994 and 1998, 56 patients had prostate cancer diagnosed with TRUS-guided biopsies; all patients had sextant 18 G cores taken from both lobes. The clinical stage on DRE was T1c in 58% and T2a in 42%; the mean (range) patient age was 60 (46–69) years, the initial PSA level 10.5 (1.4–35.9) ng/mL and the Gleason score 5.6 (2–9). All patients subsequently underwent radical retropubic prostatectomy (RRP).
Results The results are tabulated for two subgroups according to the involvement of one or both lobes from diagnostic TRUS biopsies. The final specimen histology data are shown, including the incidence of positive surgical margins (PSMs) overall, and the rate of PSM on the contralateral/benign side.

Subgroup (n)	*One lobe, n (%)*	*Two lobes, n (%)*
Total +ve TRUS (56)	29 (52)	27 (48)
Final histology		
cancer both lobes	22 (76)	N/A
Any PSM	13 (45)	21 (78)
Contralateral PSM	6 (21)	N/A

Conclusions Unilateral prostate cancer involvement in TRUS biopsies is associated with a high incidence of bilateral disease on final histology. Alarmingly, a PSM was identified on the 'benign' side in 21% of cases where NSRP might be advocated. This study highlights the hazards in case selection for NSRP based on DRE and TRUS findings.

P116

Long-term outcomes and morbidity after ^{125}I brachytherapy for prostate cancer: a UK series

G. Hellawell, K. Ho, K. Le Monnier, D. Cole, E. Whipp, G. Fellows and S. Brewster *The Departments of Urology and Oncology, Churchill Hospital, Oxford and the Bristol Oncology Centre, Bristol, UK*

Introduction Brachytherapy for the treatment of localized prostate cancer is enjoying a resurgence of enthusiasm following technical advances pioneered in the 1980s. Proponents of the modern technique argue that long-term disease-free survival is comparable with that of radical surgery, with less mortality and morbidity. We have reviewed the long-term morbidities and outcomes of a series of patients who underwent modern brachytherapy.
Patients and methods The records of 51 men (mean age 67 years) with previously untreated, clinically localized prostate cancer who had ultrasound-guided transperineal ^{125}I-implants at two UK centres between 1984 and 1990 were reviewed. Tumours were graded as Gleason score $\leqslant 4$ in 15 patients, 5–7 in 25 and >7 in four patients. The radiation dose was 129–149 Gy. Follow-up data were obtained by telephone interview with the patients, their family or local doctor.
Results The mean follow-up was 68.4 months; 38 (75%) patients have died, of whom 28 (74%) died from prostate cancer. Of the remaining 13 patients, eight remain disease-free. Persistent tumour or local progression of disease was present in the other five patients, with three developing metastases. The median disease-free survival was 66.1 months. Twenty-four patients reported complications; 11 with long-term urinary incontinence and eight with rectal complications.
Conclusion These early long-term UK results are disappointing, despite generally favourable tumour demographics. They are inferior to reported surgical and EBRT series, and the Seattle brachytherapy data. The series is small, from the pre-PSA era, and has potential technical flaws. However, the study provides justification for caution as brachytherapy becomes more widely practised in Europe and worldwide.
Funding: PPP Healthcare Medical Trust

16.00–17.00
Poster Session 12
Basic Science – Physiology 2

P117

Vanilloid receptor subtype 1 and ATP-gated ion channel P2X3 in human urinary bladder

C.M. Brady. P. Yiangou, P. Facer, A. Ford, O.J. Wiseman, C.J. Fowler and P. Anand *Imperial College School of Medicine, Peripheral Neuropathy Unit, Hammersmith Hospital, London, UK*

Objectives To determine the presence, distribution and molecular forms of the vanilloid receptor VR1 for the first time, and confirm the presence and distribution of the ATP-gated ion channel P2X3, in the human urinary bladder.
Materials and methods Normal urinary bladder tissues were obtained at postmortem from four subjects. Eight urinary bladder biopsies were also taken from some patients with detrusor hyper-reflexia treated with intravesical resiniferatoxin (RTX). The specimens were assessed using affinity-purified specific antibodies to VR1 and P2X3 by Western blotting and immunocytochemistry, and compared with immunostaining using antibodies to the pan-neuronal marker PGP 9.5 and Schwann cell marker S-100.
Results VR1- and P2X3-immunoreactive fine nerve fibres were scattered throughout the suburothelium of the normal bladder and cystoscopic biopsies, and traversed the muscle layer. They had a similar distribution to PGP 9.5-immunoreactive fibres, but there were fewer, suggesting localization in subsets of axons. Western blot studies showed an expected 100-kDa VR1 protein, and a P2X3-immunoreactive 66-kDa protein.
Conclusion VR1 and P2X3 are present in the human urinary bladder and may contribute to distinct pathophysiological states of bladder overactivity, in accord with their differential expression in sensory neurones. Intravesical vanilloids act via the VR1 receptor and are effective in the treatment of detrusor hyper-reflexia. P2X3 may represent a selective therapeutic target for other causes of overactive bladder.
Funding: Napp Laboratories, UK.

P118

Decreased urinary bladder apoptosis in a rabbit model of diabetes mellitus

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Introduction Urinary bladder dysfunction is a recognized complication of diabetes mellitus (DM). This is thought to be partly related to altered bladder morphology, as there is evidence that DM is associated with increased bladder weight. In DM, increased cellular proliferation is well established and is thought to account for this. However, there is evidence to support the view that in other pathological states affecting the urinary tract, altered apoptosis (programmed cell death) may also play a role. We investigated, in a rabbit model of DM, whether there are any changes in bladder apoptosis.
Materials and methods Diabetes was induced in six adult New Zealand White rabbits with alloxan (65 mg/kg); six age-matched controls were used for comparison. After 6 months, following cervical dislocation, the urinary bladders were excised, weighed and subsequently stored at − 70°C until used. The TdT-mediated dUTP nick-end labelling (TUNEL) technique was used to detect and quantify apoptosis in both DM and age-matched control urinary bladder detrusor and neck sections. This involved labelling DNA strand breaks and analysing them by fluorescence microscopy.
Results Diabetes was confirmed as this group had significantly ($P < 0.001$) elevated mean (SD) serum glucose levels of 26.3 (1.41) mmol/L, compared with the controls at 7.5 (0.39) mmol/L. The urinary bladder weights were also significantly ($P < 0.001$) greater in the DM rabbits than in the controls, at 4.2 (0.3) and 2.1 (0.2) g, respectively. Apoptosis was significantly less in the urothelial cells of both the diabetic detrusor and bladder neck ($P < 0.001$ for both) than in the controls.
Conclusions Our results confirm previous findings that DM is associated with increased bladder weight. Although this is associated with increased cellular proliferation, we have shown that decreased apoptosis may be important. Therefore, in DM, decreased apoptosis may play an important role in the pathophysiology of diabetic cystopathy.
Funding: Charles Wolfson Charitable Trust.

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Nitric oxide synthases expression in the rat urogenital system

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Introduction Nitric oxide (NO) is a neurotransmitter in the lower urinary tract, and in many other tissues. NO is synthesized from L-arginine by NO synthases (NOS). Nerve profiles displaying NOS immunoreactivity have been described in the human, pig and sheep ureter. NOS nerves are distributed to the smooth muscles, around arteries and in subepithelial layers. Three isoforms of NOS have been identified, but the role of the respective isoforms in the urogenital system is not well understood. The purpose of this study was to determine the distribution of the neuronal NOS (NOS1) and endothelial NOS (NOS3) isoforms in the rat urogenital system.
Materials and methods Immunohistochemical studies were undertaken on paraffin-embedded sections of bladder, urethra, ureter and genital organs, using specific antibodies against NOS1 and NOS3.
Results NOS1-positive nerve fibres and cells were detected in the smooth muscle layer of the bladder, ureter and urethra. NOS1-immunoreactivity was also found in the submucosa. Cell bodies in the pelvic ganglia around the genitalia were strongly positive. The epithelial lining of the prostate, especially the lateral lobes, were also NOS1-positive. NOS3 immunoreactivity was present in the endothelial cells of the vessels of the urogenital system. An unexpected finding was the presence of NOS3-immunoreactivity in the striated sphincter muscle of the urethra in both sexes.
Conclusion NOS1 is most abundant in the ganglia and nerve fibres in the smooth muscle layers and submucosa of the urogenital organ, whereas NOS3 is present in the urethral sphincter and the blood vessels. Our results are compatible with an important role for NO in the relaxation of the urethral sphincter and smooth muscles of the rat urogenital system.
Funding: John L. Emmett Foundation

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Ultrastructural evidence of voiding dysfunction in the diabetic bladder

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Introduction Up to 83% of diabetic patients develop lower urinary tract dysfunction. Ultrastructural changes in the bladder have been shown to correlate with the voiding dysfunction patterns. Our aim was to study the structural changes occurring in the diabetic bladder associated with voiding dysfunction.
Materials and methods For this study, *in vivo* cystometry under anaesthesia was undertaken in rats with diabetes mellitus (DM) at various stages of disease (8, 10, 20 weeks of age). The rats were then killed, the bladder harvested and weighed, the bladder samples fixed in 10% formalin or in 2.5% glutaraldehyde, and sectioned and stained with haematoxylin and eosin. Ultrathin sections were cut, stained with the standard uranyl nitrate/lead citrate sequence, and examined and photographed in a transmission electron microscope.
Results Sample specimens were obtained from eight DM rats and four age-matched controls. There were significant increases in bladder capacity, compliance and wet-weight (all $P<0.001$) of the bladders of DM rats. Light microscopy showed: (a) increased interstitial oedema; (b) separation of detrusor smooth muscle cells (DSMC); (c) increased collagen deposits; and (d) hypertrophy of DSMC. Electron microscopy showed: (a) a patchy dense band pattern; (b) scattered and disorganized distribution of collagen bundles; (c) caveolar disintegration; (d) changes in mitochondria with decreased cristae and loss of internal structure; (e) separation of contact plates.
Conclusions There are distinct gross and ultrastructural changes in the bladder of this transgenic rat model of DM which are associated with *in vivo* voiding dysfunction. Confirmation of these findings in the bladder of human patients with DM is needed.
Funding: NIH NIDDK Grant

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Impaired nitric oxide-mediated cavernosal relaxation and upregulation of cavernosal nitric oxide synthase in a model of partial BOO

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Introduction Several studies have reported an increased risk of erectile dysfunction (ED) in men with a high symptom score of BPH, but thus far there has been little physiological evidence to support this. Alterations in cavernosal nitric oxide (NO) signalling have been documented in animal models of conditions which predispose to ED, such as diabetes. We have investigated whether such changes exist in the rabbit model of partial BOO.
Materials and methods Partial BOO was surgically produced in six adult male New Zealand White rabbits. Six weeks later, after cervical dislocation, cavernosal smooth muscle (CSM) strips were mounted in organ baths and pre-contracted with phenylephrine (100 μmol/L) in the presence of atropine (1 μmol/L), guanethidine (5 μmol/L) and indomethacin (10 μmol/L). Sodium nitroprusside (SNP, a NO-donor) was added in increasing concentrations, a concentration-relaxation curve was produced and the IC_{50} calculated. Autoradiography was also undertaken using [^{3}H]-NG-nitro-L-arginine to assess NO-synthase expression (quantified by densitometry). Samples were stained using NADPH-diaphorase as a measure of NO-synthase function. These experiments were repeated on sham-operated controls for comparison.
Results The mean IC_{50} for SNP-induced CSM relaxation was significantly higher in rabbits with partial BOO (4.7 μmol/L) than in controls (1.8 μmol/L; $P=0.02$). Autoradiography after 3 months indicated NO synthase expression was significantly greater in the CSM of rabbits with partial BOO ($P<0.001$). This was supported by increased diaphorase staining in CSM from the obstructed animals.
Conclusions Rabbits with partially obstructed bladders have impaired mechanisms mediating erectile function. This provides further evidence linking BPH and ED, and may provide some insight into the mechanisms involved.

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Cyclo-oxygenase inhibition and the bladder neck – a pharmacological target for the treatment of bladder outlet symptoms?

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Introduction The role of the nervous system in the regulation of ureteric modulation is poorly understood and there has been little work on human tissue. The passage of renal calculi is aided by ureteric contraction but ureteric spasm is a painful symptom in renal colic. Pharmacological therapy may yet prove a useful adjunct in the treatment of renal calculi disease. We undertook physiological studies on human ureter sampled at nephrectomy. Our aim was to determine whether a contractile response induced by electrical field stimulation (EFS) could be affected by cyclo-oxygenase (COX) inhibition.
Materials and methods Over a 10-month period the ureter was sampled from 18 patients undergoing nephrectomy or urinary diversion. A standard organ-bath superfusion apparatus was used to measure the physiological response of the ureter. In the normal state the samples were superfused with pre-oxygenated, physiological Krebs' solution at 37°C (pH 7.3–7.4). The response to EFS was obtained before and after a 30 min application of COX inhibition with sodium diclofenac (10 μmol/L).
Results Surgical samples from 18 patients allowed physiological measurements on 72 strips; 57 strips (79%) showed spontaneous activity. Contraction was stimulated using single-pulse stimulation of 3 ms duration (50 V) and frequencies of 1, 2, 4, 8, 16, 32 and 64 Hz. After a 30 min exposure of the samples to 10 μmol/L sodium diclofenac the response was significantly decreased at frequencies of 16, 32 and 64 Hz ($P<0.05$). The calculated frequency for the half-maximum response was significantly different before and after COX inhibition ($P<0.05$).
Conclusions We showed that the contractile response of ureteric smooth muscle induced by EFS can be altered by COX inhibition. This may have therapeutic implications in modifying ureteric activity to aid the passage of ureteric calculi.

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The role of M2 and M3 muscarinic receptors in the intracellular calcium responses of cultured human detrusor smooth muscle

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Introduction Newer agents for treating detrusor instability are more selective for the M3 muscarinic receptor, but they are no more effective than less selective agents. Human urinary bladder has an M2 : M3 muscarinic receptor ratio of $\approx 3:1$. Human detrusor smooth muscle (HDSM) contraction is caused by M3 receptor stimulation and is mediated via inositol phospholipid hydrolysis.

Materials and methods Explant cultures of HDSM were established and experiments undertaken on confluent monolayers. Intracellular calcium responses were measured using Fura-2 (a calcium-sensitive dye).
Results The calcium response was antagonized by atropine, with a mean (SD) pA2 of 8.5 (0.13). The M3 antagonist 4-DAMP showed a reduced effect on the inhibition of calcium responses to muscarinic stimulation, with a pA2 of 7.4 (0.1). The M2 antagonist methoctramine showed no significant effect, the pA2 being 6.2 (0.1). The effect of 4-DAMP was augmented by pre-treatment with pertussis toxin (100 ng/mL for 18 h), with a pA2 of 8.1 (0.1). In nominally calcium-free conditions (0.1 mmol/L EGTA) the effect of 4-DAMP was again augmented.
Conclusion These data suggest that M3-mediated intracellular calcium release may not be the sole mechanism of detrusor smooth muscle contraction. These alternative mechanisms are being elucidated further. These different routes of contraction may act as an alternative site for the pharmacological treatment of unstable bladder contractions.

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The tissue basis of atropine resistance in unstable human detrusor

D. Skennerton, R. Harvey, M. Bayliss, C.H. Fry *Institute of Urology and Nephrology, London, UK*

Introduction Detrusor from patients with stable bladders is solely activated by the neurotransmitter acetylcholine. However, in tissue from patients with urodynamically confirmed idiopathic instability an atropine-resistant component of the contraction is present, mediated by a second transmitter, ATP. Why ATP exerts an action in these bladders is unknown. We examined the hypothesis that reduced degradation of ATP in the post-ganglionic parasympathetic synapse can explain this phenomenon.
Materials and methods Samples were obtained with consent and ethical approval from patients with stable and idiopathically unstable bladders. Isometric tension was measured *in vitro* from superfused strips (< 1 mm diameter). Samples were exposed to ATP and α,β methylene ATP (ABMA) in non-cumulative doses from 0.01 μmol/L to 10 mmol/L. The EC_{50} values were then expressed as pEC_{50} ($= -\log EC_{50}$). Extracellular ATPase activity (ARL67156-sensitive) was measured in frozen samples from the initial rate of ATP hydrolysis, using a luciferin-luciferase assay.
Results ATP was significantly more potent in strips from unstable than from stable bladders, with mean (SD) pEC_{50} values of 3.89 (1.06) ($n=23$) and 3.03 (1.01) ($n=19$, $P=0.01$), respectively. The un-hydrolysable ATP analogue ABMA was significantly more potent, with a pEC_{50} of 5.56 (0.11) ($n=6$, $P<0.01$). Extracellular ATPase activity was significantly less in samples from unstable bladders, at 0.15 (0.06) vs 0.42 (0.11) nmol/min/mg (using 2 mmol/L ATP substrate, $n=6$).
Conclusion ATP is less potent than ABMA in generating contractions in human detrusor, implying that the muscle samples hydrolyse some ATP, thus reducing the effective concentration. However, the potency is significantly less in samples from stable than from unstable bladders, indicating that the rate of ATP hydrolysis is reduced in the samples from unstable bladders. This was corroborated by measurements of extracellular ATPase activity using an enzymatic assay. We propose that such reduced ATPase activity accounts for atropine-resistant contractions in the unstable bladder.
Funding: Royal College of Surgeons

P125

Comparison of the intracellular Ca^{2+} responses to agonists in freshly isolated and cultured human detrusor myocytes

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Introduction Bladder reconstruction has recognized complications. It would be desirable, using human detrusor myocyte cultures, to create a tissue model (to test interventions) and an autologous implant to reduce the complications of surgery. We are currently characterising cultured cells and comparing them with fully differentiated detrusor cells by measuring responses to agonists and mechanisms mediating contraction.
Materials and methods Cells were isolated from human cystectomy samples using collagenase digestion. A fraction was loaded with Fura-2, to measure intracellular calcium [Ca^{2+}]i at 37°C. Remaining cells were cultured in a D-valine-based medium [*J Urol* 2001; in press] until confluent. Cultures were trypsinized and cells loaded with Fura-2, as above.
Results Freshly isolated cells responded to several agonists by generating transient increases in [Ca^{2+}]i. Carbachol and ATP showed dose-dependent effects (EC_{50} 3.3 μmol/L, SD 0.70; $n=6$; and 0.3 μmol/L, SD 0.28, $n=22$, respectively). Ca transients comparable with the EC_{50} concentrations of agonists were generated by 10 mmol/L caffeine and 80 mmol/L KCl. Cultured cells gave carbachol responses of similar magnitude (EC_{50} 3.1 μmol/L, SD 0.9, $n=6$) to fresh cells. Responses to ATP were similar in form but significantly different in sensitivity (EC_{50} 1.5 μmol/L, SD 1.1, $n=5$, $P<0.05$). The responses to 10 mmol/L caffeine and 80 mmol/L KCl were attenuated compared with the agonist-induced responses.
Conclusion These data show that cultured human detrusor myocytes are as sensitive to muscarinic agonists as are freshly isolated cells. They were less sensitive to a purinergic agonist. Responses to KCl and caffeine suggest that the Ca-handling properties of intracellular stores and the Ca-induced Ca-release mechanism are altered.
BUF /Blackwell Science Ltd, St Peter's

P126

PUV in an animal model – electromechanical properties of detrusor smooth muscle

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Introduction: PUV leads to prenatal infravesical obstruction that causes developmental abnormalities to the upper and lower urinary tracts. This study examined the fetal pathophysiology of this condition, with reference to the electromechanical properties of the bladder.
Materials and methods A fetal lamb model with induced partial infravesical obstruction was used. In three fetuses BOO was induced in mid-gestation (78–80 days) and detrusor smooth muscle function examined *in vitro* 4 weeks later. Four sham-operated fetuses underwent a similar procedure. Smooth muscle function was characterized by: (i) constructing nerve-mediated (sensitive to 1 μmol/L tetrodotoxin) force-frequency relationships in the presence and absence of atropine (1 μmol/L) or α,β-methylene-ATP (ABMA, 10 μmol/L); and (ii) contractures elicited by KCl (120 mmol/L) and carbachol (10 μmol/L).

Results Nerve-mediated atropine-resistant contractions were absent in either group. The absolute force (mN/mg) developed by obstructed bladder strips was significantly ($P < 0.05$) less than that from sham-operated fetuses. This was the case when electrical stimulation (0.65, SD 0.18 vs 2.98, 11.66), KCl (0.60, 0.21 vs 2.39, 0.66), carbachol (2.91, l.03 vs 8.28, 0.54) or ABMA (0.63 vs 2.94, 2.15) were used. The ratio of tension generated by carbachol and electrical stimulation was significantly ($P < 0.05$) greater in strips from obstructed fetuses (2.3, 0.40 vs 1.3, 0.19). There was no difference in ratio of the tension produced by carbachol and KCl (5.5, 3.2 vs 3.6, 0.8; obstructed vs sham).

Conclusion In the obstructed fetus, detrusor smooth muscle contractility is significantly impaired. The greater proportional decrease of nerve-mediated contractions suggests that there is a relative denervation of the tissue. These findings are similar to those from experiments with obstructed human bladder. This model may therefore used to assess the consequences of PUV in boys.

Thursday 28 June
10.00–11.00
Paediatric Urology

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Long-term sexual function in intersex conditions with ambiguous genitalia

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Introduction The current management for intersex conditions includes clitoral reduction surgery for those patients with ambiguous genitalia who are being raised as female. Evaluation of this management is difficult because there are few long-term studies assessing sexual function and other outcomes.
Patients and methods The study included a questionnaire and a retrospective hospital-note review. The questionnaire comprised details on diagnosis and treatment, with a modified sexual function inventory (GRISS) which provided scores encompassing seven areas of female sexual function. All hospital notes were collected and analysed for diagnosis and surgical detail. All respondents were invited for a clinical examination.
Results Thirty-seven intersex women (>18 years old), all with ambiguous genitalia at birth or in childhood, completed the questionnaire; 11 were patients and 26 were recruited through the UK Androgen Insensitivity Syndrome Support Group. Of the 37 patients 16 (43%) attended for a clinical examination; 10 (29%) had had clitoral surgery deferred and so had currently not undergone this surgery, of which one had never been sexually active. Of the 27 (73%) who had undergone clitoral surgery, nine (33%) had never been sexually active, leaving sexual function data on 18 patients who had undergone clitoral surgery and nine who have virilized female genitalia and had not undergone clitoral surgery. The mean overall sexual function scores were worse in the group with clitoral surgery. On assessing orgasm scores alone, the group with clitoral surgery had significantly abnormal scores for difficulty with orgasm, with five of 18 having complete anorgasmia.
Conclusions Clitoral surgery can damage adult sexual function.

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Is there any correlation between sacral ratio and adolescent enuresis? – a preliminary report

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Objective To correlate persistent enuresis with the sacral ratio (SR) and to determine sacrococcygeal development, as this may result in cessation of primary nocturnal enuresis in adolescence. The results were compared between the sexes and with an aged-matched control group.
Patients and methods One hundred patients with a history of persistent nocturnal enuresis (PNE, mean age 15.3 years, range 12–18) were assessed using urinary tract ultrasonography, urine analysis, urine culture and lumbosacral X-ray. The results were compared with 100 age-matched healthy children. Lumbosacral abnormalities, e.g. spina bifida occulta (SBO), and the SR (normal >0.74) were analysed in both groups. A lumbosacral X-ray (anteroposterior and lateral views) were taken in all children with a history of PNE. The urological and neurological investigations showed any structural organic abnormalities in the genitourinary tract and nervous system.
Results SBO was identified in 73% and a reduced SR in 81%. There was a significant correlation between SBO and a reduced SR, between SBO and uroflowmetry patterns, and between a reduced SR and the uroflowmetry pattern.
Conclusions This preliminary study showed that lumbosacral abnormalities (SBO, low SR) correlate closely with PNE. We recommend an evaluation of all children with PNE, and in whom previous treatment has failed, by urinary tract ultrasonography, uroflowmetry, and anteroposterior and lateral plain lumbosacral X-rays, before undertaking more invasive investigations. To our knowledge this is the first report of these associations and requires further investigation.

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Effect of short-chain fatty acids on urothelial cell kinetics *in vitro* and *in vivo*: implication for treatment in enterocystoplasty

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Introduction The inflammatory changes seen in enterocystoplasty may be similar to diversion colitis and likewise may be treated by instillations of a cocktail of short-chain fatty acids (SCFAs) containing butyrate (40 mmol/L), propionate (30 mmol/L) and acetate (60 mmol/L). Intravesical SCFAs would affect the urothelium and we therefore assessed their effect on urothelium in culture, and in rats.
Materials and methods Primary urothelial cells cultured from normal biopsy specimens and urothelial (RT112, MGH-U1) and colon (CaCo-2, HT29) cancer cell lines were incubated with butyrate (0.08–160 mmol/L), propionate (0.46–240 mmol/L) and acetate (0.46–240 mmol/L) separately and as a cocktail. Cell proliferation was measured using the tetrazolium (MTT) assay. Flow cytometry of propidium iodide-stained cells was used to investigate the effect on the cell cycle. The intravesical tolerance of SCFAs was assessed using 14 adult female rats; SCFAs were instilled for 1 h and the bladders harvested at 6 h, 1, 3, 5, 7 and 14 days.
Results SCFAs inhibited cell proliferation; in primary urothelial cells, the concentration required to inhibit cell growth by 50% of the control (IC_{50}) after incubation for 1 h was 20 mmol/L butyrate, 120 mmol/L propionate and 240 mmol/L acetate. The effects were similar in the cancer cell lines. Flow cytometry showed arrest in G1 and an increase in the sub-G1 (apoptotic) population. Intravesical SCFAs were tolerated well and all harvested bladders were assessed as histologically normal.
Conclusion SCFAs inhibit the growth of primary and transformed urothelial cells in a time- and dose-dependent manner. Butyrate was the most potent SCFA when compared with the concentrations used in the cocktail. Cell-cycle analysis suggests that growth inhibition is caused by G1 arrest and the induction of apoptosis. SCFAs induced no histological changes in the intact rat urothelium. Although reassuring, further *in vivo* assessment is required before clinical application is considered.
Funding: RCS

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Double 'VQ' technique for simultaneous Malone antegrade enema and Mitrofanoff stoma reconstruction

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Objective To determine the short-term results and complications of stoma reconstruction in a simultaneous Malone antegrade continent enema (MACE) and Mitrofanoff principle, and report a double 'VQ' technique for preventing complications at the stoma level.
Patients and methods Between September 1999 and June 2000, 15 patients (mean age 6.5 years, range 4–14, nine boys and six girls) underwent Mitrofanoff procedures in conjunction with a MACE procedure and augmentation cystoplasty. Thirteen patients had neuropathic bladders, and two had bladder and bowel dysfunction with no detectable neurological abnormalities. Ten patients had an antireflux Mitrofanoff channel constructed using the distal part of the appendix with its divided mesentery. The proximal half of the appendix was preserved as a modified MACE procedure. Five children had a Mitrofanoff, using the appendix and caecal flap reconstruction for the MACE. The mean (range) length of appendix used was 10.3 (9–15) cm; there was no correlation between the length of appendix and age of the child. Each stoma was constructed with two different skin flaps. The two channels were initially anastomosed with two separate triangular posterior 'V'-shaped skin flaps, on the right lower abdominal wall. Both mucosae were completely buried with a single or double quadrilateral skin flap (VQ technique).
Results All patients are continent day and night and are out of diapers. The mean (range) follow-up was 6.5 (6–17) months. A parastomal hernia formed in one patient. All 30 stomas are functioning with no evidence of stenosis.
Conclusion The divided appendix with two separate pedicles is an ideal channel for simultaneous Mitrofanoff and MACE procedures when the appendix is >9 cm long with a suitable branching mesentery. Whenever the appendix is short we prefer to use it as the Mitrofanoff channel and create a pedicled tube flap from the caecum for the MACE procedure. Most of the minor complications are preventable by meticulous technique. The double 'VQ' stomas have the lowest incidence of complications and produce the most satisfactory cosmetic appearance.

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Enterocystoplasty and growth failure: a critical re-appraisal

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Introduction The assumption that enterocystoplasty in children has a detrimental effect on skeletal growth has almost exclusively been based upon a chance finding in a retrospective study 10 years ago. We re-evaluated the same research question in a larger cohort and with a longer follow-up.
Patients and methods Between 1982 and 1997, 242 children and adolescents underwent enterocystoplasty. Patients with conditions involving organ systems apart from the urinary tract, and those with myelomeningocele, malignant diseases, reduced GFR and incomplete notes, were excluded. In the definitive study cohort (123; mean age at operation 8.6 years; mean age at investigation 16.8 years) enterocystoplasty had been undertaken using colon in 70, ileum in 37, a combination of both in 11, ileocaecal segments in three and stomach in two patients.
Results In all, 1215 height and weight measurements had been recorded. The distribution of percentile positions before and after enterocystoplasty showed a normal configuration with 83% and 80% of patients growing within two standard deviations from the 50th percentile. After surgery, 85% either remained on the same or reached a higher centile. Nineteen patients (15.5%) showed a decrease in position, with a similar tendency in the weight centile. A clinically relevant growth disorder was recognized in four patients with a complete endocrinological evaluation; in none of these was enterocystoplasty thought to be an aetiological factor.
Conclusions It is very unlikely that the loss of the preoperative percentile position on the growth curve in 15% of children after enterocystoplasty is a consequence of that particular surgery. It is rather an unspecific phenomenon that has to be considered in any clinical population of the same size and age distribution after the same length of time.
Funding: DFG

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Laparoscopic varicocelectomy in adolescence is safe after ipsilateral inguinal surgery

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Introduction Retroperitoneal ligation of the testicular artery along with the internal spermatic veins has been reported to be a safe and effective method of treating adolescent varicocele. Potentially, a secondary blood supply to the testicles (cremasteric and/or vas artery) may become compromised from previous ipsilateral inguinal surgery (hernia, orchidopexy or hydrocele repair). We evaluated the outcome of laparoscopic varicocelectomy in children after previous ipsilateral inguinal surgery.
Patients and methods Over a 9-year period (1991–2000), 27 patients had laparoscopic varicocele repair, where both the spermatic artery and vein were clipped high above the internal ring; 13 of these patients had undergone previous ipsilateral surgery. These included five inguinal hernia repairs, two orchidopexies, three hydrocele repairs and three previous varicocele repairs. All patients were followed up clinically at 3 months and 1 year after surgery.
Results No patient developed ipsilateral testicular atrophy; moreover, the testis size remained stable or was associated with compensatory growth in all patients. One patient developed fever after surgery, with no signs of wound infection, but otherwise no complications related to laparoscopy occurred. To date, one patient has reported recurrence of varicocele and two developed reactive hydrocele, one of which resolved spontaneously.
Conclusion Retroperitoneal high ligation of the internal spermatic vein and artery does not appear to compromise the collateral blood circulation to the affected testis, after previous inguinal surgery involving the ipsilateral testicle.

10.30–11.30
Poster Session 13
Renal Cancer

P127

Nephron-sparing surgery: referral pattern, selection of patients and outcome in a specialized renal cancer clinic

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Introduction In 1998 a specialist renal cancer clinic was established in our regional cancer centre. The aim of the present study was to review the experience of nephron-sparing surgery (NSS) in this unit.
Patients and methods In a 27-month period, 45 patients (aged 29–72 years) were referred for possible NSS. Patients were re-staged with 3 mm slice helical CT with multiplanar reconstruction and selective renal angiography The indications and number of patients undergoing NSS were:

Indication	*No. patients: total*	*undergoing surgery*
Chronic renal impairment	18	4
Bilateral tumours	4	0
Solitary kidney	8	5
Tumour <3 cm	3	1
Von Hippel Lindau	5	3
Cystic/indeterminate lesions	8	8

Results Repeat imaging up-staged 15 patients, including three of four with bilateral tumours; 17 underwent attempted partial nephrectomy and 13 were successful. Four required radical nephrectomy because of the operative findings. There were 1–6 tumours. Two of five patients with a solitary kidney required temporary dialysis after surgery. There was one persistent urinary leak, treated by ureteric stenting. One postoperative haemorrhage was treated by radiological embolization. Negative frozen-section margins were all confirmed with definitive pathology.
Conclusions The establishment of our specialist clinic has led to many patients being referred by colleagues for consideration of NSS. The results highlight the necessity of careful preoperative evaluation, but NSS is a safe and reproducible technique in a specialized unit.

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Nephron-sparing surgery for renal cell cancer

C. Hagan, T.H. Lynch and P.F. Keane *Department of Urology, Belfast City Hospital, Belfast, N. Ireland*

Introduction Nephron-sparing surgery (NSS) has an established role in the management of RCC occurring bilaterally or in a solitary kidney. Some authors recommend NSS for small RCC in the presence of a normal contralateral kidney. We assessed retrospectively the outcome after NSS for RCC, in our institution.
Patients and methods Between 1990 and 2000, 24 patients with RCC underwent NSS. The median (range) follow-up was 51 (4–118) months; 10 (42%) were incidental tumours. Six patients (25%) had tumour in a solitary kidney, six (25%) bilateral synchronous tumours, four (17%) Von Hippel-Lindau, four (17%) compromised function in the contralateral kidney and four (17%) a functionally normal contralateral kidney. Twelve (50%) patients underwent wedge excision, 10 (42%) partial nephrectomy and two (8%) required bench surgery with autotransplantation. All patients were reviewed with 6-monthly CT or ultrasonography.
Results Twenty patients are alive, with one cancer-related death caused by metastases. The disease-specific survival at 4 years was 94%. There have been no local recurrences. Twenty-one tumours were T1, of which 19 (86%) were <4 cm in diameter; three tumours were stage pT3a. All tumours were clear-cell nonpapillary RCC. One patient is dialysis dependent; four patients had post-operative urine leaks, three of which resolved spontaneously and one required re-exploration.
Conclusion Cancer-specific survival rates after NSS for small renal tumours are similar to those after radical nephrectomy. There is a low complication rate and the risk of local recurrence of clear cell tumours is small.

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Cytoreductive nephrectomy in the presence of metastatic disease: is this a realistic option in renal cancer patients?

E. Bromwich, D. Hendry, G. Jones, P. Vasey and M. Aitchison
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Introduction Two recent multicentre trials [*Eur Urol* 2000; 37 (suppl 2): 55 and *Proc ASCO* 2000, Abstract 3] reported a survival advantage for patients with metastatic renal cancer who undergo nephrectomy followed by treatment with β-interferon, compared with those treated with β-interferon alone. In 1998 a specialized referral clinic was established in a regional cancer unit for patients with renal cancer. Those with M+ disease were considered for nephrectomy. Our experience with these patients is reviewed.
Patients and methods Of a total of 232 patients referred to the clinic, 154 with M0 disease underwent nephrectomy with curative intent; 67 (mean age 64 years, range 38–80) with known metastases were considered for cytoreductive nephrectomy. Nephrectomy was undertaken if the primary tumour was considered operable and the patient's performance status was 0–1.
Results In all, 17 patients (mean age 54 years, range 38–61) fulfilled the criteria for referral and 16 underwent surgery. Cytoreductive nephrectomy was not possible in 75% of patients with M+ disease because of their performance status and/or operability at presentation.
Conclusion Younger patients are more likely to be suitable for nephrectomy. Cytoreductive nephrectomy was feasible in 7% of the patients in our renal cancer clinic and is therefore unlikely to have a major effect on survival for this disease.

P130

Comparison of laparoscopic and open radical nephrectomy for RCC

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Introduction Laparoscopic nephrectomy for benign and malignant disease is a developing field. We report on our single-centre

experience of treatment of RCC by open and minimally invasive methods.
Patients and methods We retrospectively examined the case histories of patients who underwent a radical nephrectomy procedure between 1 January 1998 and 31 December 2000; patients who had caval or metastatic disease were excluded. Nineteen patients had open radical nephrectomies, whereas seven had their tumours removed laparoscopically. We examined their blood loss, operating time, and the number of inpatient days before discharge.
Results The mean (range) age of the patients who had an open procedure was 60.4 (31–79) years and was 48.7 (27–65) for those treated laparoscopically. The maximum diameter of specimens removed was similar, with a mean (range) of 12.6 (8–25.5) and 12.7 (10.5–17.5) cm for the open and laparoscopic groups, respectively; likewise, the mean weight was 551 (162–2351) and 511 (275–860) g, respectively. However, the two groups had a different length of stay in hospital; the median (range) stay for the laparoscopy group was 5 (3–12) days and in the open group was 10 (5–16) days. The number of postoperative inpatient days was significantly different between the procedures ($P < 0.0035$, Mann–Whitney *U*-test).
Conclusion This study shows that radical nephrectomy is superior to open surgery with respect to blood loss and early mobilization. In the past, the extraction of the whole kidney has been difficult, but we advocate the use of a small muscle-splitting incision in the iliac fossa to retrieve the intact specimen for histopathology. Laparoscopic radical nephrectomy is a less-invasive alternative to open surgery for patients with localized RCC. Similar sized tumours may be retrieved. Patients mobilize faster, require less analgesia and may be discharged earlier if they undergo a laparoscopic procedure.

P131

Is a bypass necessary in patients undergoing nephrectomy for RCC extending into the inferior vena cava?

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Introduction In RCC there is involvement of the inferior vena cava (IVC) in 5% of cases and this finding is more common in right-sided tumours. It is usual practice to remove such tumours if the patient is fit enough and has no high-volume metastatic disease. Some have advocated a cardiac or venous bypass for such operations. We have prospectively examined techniques for local vascular control in such patients.
Patients and methods Between 1992 and 2000, 19 patients (14 men and five women, age range 45–84 years) with RCC within the IVC underwent radical nephrectomy; the tumour was right-sided in 17. All patients underwent CT and Doppler ultrasonography before surgery; some also had MRI and trans-oesophageal Doppler scans. The IVC extension was sub-hepatic in nine, intra-hepatic in six and intra-cardiac in four. Two patients had extension into the right ventricle and hence underwent cardiac bypass; the other procedures were carried out through a thoraco-abdominal approach with no bypass. 'Snuggers' were used to control the distal IVC, contralateral renal vein and proximal IVC. A Foley catheter was passed above the thrombus through a cavotomy, the balloon inflated and the thrombus removed.
Results The IVC extension was removed in all cases, with no deaths during surgery. In one case an undiagnosed hepatic vein extension embolized to the pulmonary artery 8 h after surgery and had to be removed on bypass. Four patients have died with metastatic disease.
Conclusion Cardiac bypass is advisable to remove RCC extensions into the hepatic veins, right ventricle and larger masses in the right atrium. However, most patients can be managed safely by local vascular control and the use of a Foley catheter and balloon to prevent embolization.

P132

Management of RCC with tumour thrombus involving the inferior vena cava: a study in one UK institution

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Introduction Tumour thrombus involving the inferior vena cava (IVC) affects 4–10% of patients with RCC. Surgery to excise these tumours with suprahepatic caval involvement usually involves cardiac bypass and hypothermic cardioplegia. We present a retrospective analysis of 32 consecutive patients who underwent radical nephrectomy and IVC tumour thrombectomy. The objective was to determine the need for cardiac bypass, the postoperative morbidity, mortality and patient survival in this group of patients.
Patients and methods Between May 1993 and May 2000, 32 patients (mean age 62.5 years) underwent radical nephrectomy and vena caval tumour thrombectomy; 25 (78%) had tumour thrombus extending above the hepatic veins. Of these, 14 (56%) had tumour thrombus extending above the diaphragm. Ten of these 14 patients underwent cardiac bypass with hypothermic circulatory arrest to aid in removing the tumour. Ten patients had metastatic disease at the time of presentation (nine in the lung and one adrenal).
Results There was one death each in the cardiac bypass and no-bypass groups. The overall survival was 20.3 months; six patients in the bypass group died from disease progression (mean survival 13.5 months) whilst four are still alive (at 24, 6, 4 and 3 months, respectively). Of the nine patients with metastatic lung disease at presentation (mean survival 18.2 months), three are still alive at 35, 24 and 18 months, respectively.
Conclusions In patients with caval tumour thrombus, cardiac bypass is necessary only with intracardiac extension. Patients with metastatic lung disease and caval tumour thrombus should not be denied surgery, as long-term survival is possible.

P133

Outcome and survival with *in-situ* RCC

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Introduction About a third of patients presenting with RCC have locally advanced or metastatic disease. Anecdotally, some have a longer than expected survival with the primary tumour left *in situ*, when management is limited to symptomatic and palliative measures which include embolization of the tumour, radiotherapy to metastases or systemic immunological therapy. A group of patients with *in situ* RCC was identified retrospectively and their management, outcome and survival assessed.
Patients and methods All patients diagnosed with RCC from January 1994 to January 1999 in whom the primary tumour was left *in situ* were identified from hospital notes. Age, sex, mode of presentation, date and method of diagnosis, CT findings, TNM stage, management method, length of follow-up and outcome were documented.
Results Twenty-four patients were identified (eight women and 16 men, mean age 70 years, range 54–89). The mode of presentation included haematuria, loin pain, symptoms attributable to metastases, and incidental finding of tumours. The diagnosis in all cases was made by CT. The pathological stage at diagnosis was T1 in three, T2 in six, T3a in four, T3b in seven, T3c in one and T4 in three patients. There were nodal metastases in 10 patients at presentation and 14 had distant metastases. Eleven of the patients received symptomatic treatment only, eight received embolization of the primary tumour, seven underwent radiotherapy to metastases, and one patient accepted a course of immunotherapy. Survival ranged from 1 to 55 months, with 12 patients surviving >1 year, five reaching 2 years and none surviving 5 years from diagnosis at the time of analysis. Of 15 patients with tumours of stage T3a or

more, 12 of whom had metastases at presentation, the mean (range) survival was 12.2 (1–48) months, with three patients still alive at 11, 22 and 48 months from diagnosis.
Conclusion Compared with a recent report stating that patients with operable metastatic RCC have a survival advantage if given immunotherapy after cytoreductive nephrectomy, compared with immunotherapy alone (mean survival 12.5 and 8.1 months, respectively), and an overall survival advantage of 50% [*J Urol* 2000; 163 (suppl 4): A685), these results confirm that the patient with locally advanced disease with or without metastases can survive for a considerable period with no surgical or systemic immunological therapy, and such intervention may offer no significant improvement in outcome and survival compared with symptomatic treatment only. This work will form the basis of a regional database of patients managed with *in situ* RCC.

P134

Percutaneous radiofrequency ablation in the management of RCC

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Introduction The use of diagnostic imaging has resulted in the increased detection of incidental small RCCs. Several of these patients are elderly, with significant comorbidity and are unfit for major surgery. The aim of this study was to determine the role and efficacy of radiofrequency ablation (RFA) in the treatment of RCC in high-risk patients.
Patients and methods Between July 1999 and August 2000, five patients (mean age 76.6 years) underwent RFA for incidentally detected renal tumours, using CT/ultrasonographic guidance. Five RCCs (mean size 3.6 cm) were treated with seven sessions of RFA, using internally cooled probes, with the patient under sedoanalgesia. Treatment sessions lasted a mean (range) of 11.4 (6–14) min. All patients were followed up (3–17 months) with regular contrast-enhanced CT.
Results All patients were discharged within 24 h of the procedure with no complications. No enhancement of the tumours, consistent with radionecrosis, was apparent in three patients within 7 days of primary treatment; two patients required a further treatment to achieve total tumour ablation. Four patients remain tumour-free and one patient has since died from an unrelated medical condition.
Conclusion RFA is a safe and minimally invasive treatment for RCC and is well tolerated. It is a highly effective treatment for those patients unfit for major surgery, although a longer follow-up is needed to assess further its long-term efficacy in the management of RCC.

P135

Laparoscopic radical nephrectomy for RCC

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Introduction Laparoscopic renal surgery has developed over the past 8 years and is now being offered to a greater selection of patients. Laparoscopic radical nephrectomy (LRN) has only recently started to gain wider acceptance. There was initial concern about achieving appropriate oncological resection of tumour and about port-site recurrences from tumour seeding. The aim of this study was to evaluate the efficacy and feasibility of using LRN for RCC.
Patients and methods The first 20 patients (11 men and nine women, mean age 58.2 years, SD 8.5, 11 left and nine right kidneys removed) who underwent a LRN for RCC were analysed. The LRN was undertaken using a transperitoneal approach with three to four ports using the same oncological principles as for open radical nephrectomy. The kidney was removed using a laparoscopic bag via an enlarged trocar port. No tumour had CT evidence of lymphatic, vascular or perirenal invasion.
Results Nineteen kidneys were successfully removed laparoscopically; the one conversion was caused by extreme renal fibrosis and occurred after securing the renal hilum laparoscopically. The mean (SD, range) operative duration was 143.4 (22.3, 90–240) min. A blood transfusion was required in one patient (two units). Oral intake was commenced for fluids in 1.6 days and diet in 2.6 days. The mean (SD) hospital stay was 5.5 (2.1) days. Analgesia was parenteral for 1 day and oral from day 2 onwards. The complications included eight minor (fever in six, cardiac in one and ileus in one) and one major (a perforated duodenal ulcer). There were no recurrences. The mean specimen weight was 392.6 g; the tumour was in the upper pole in seven, mid pole in five, lower pole in seven and multicentric in one. The mean (SD) tumour size was 4.1 (0.4) cm. Histopathology showed 12 T1G2, six T1G3 and one T2G2 RCCs, and one oncocytoma removed.
Conclusions LRN can be effective for RCC, safely and with excellent tumour control for low-grade disease, maintaining strict oncological principles.

P136

Immunohistochemical markers for detecting microvascular invasion in RCC

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Introduction Of patients with newly diagnosed RCC, ≈ 30% have unsuspected metastatic disease present at diagnosis. Consequently, outcomes differ in patients with histologically similar tumours. There is published evidence suggesting that patients with microscopic vascular invasion (MVI) are at considerable risk of progression within 5 years after presumed curative surgery. We investigated changes in the histological assessment, to increase the detection of MVI.
Materials and methods The number of slides/cm of tumour examined was gradually increased, starting from 1 slide/cm. We attempted a more accurate detection of the MVI by using immunohistochemical markers, EVG (specific for elastin), FVIII and CD31; CD31 has been identified as being more specific for the vascular endothelium than the other stains listed. The slides were independently examined by two pathologists. Fifteen patients undergoing potentially curative or palliative nephrectomy were included. In three in whom the routine pathological examination reported no evidence of MVI, staining with CD31 was positive. Results were similar by the two reporting pathologists. Increasing the number of slides/cm had no effect on the detection of MVI. The percentage of MVI detected using EVG and FVIII was no different from that reported using the current method, but CD31 appeared significantly better in detecting MVI.
Conclusion A more accurate detection of MVI might alter significantly the outcome of these patients, as it will allow the selection of those patients who would benefit from additional treatment with biological response modifiers.

P137

Is there a scientific basis for the use of herceptin immunotherapy in RCC?

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Introduction The 5-year survival for patients with stage IV RCC is ≈ 10%; additional treatment modalities are needed because RCC is largely radio- and chemo-resistant, and results with immunotherapeutic agents such as interleukin-2 and interferon-α have had limited success. Herceptin is a mAb to the HER-2 receptor. Overexpression of HER-2 in patients with breast cancer is used as the selection criterion for clinical treatment with herceptin immunotherapy. HER-2 status is determined using specific techniques approved by the Food and Drug Administration in the USA. Our centre is one of the British quality-control centres for applying such techniques. In this study we assessed HER-2 status in RCC using these approved techniques to determine whether there is any scientific basis for the use of herceptin in patients with RCC.

Materials and methods The study group comprised patients with a histological diagnosis of RCC after nephrectomy; 5 μm tissue sections were used throughout. Gene amplification was assessed using fluorescent *in situ* hybridization (FISH) with probes for chromosome 17 and HER-2. Protein expression was assessed using the CB11 mAb, the results being scored by two independent observers.

Results Twenty-seven RCCs and seven benign specimens were evaluated (six stage 1, six stage II, eight stage III and seven stage IV tumours). No gene amplification was detected in any of the tissue sections. The median (range) HER-2/chromosome 17 number for the tumours was 0.99 (0.8-1.17). Nine tumours were polysomic for chromosome 17 and seven were polysomic for HER-2. There was no association between polysomy and tumour stage. Three of 27 (11%) tumours over-expressed the HER-2 protein, compared with six of seven of the benign tissue ($P < 0.001$).

Conclusions Using FISH and immunohistochemical gene amplification, the protein over-expression of HER-2 is not common in RCC. The results of this study cast doubt on the suitability of herceptin in the treatment of RCC.

10.30–11.30
Poster Session 14
Reconstruction

P138

Long-term results of ileal ureteric substitution

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Introduction Ileal ureteric substitution can be used when there is extensive ureteric loss and is a relatively uncommon procedure. This report details the experience in one centre of this surgically challenging procedure.
Patients and methods Eight patients (median age 52 years, range 36–74) who underwent the procedure in our unit were assessed retrospectively; all had a percutaneous nephrostomy inserted before surgery. A 15–20 cm length of small bowel was anastomosed in an isoperistaltic fashion. None of the ileal segments was tapered before anastomosis and no anti-reflux procedure was used.
Results Eleven ureteric units were replaced; the median (range) follow-up was 111 (65–198) months. Five patients had retroperitoneal fibrosis and two had complications of stone disease. Urinary infection was the commonest complication in the short-term (five) and four patients developed upper tract dilation. One patient has subsequently undergone a TURP and one uses CISC. Renal function was preserved in seven patients. Metabolic acidosis occurred only in those patients with bilateral ureteric substitution.
Conclusions Ileal ureteric substitution is a complex procedure reserved for difficult cases and is durable in the long-term. Bilateral ureteric replacement is associated with subsequent long-term metabolic problems. Renal function is not adversely affected by the procedure.

P139

Buccal mucosa graft for tuberculous ureteric strictures

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Introduction Buccal mucosa has an already established role in managing urethral strictures. Genitourinary tuberculous is a common disease in India and thus the use of buccal mucosa was evaluated for long ureteric strictures.
Patients and methods Two young women and a man with long ureteric strictures secondary to genitourinary Koch's tuberculosis were treated after 6 weeks of medical treatment. The first patient presented with a long upper ureteric stricture 2 months after augmentation cystoplasty for a 'thimble' bladder. After excising 2 cm of ureter a 9.7 cm stricture was treated using an 'onlay' technique, wrapped by mobilized omentum. The other two patients had lower and middle long strictures not amenable to a Boari flap; hence, with or without ureteric reimplantation, buccal free grafts were used. The patients were assessed after 8 weeks, 3, 6 and 12 months using IVU, retrograde pyelography and isotope scans
Results During the follow-up both healing and drainage were good. Ureteroscopy in each patient showed excellent regeneration of the urothelium.
Conclusion Earlier experience of managing genitourinary tuberculous strictures gave disastrous results with a Davis intubated ureterotomy and hence scaffolding by a free graft of buccal mucosa was considered a good option for these long strictures. It is easy to harvest with the omentum scaffold and provides a good vascular supply. The ureter drains by gravity, but a long-term follow-up is required.

P140

The problems of penile urethroplasty

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Introduction We recently published our results with penile urethroplasty, which show that a two-stage reconstruction gives better results than a one-stage reconstruction for a complete circumferential repair, in terms of their long-term re-stricture rates. Nonetheless, a two-stage reconstruction carries a distinct short-term morbidity.
Patients and methods The results of 119 one-stage and 21 two-stage bulbar urethroplasties were compared with 20 one-stage (Orandi) and 82 two-stage penile urethroplasties.
Results The short-, medium- and long-term re-stricture rates were very similar with all these procedures, at $\approx 12\%$, but the short-term revision rates for other complications were very different. The short-term revision rates were 21% and 20% after first-stage and second-stage urethroplasty of the penile urethra, and 20% after a one-stage (Orandi) penile urethroplasty. The short-term revision rate after a one-stage or two-stage bulbar urethroplasty was zero.
Conclusions Penile urethroplasty, whether a one- or two-stage repair, is intrinsically prone to complications such as haematoma or infection, which in turn lead to secondary complications such as fistulation, which do not occur in the bulbar urethra (or more proximally). Meticulous haemostasis and the use of prophylactic antibiotics may help.

P141

Radical myectomy – medium-term results

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Introduction Since 1994, 58 patients with an overactive bladder have undergone a radical myectomy. Twenty-one were operated on for recalcitrant congenital detrusor instability; 17 for idiopathic instability who have also failed conservative therapy and 20 patients with congenital (11) or acquired (nine) neuropathy with hyper-reflexia.
Patients and methods At least half the detrusor was removed from below upwards after dissecting down to the urothelium around the circumference of the bladder. The urothelium was then covered with an omental layer. Most of the congenital neuropaths had additional procedures, usually an artificial sphincter (eight).
Results The best results were achieved in those with congenital instability and those with congenital hyper-reflexia. All but two of the congenital group (91%) were cured although many took up to 12 months to achieve the maximum benefit. No patient had to catheterize. Of the 11 myelodysplastic patients, there was only one failure and all but two were stable at 12 months. However, two patients developed large intravesical calculi. The nine acquired neuropaths fared less well and only three were rendered symptom-free. Those with idiopathic instability fared less well; 11 had some improvement in symptoms (even though nine had become stable). One patient has to self-catheterize. There were five failures, all aged over 50 years.
Conclusion Treatment in the congenital group is technically easy and they are almost always cured. The myelodysplastic group was technically difficult but achieved excellent results. The idiopathic

group was disappointing; surgery in the older idiopath was again technically difficult and nearly always failed. Which patients benefit from myectomy in our hands is becoming clearer.

P142

Adherence of *Escherichia coli* strains causing infections in patients with a reconstructed bladder

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Introduction Transposition of intestinal segments into the urinary tract results in long-term complications. Recurrent UTI and excess mucus production are two such long-term complications that affect the quality of life of these patients. We investigated the basis of colonisation and persistence of *E. coli* isolates within the reconstructed bladder.
Material and methods Mucus and punch-biopsy samples were obtained from seven patients who had been shown previously to have persistent *E. coli* UTIs. Binding studies to mucus and purified mucins immobilized on microtitre plates were carried out. We used *E. coli* strains expressing known fimbrial adhesins (type 1 fimbriae and P-pili). The same strains were also used to analyse binding to biopsy sections by fluorescence microscopy.
Results Mannose-sensitive (type 1 fimbriae) adhesins were shown to mediate attachment of strains to mucus, mucin and ileal biopsies. Binding to biopsy sections represented attachment to both mucus and epithelium. The possible binding site of type 1 fimbriae within the mucin glycoprotein structure is shown. There was no clear evidence of binding mediated by P-pili.
Conclusion Most *E. coli* strains causing persistent infections in patients with transposed intestinal segments express type 1 fimbriae. This adhesin facilitates the binding to both mucus and epithelium of the transposed segment. Bacterial persistence is likely to result from the adherence to mucus in conjunction with stasis as a result of incomplete emptying of the reconstructed bladder.

P143

Total pelvic clearance – is it worthwhile?

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Introduction Therapeutic options are generally limited in patients with primary or recurrent locally advanced pelvic malignancy. However, in some cases total pelvic clearance (TPC) may achieve palliation and/or cure. This study describes our experience with this procedure.
Patients and methods Between 1990 and 2000, 28 patients (17 women and 11 men) underwent TPC (mean age 54 years); 12 had Duke's C colorectal adenocarcinoma and eight had stage IV squamous cell carcinoma of the cervix/vagina. Most of the patients had pain associated with symptoms such as foul-smelling discharge, ulceration and bleeding. Patients who underwent TPC within the last year completed a quality-of-life assessment. Surgery was undertaken by a pelvic team consisting of urologists, colorectal surgeons and gynaecologists.
Results TPC was the primary treatment in only five patients (with neoadjuvant radiotherapy in three), all others having had surgery, chemotherapy and/or radiotherapy previously. Twelve patients (43%) had perioperative complications ranging from UTI to septicaemia and adult respiratory distress syndrome, but none died within 3 months of surgery. Eleven patients have died since surgery, with a mean (range) survival of 12.2 (3–35) months. Ten patients were disease-free when last reviewed, with a mean survival of 33.9 (7–84) months; seven patients had evidence of recurrent disease.
Conclusion TPC is a complex procedure associated with significant morbidity, but with careful patient selection and a multidisciplinary approach, good palliation and, in some cases, a cure can be achieved in this desperate group of patients.

P144

Reconfigured antirefluxive ileal ureter: a novel surgical technique

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Introduction The ileal ureter was not generally accepted because of the controversy about long-term renal function, metabolic impairment and the need for a antireflux procedure. Thus we compared two techniques for ureteric replacement in dogs.
Materials and methods Two groups of five dogs were used; in group 1, the dogs had a refluxing ileal ureter constructed. In group 2 the dogs underwent a novel technique entailing the isolation of 3 cm of ileum, a transverse ileotomy for 80% of the circumference, a longitudinal incision of each of the created rings of ileum on opposite sides adjacent to the mesentery, and unfolding of the incised rings, resulting in a 9–11 cm long ileal strip which was tubularized into a narrow ureteric substitute, with a nonrefluxing submucosal ileo-neocystostomy. The intact reno-ureteric units served as controls. The dogs were observed for 12 weeks.
Results In group 1 the serum creatinine level increased from 7 mg/L before surgery to 11 mg/L afterward ($P < 0.003$), with no significant difference in group 2 or between the groups. IVU and MAG3 renal scans showed a preserved upper tract in both groups. Ascending cystography after surgery showed reflux in group 1 and no reflux in group 2; urine culture showed significant bacterial growth in all. The acid-base and electrolyte balance was maintained.
Conclusions The results of this study do not indicate that either technique is best. However, the novel technique is safe and reproducible clinically. Its potential advantages are the minimal bowel length used, a small absorptive area (minimizing metabolic disturbances) and the feasibility of a standard safe non-refluxing ileo-neocystostomy.

P145

Urological injury associated with obstetric trauma: the changing pattern in Saudi Arabia

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Introduction An improvement in obstetric care usually reduces the incidence of lower urinary tract injury. We reviewed 56 such injuries referred to our institution and managed over a period of 26 years, to evaluate changes in presentation and management.
Patients and methods In this retrospective study, the medical records of 56 women (median age 35.8 years, range 18–56) were reviewed, particularly for the type of injury, aetiology of the injury, presentation, and the type and outcome of treatment. The period of review was divided into the first 16 years (1975–1990) and the last 10 years (1991–2000) for comparison.
Results Prolonged labour was the cause of injury in 20 (70%) of the patients during the initial period, compared with eight (30%) during

the latter period. Fifty-three patients had fistulae; these were more complex during the initial period, and 11 of the patients had urethrovaginal (nine) and rectovesical (two) in addition to vesicovaginal fistula. The clinical presentation included total incontinence in 52, stress leakage in one and pyelonephritis in three patients. Twenty-eight patients had undergone up to five previously attempted repairs elsewhere. Of 53 patients treated surgically, urinary diversion was needed in 20. More patients (49%) required urinary diversion and the repair of the fistula was successful in fewer (41%) in the initial period. During the last 10 years the repair of fistula was successful in 20 (74%) of the patients and urinary diversion was necessary in six (23%).

Conclusions With better obstetric care, prolonged labour may be a less common cause of urological injury in Saudi Arabia. The lower urinary tract mat still be injured as a result of complications of obstetric procedures, but the extent of injury is much less and fistula repair more successful, with urinary diversion rarely required.

15.00–16.00
Poster Session 15
BPH - General

P146

Effect of doxazosin on bladder function after BOO in rats

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Introduction Hypoxia induced by BOO plays a major role in hypertrophic/degenerative responses to BOO. Doxazosin is an effective α-antagonist used for symptomatic BPH. Although the therapeutic effect of doxazosin is through relaxation of prostatic smooth muscle, clinical efficacy may be mediated by inhibiting spinal α-adrenergic receptors and direct bladder effects (vascular α receptor inhibition). We evaluated the effect of doxazosin on bladder blood flow and dysfunction induced by BOO in rats.
Materials and methods The study comprised two parts. In part 1, eight rats were divided equally into two groups; group 1 received oral doxazosin (30 mg/kg) for 4 weeks and group 2 vehicle only (5% DMSO). After 4 weeks, the bladder blood flow was assessed and the bladders excised, frozen and analysed. In part 2, 32 adult male rats were divided equally into four groups; groups 1 and 2 received oral doxazosin (30 mg/kg) for 4 weeks and groups 3 and 4 vehicle only (5% DMSO). At 4 weeks, groups 1 and 3 received BOO and doxazosin for 2 more weeks. After 6 weeks of doxazosin the bladders were excised and weighed; strips were assessed in contractile studies.
Results In part 1, 4 weeks of doxazosin increased blood flow to the bladder; the increase in bladder weight in group 2 was significantly greater than in group 1 ($P<0.05$). In part 2, BOO resulted in significant decreases in the contractile response to field stimulation in treated and untreated rats ($P<0.05$). The decrease in response was significantly greater in the untreated rats ($P<0.05$). The response to KCl was significantly reduced by BOO in untreated groups but not in the treated groups ($P<0.05$). The time to maximum tension was significantly greater in response to carbachol, ATP and KCl ($P<0.05$). The increase was significantly greater for the vehicle-treated obstructed groups stimulated by KCl than for the doxazosin-treated groups ($P<0.05$).
Conclusions Doxazosin increased blood flow to the bladder, reduced the degree of bladder hypertrophy and reduced the severity of the response to BOO in rats; this was ascribed to pharmacological effects on α-adrenergic systems outside those in the prostate. These include effects on bladder blood flow, micturition centres of the CNS, spinal reflexes, and α-adrenergic receptors in the urethra and bladder.
Funding: Pfizer, Inc.

P147

A randomized, double-blind, crossover study investigating the efficacy of doxazosin (gastrointestinal therapeutic system) and tamsulosin in patients with BPH

R. Kirby *St. George's Hospital, London, UK*

Introduction Selective α1-antagonists are effective in improving urinary function and symptoms for patients with BPH. The effects of doxazosin gastrointestinal therapeutic system (GITS, an extended-release formulation) and tamsulosin on urinary flow rates and total IPSS were compared.
Patients and methods Data from a randomized, double-blind, crossover study of 47 men (aged 50–80 years) were analysed. Patients were treated in four phases: phase I, placebo run-in (2 weeks); phase II, first study drug doxazosin GITS or tamsulosin (8 weeks); phase III, wash-out with placebo (2 weeks); and phase IV, second study drug tamsulosin or doxazosin GITS (8 weeks). Doxazosin GITS began at 4 mg/day and tamsulosin at 0.4 mg/day; doxazosin GITS was titrated to 8 mg/day and tamsulosin to 0.8 mg/day after 4 weeks of therapy if the increase in maximum urinary flow rate (Q_{max}) was <3 mL/s and the reduction in total IPSS was $<30\%$. Endpoint efficacy data were analysed using an analysis-of-covariance model with terms for sequence, phase and sequence within patient and baseline as covariate.
Results Doxazosin GITS and tamsulosin significantly relieved LUTS and significantly increased Q_{max} from baseline ($P=0.001$). Preliminary analyses showed doxazosin GITS produced significantly ($P=0.019$) greater improvements than tamsulosin in total IPSS at the last treatment visit of efficacy phases II and IV combined. There was a marginal difference in improvement in Q_{max} in favour of doxazosin GITS over tamsulosin (mean change from baseline 2.6 mL/s and 1.7 mL/s, respectively, $P=0.089$). The IPSS at baseline and at the last treatment visit of the efficacy phase in the intention-to-treat population (adjusted means, with SEM or SD) were: total score 16.4 (6.41) and 16.1 (6.76); and 8.2 (5.11) and 9.8 (6.65), respectively. The adjusted mean change from baseline was −8.0 (0.46) and −6.4 (0.46), respectively ($P=0.019$; within group $P=0.001$ for both.
Conclusions Doxazosin GITS was significantly more effective than tamsulosin in relieving LUTS in men with BPH.
Funding: Pfizer, Inc.

P148

Tamsulosin in the treatment of urinary retention; a prospective, placebo-controlled trial

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Introduction The aim of this study was to assess the effectiveness of tamsulosin in relieving urinary retention at 2 days and 2 weeks after starting treatment, and to identify the patient factors predictive of outcome.
Patients and methods In a prospective, randomized, placebo-controlled trial, 49 patients with acute urinary retention presumed (by exclusion) to be related to BPO received either tamsulosin (30) at 400 μg daily, or placebo (19) for 2 weeks. The catheter was removed after the second dose. Those unable to void were re-catheterized and given a second trial without catheter (TWOC) at 2 weeks. The outcome measure in the two groups was the ability to void at the designated times.
Results After the TWOC at the second dose, 19 of 30 (63%) patients on tamsulosin and seven of 19 (37%) on placebo voided (not significant, chi-squared test). Of the patients who failed the TWOC at the second dose and were re-catheterized, none voided successfully at 2 weeks. The tamsulosin and placebo arms were well matched for age (tamsulosin 71.8 years, placebo 70.0 years). The mean age of patients with a successful TWOC, regardless of treatment arm, was 69.0 years, whilst the mean of age of those who failed was 73.3 years. The treatment arms were also well matched for the volume of retained urine at the first catheterization (tamsulosin 850 mL, placebo 860 mL). The mean bladder volume of patients with a successful TWOC, regardless of treatment arm, was 760 mL, compared with 955 mL in those who failed. The chi-squared test for age and volume of retained urine showed these results to be statistically insignificant at the 5% level.

Conclusion Treatment with tamsulosin appears to be effective in improving the success rate of voiding after an episode of acute urinary retention, but the sample size was too small to confirm this result statistically. The study suggested that patient age and volume of retained urine on presentation may influence outcome, and showed that a second TWOC at 2 weeks was not beneficial.

P149

Acute urinary retention: what is the impact on quality of life?

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Introduction Acute urinary retention (AUR) is a common urological emergency, usually involving admission, insertion of a catheter and/or an operation to relieve BOO. This study assessed the impact of admission for AUR on patients' health-related quality of life (HRQoL) when compared with those undergoing an elective urological admission requiring a catheter (TURP) and an emergency admission (renal colic).
Patients and methods Consecutive men admitted with AUR, renal colic or for a TURP were recruited. A self-completion questionnaire assessing HRQoL (e.g. general health, activities of daily living, anxiety, pain and urological symptoms) was administered to all three groups on five separate occasions (within 72 h of admission and at 1, 2, 3 and 6 months after admission).
Results Data on all 100 patients recruited during the 24-month period (August 1998 to July 2000) will be available at presentation. Currently it is complete for 32 patients (mean age 69.6 years, range 43–87). The mean HRQoL scores were low on admission for all three groups but the patients admitted with renal colic and for TURP showed a greater improvement on discharge than did the AUR group. The pain experienced by patients adversely affected all aspects of HRQoL but in particular interfered with sleep and enjoyment of life.
Conclusion HRQoL scores for patients admitted with AUR remained lower than those for patients with renal colic or TURP for 6 months after discharge. This study is the first to show that AUR appears to have a significant and persistent effect upon patients' HRQoL.
Funding: Merck

P150

The relation between IPSS and objective variables in the diagnosis of BOO: statistical analysis and application of an artificial neural network

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Introduction This study objectively evaluated the IPSS, and correlations with objective variables, with an artificial neural network (ANN) in predicting BOO.
Patients and methods The study comprised 460 men who were prospectively included (mean age 60.4 years, SD 9.4). All patients underwent a DRE, PSA measurement, flow rate, TRUS, cystoscopy, filling and voiding cystometry and pressure-flow studies. Patients answered an Arabic translation of the IPSS. Spearman's coefficient (r) was calculated for the correlations among variables. A feed-forward back-propagation ANN was designed. The input layer included seven neurones, the hidden layer 15 and the output layer three. The training set comprised records of 305 patients, with 155 records in the testing set. The input consisted of the items of the IPSS and the output variables was 'obstructed', 'unobstructed' and 'equivocal', compared with the results of the pressure-flow study.
Results There was no correlation between individual questions of the IPSS and objective variables, whether the obstructive, irritative or total score was correlated with the variables. Using the ANN, in the training set the diagnostic accuracy for predicting obstruction was 94%, and in the testing set was 87%. The overall accuracy in the testing set was 73%.
Conclusion Symptom scores cannot be used in diagnosing BOO or evaluating or comparing different treatment modalities for BPH. The ANN model was helpful in predicting BOO, with good accuracy. The ANN model could be used to spare 73% of patients invasive urodynamics.

P151

Shared management of men with LUTS: an outreach flow clinic approach

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Introduction In consultation with the local GPs, an outreach flow clinic was established in 1995 in our affiliated cottage hospital, to reduce the waiting time for the assessment of men with LUTS and to bring the investigation of these patients closer to them. We present a 2-year retrospective audit of the service, which we believe is a good model for departments covering wide geographical areas.
Patients and methods On assessing men with LUTS, the GP takes a history and performs a physical examination, including a DRE. Urine analysis, a full blood count, PSA, serum electrolytes, urea and creatinine are then requested. Patients with significant abnormality were referred immediately to the urologist. Others were referred to the flow clinic, with their results. The clinic sends appointment letters with a frequency/volume chart and IPSS form. After the flow tests and postvoid residual scan, all results (with the GP's letter) are sent to a designated consultant urologist who reviews and makes recommendations for management to the GP.
Results In all, 156 patients were investigated through the above pathway during the period of the audit, of whom 147 were men (mean age 69.2 years, range 32–91). The waiting time for investigation was 1–8 weeks (mean 4, mode 4); 70% of patients had a mild or moderate IPSS, 57 (39%) were referred to urology, while 87 (59%) were managed by the GPs, of whom only 3% (two patients) had been referred back to the urologist for bothersome symptoms. Three patients had left the area.
Conclusion With the urologist's supervision, up to 60% of men with LUTS may be managed at the primary care level. Patient selection is vital.

P152

A probability-based system for combining simple office variables as a predictor of BOO

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Introduction Predicting BOO from an office assessment for each patients with LUTS remains unreliable; a clinic-based index was developed to improve the prediction of BOO from simple variables available within a clinic.
Patients and methods Consecutive patients with LUTS were evaluated with the IPSS, a DRE, free uroflow (Q_{max}), postvoid residual urine (PVR), TRUS volume measurement and a pressure-flow study. An index (the predicted BOO index, BOOI) was created

using multiple linear regression from a derivation set of half the patient group, and the model assessed in a separate validation set. **Results** The Q_{max}, total prostate volume and PVR significantly predicted the BOOI ($n=384$, adjusted $r^2=0.50$, $P<0.001$), whilst other variables or interactions were unhelpful. These variables were used to create the index (i.e. the predicted BOOI). The PVR could be omitted with no significant loss in the predictive power of the index. When applied to the validation set, an index of >60 (17% of the study population) increased the pre-test probability of obstruction from 45% to 86% (positive predictive value), whilst an index of <20 (23% of study population) reduced the chance of significant obstruction to 4% and any level of obstruction from 72% to 31%. **Conclusions** This is the first series to present urodynamic data using new indices of bladder voiding function. The index enables the prediction of the likelihood of obstruction from a simple office assessment. Using this index, clinicians are able to form an individualised probability assessment for each patient with LUTS. For those where the confidence of diagnosis is high (40% of this study group) appropriate interventions could be instigated with no recourse to invasive urodynamic study.

P153

Residual urine fraction has better correlation with lower urinary tract variables

N.N.K. Lynn, G.N. Collins, P.J.C. Brooman, S.C.W. Brown and P.H. O'Reilly *Department of Urology, Stepping Hill Hospital, Stockport, UK*

Introduction The postvoid residual urine volume (PVR) is an important variable in assessing men with LUTS. We determined the relationships between PVR, residual urine fraction (RF), age, total prostate volume (TV), maximum urinary flow rate (Q_{max}) and the IPSS.
Patients and methods A series of 168 consecutive men with LUTS were assessed; the Q_{max} described by the patients as typical for them, with a minimal voided volume (VV) of >150 mL, was used, as it was shown to be reproducible. The PVR was measured by 5 MHz transabdominal ultrasonography. Patients with PVR of >100 mL were asked to empty their bladders for the second time and this value was used. The RF was calculated as PVR/(PVR + VV). The TV was measured by TRUS (7.5 MHz transducer) using a standard protocol. Spearman's correlation coefficient (rho) was calculated for RF , VF, PVR, TV and Q_{max}.
Results The mean (range) for age, TV, Q_{max} and PVR were 65.8 (43.0–87.0) years, 47.8 (9.3–134.0) mL, 14.3 (5.0–38.0) mL/s and 101 (0–900) mL. The rho values for PVR against age, TV, Q_{max} and IPSS were 0.083 ($P>0.05$), 0.023 ($P>0.05$), −0.137 ($P>0.05$) and 0.01 ($P>0.05$), respectively. The rho values for RF against age, TV, Q_{max} and IPSS were 0.23 ($P<0.01$), 0.21 ($P<0.01$), −0.27 ($P<0.01$) and 0.015 ($P>0.05$), respectively.
Conclusion Compared with the PVR, the RF has a better correlation with lower urinary tract variables in men with LUTS.

P154

Can cystatin C identify patients with BOO and acute urinary retention who are at risk of significant renal impairment?

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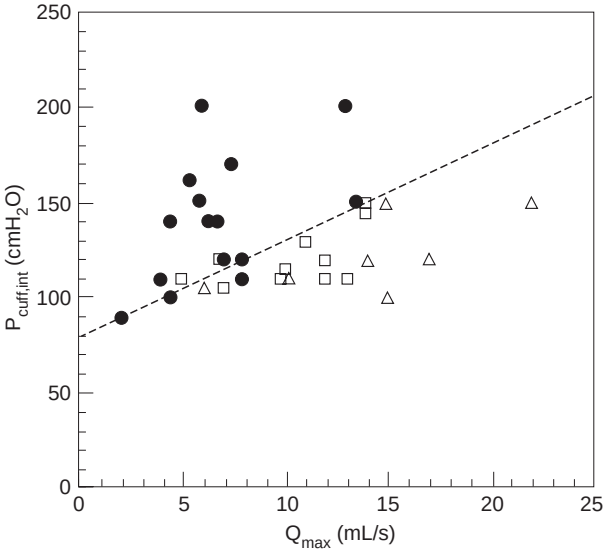
Introduction Serum creatinine is an established marker of renal function, but only starts rising once half the GFR has been lost. Cystatin C is a more sensitive marker, rising when about 25% of GFR is lost; it can be easily measured using the same analysers as creatinine. A significant proportion of men admitted in acute urinary retention (AUR) have a normal creatinine level, but up to half of them have a decreased GFR, as measured by cystatin C. We propose that these patients will develop a further decline in GFR while awaiting TURP and that this decline will be significantly worse than in the group with normal creatinine and normal cystatin C levels. Hence, the level of cystatin C on admission may predict the GFR after TURP.
Patients and methods All men admitted in AUR were assessed for height, weight, blood pressure, creatinine, cystatin C and residual volume of urine. The GFR was calculated using the Cockcroft-Gault formula, which is better than the measured creatinine clearance. These values were then reassessed after catheterization, before and 6 weeks after TURP.
Results To date, 20 patients (age range 60–93 years) have been recruited; of these, 13 (65%) had evidence of renal impairment on admission, 12 with a raised cystatin C (three had a normal creatinine level) and 10 with a raised creatinine (one with a normal cystatin C level). The results so far show a statistically significant relationship between cystatin C and creatinine level on admission, which becomes insignificant a few days after catheterization. Renal function tends to improve with catheterization. We hope to have recruited 60 patients by June 2001, providing more significant results.
Funding: St Helier Hospital

P155

Can noninvasive bladder measurements identify men with BOO?

C.J. Griffiths, D. Rix, A. Macdonald, W. Robson, M. Reddy, M.J. Drinnman, R.S. Pickard and P.D. Ramsden *Departments of Medical Physics and Urology, Freeman Hospital, Newcastle-upon-Tyne, UK*

Introduction A noninvasive technique for measuring the bladder contraction pressure has been developed, based on the progressive inflation of a penile cuff during voiding. This gives continuous data of cuff pressure and flow rate up to the point where flow is interrupted. Previous work has shown that the cuff pressure at the interruption of flow correlates closely with simultaneously measured isovolumetric bladder pressure. We present the results of plotting cuff pressure at the interruption of flow against the maximum flow rate (Q_{max}) for men classified as obstructed, equivocal or unobstructed, according to the provisional ICS method for defining obstruction from an invasive investigation.
Patients and methods Data were obtained from 32 men with LUTS and from seven volunteers. For each, a conventional pressure flow study (PFS) was carried out using an 8 F double-lumen catheter. This was repeated in combination with the new test. A paediatric blood pressure cuff was fitted round the penis and, once voiding had commenced, the cuff was inflated in steps of 10 cmH_2O at intervals of 0.75 s until flow was interrupted (or a maximum of 200 cmH_2O reached). The Q_{max} and detrusor pressure at maximum flow ($Pdet_{Qmax}$) were obtained from the invasive PFS and plotted on the provisional ICS nomogram to classify each subject as obstructed, equivocal or unobstructed. Then similarly, using the same format for the axes, Q_{max} was plotted against the cuff pressure at which flow was interrupted, $Pcuff_{int}$, for each subject, using a symbol to indicate their invasive classification.
Results Data from six patients were excluded from the analysis; one failed to void, two strained excessively and three were studied using a narrow cuff which we now know to be unreliable. The patients were classified on the basis of the invasive PFS data as obstructed (15); equivocal (11, including four volunteers!); or unobstructed (seven). The figure shows noninvasive data from the same subjects, retaining the symbols from their invasive classification.



Conclusions The graph shows a clear differentiation between obstructed men, lying to the upper left, and equivocal or unobstructed men, to the lower right. The line drawn emphasizes this distribution. The position and slope of this line, compared to those on the ICS nomogram, can be justified from a theoretical standpoint. We conclude that noninvasive voiding studies using the cuff inflation technique can provide clinically useful information on obstruction.

P156

Comparison of bladder pressure, urethral pressure and cuff pressure during interruption of flow by inflation of a penile cuff

M.J. Drinnan, A. Johnston, A.M. MacDonald, W. Robson, R.S. Pickard, P.D. Ramsden and C.J. Griffiths *Departments of Medical Physics & Urology, Freeman Hospital, Newcastle Upon Tyne, UK*

Introduction The measurement of voiding pressure is helpful in assessing men with LUTS who may have BOO. We propose to derive the measurement by using a penile cuff to interrupt flow, as for non-invasive blood pressure measurement. The aim of this study was to assess an underlying assumption of this approach, i.e. that bladder pressure is transmitted to the penile urethra, and that flow is therefore interrupted just as the rising cuff pressure exceeds bladder pressure.
Patients and methods A triple-lumen 9 F catheter was positioned with ports in the bladder for filling and pressure measurement. The third port was located 15 cm from the external meatus to record urethral pressure proximal to the cuff. The bladder was filled and during voiding, a paediatric blood-pressure cuff was gradually inflated around the penis until flow ceased. The cuff was then deflated and the cycle repeated until voiding ended. The experiment was then repeated for a second void. Data were recorded from 11 patients referred for a pressure-flow study. Only those interruption cycles followed by a recovery in flow were analysed.
Results Of 64 inflation cycles, 22 had no flow recovery and seven had technical problems with the recording. Of the remaining 35 cycles, 30 behaved approximately as predicted: $P_{urethra}$ followed P_{cuff} to equal P_{ves}, at which point flow ceased. The mean (SD) for $P_{cuff,\ int}$ minus $P_{ves,isv}$ was 20.5 (16.0) cmH_2O, and for $P_{ves,isv}$ minus $P_{urethra}$ was 4.3 (12.7) cmH_2O. For the remaining five cycles, $P_{urethra}$ showed erratic behaviour at interruption, which may reflect a physiological response to the test. Despite this, the value of $P_{cuff,int}$ minus $P_{ves,isv}$ at interruption was 19.0 (24.0) cmH_2O.
Conclusion We quantified errors in pressure transmission from cuff to urethra, and believe that the close relation of $P_{cuff,int}$ with $P_{ves,isv}$ for all patients provides useful information about bladder pressure during voiding.
Funding: DoH, MedLINK Project M170

P157

The modified ice-water test: a better method of assessing men with BOO?

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Introduction The storage symptoms of BOO may arise because of chronic effects on the detrusor muscle, causing modulation of neurogenic responses. The fast infusion ice-water test (IWT) has a low incidence of positivity in men with BOO. However, when cold fluid is infused at a slower rate, previous studies show that a larger proportion of men have a positive test.
Patients and methods Fifty men were recruited at the routine urodynamic assessment. LUTS were assessed by a modified IPSS and any neurological disease excluded by a history. Routine cystometry was undertaken using standard equipment; 10 patients with detrusor instability or a neuropathic bladder were excluded. Obstruction was diagnosed using the Abrams-Griffiths nomogram. Forty men then underwent the IWT; saline at 0–2°C was infused at 50 mL/min and continued to a maximum volume of 250 mL. A spontaneous detrusor contraction resulting in flow was considered a positive result.
Results Twenty patients were unobstructed (mean age 64 years, range 50–80) and 20 obstructed (mean age 56 years, range 29–80). In the unobstructed group 11 (55%) had a positive test ($P<0.05$). There was no difference between groups for storage ($P=0.51$) and voiding ($P=0.71$) symptoms, but within the obstructed group men with a positive IWT had significantly more storage symptoms than those with a negative IWT ($P=0.0042$); this was not seen for voiding symptoms ($P=0.33$).
Conclusion There is a significantly greater incidence of a positive IWT in obstructed men than in unobstructed controls. This suggests that a neurogenic aetiology for the obstructed patients may be responsible for their storage symptoms. For those obstructed patients who proceed to operative treatment, the IWT will be repeated afterward. The results will help determine the utility of the test in predicting response to treatment.

15.00–16.00
Poster Session 16
Bladder Dysfunction

P158

Urinary and bowel function after radical perineal prostatectomy

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Introduction Incontinence rates after radical prostatectomy vary significantly. Patient self-assessment questionnaires have been shown to be more accurate in assessing continence than an assessment by a physician. Few studies have focused on fecal incontinence, reported in up to 18% of patients after perineal prostatectomy. The aim of this study was to investigate bowel and urinary function after perineal prostatectomy in our cohort of patients.
Patients and methods Data were acquired retrospectively via an anonymous self-administered patient questionnaire on all aspects of bowel and urinary function. The impact of additional treatments and QoL were assessed. This was mailed to 80 patients within 5 years after surgery, undertaken in two centres by the same surgeon in each centre.
Results Sixty-six patients responded to the questionnaire (82%). The mean (range) time elapsed between surgery and completion of the questionnaire was 23 (3–58) months. Overall, 56% of patients admitted to some urinary leakage, but only 6% required pad protection. Alteration in bowel habit was reported by 44% of patients after surgery. Frequency of motions (20%), urgency (18%) and loss of control of flatus (15%) were the most common complaints. Only 5% of patients admitted to faecal soiling. The risk of urine leakage declined significantly 2 years after surgery ($P = 0.008$)
Conclusions The risk of small amounts of urine leakage is high ($> 50\%$) but improves significantly after 2 years. Only 6% of patients will experience leakage severe enough to require protection. Bowel disturbances are common but the risk of faecal incontinence is low.

P159

Long-term outcome after symptomatic and urodynamic assessment of the overactive bladder

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Aim To prospectively examine outcome measures, including symptom scores and quality of life, after investigation and treatment of the overactive bladder, and to evaluate factors predictive of outcome.
Patients and methods In all, 106 women with symptoms of bladder overactivity completed validated symptom and generic QoL questionnaires (BFLUTS and SF-36) and underwent conventional (CU) and ambulatory urodynamics (AU). Sixty-nine women returned repeat questionnaires and a further questionnaire addressing satisfaction with their treatment (median follow-up 31 months).
Results Involuntary detrusor activity (IDA) was detected in 47 AU (68%) and 18 CU studies (26%); sphincter insufficiency was diagnosed on 22 AU (32%) and 30 CU studies (43%). Of 12 women undergoing bladder neck surgery, IDA was detected in six during AU and one during CU. Nine of these reported an improvement, including five with IDA. Of 26 patients prescribed anticholinergics, 13 (50%) remained on treatment, 22 had IDA on AU and 10 on CU; 16 (62%) reported improvement with anticholinergics, eight were stable on CU and two on AU. Longitudinal BFLUTS data showed that patients' satisfaction with treatment correlated most strongly with improvements in urgency, social function and lifestyle (Spearman's correlation coefficient, $r = 0.41, 0.51, 0.46$). Satisfaction with outcome correlated weakly with improvement in urge incontinence ($r = 0.31$). Baseline symptom severity was not predictive of outcome. SF-36 scores were worse than a sample of age-matched controls and showed no clinically important change after treatment.
Conclusion Urodynamic diagnosis and symptom severity are not predictive of the response to anticholinergic therapy. These findings support the empirical medical treatment of urgency and urge incontinence and do not preclude such therapy in women with stable cystometry. Women with these symptoms report poor QoL and scores do not significantly improve after treatment.

P160

Detrusor ultrastructure in BOO

R.D. Brierly, R.G. Hindley, E. McLarty, D.M. Harding and P.J. Thomas *The Department of Urology, The Royal Sussex County Hospital, Brighton, UK*

Introduction Qualitative electron microscopy studies of the human detrusor have identified precise structural changes for various voiding dysfunctions, including BOO [*J Urol* 1993; 150: 1681–95]. Specific morphological features of obstructed detrusor have been termed the myohypertrophy pattern and the degeneration pattern is described for detrusor hypocontractility. The aim of this study was to test the consistency and reliability of ultrastructural patterns in the assessment of BOO.
Patients and methods Twelve men (mean age 66 years, range 52–77) with BOO on urodynamics and 12 age-matched asymptomatic normally voiding controls (mean age 67.8 years) were biopsied. Multiple bladder biopsies were obtained from each patient endoscopically and processed for electron microscopy by standard methods. The specimens were randomized and studied at medium power ($\times 4000$) by an examiner unaware of the urodynamic findings. Any ultrastructural patterns identified subjectively were noted.
Results In the BOO group, eight of 12 were found to have the myohypertrophy pattern; half of these were associated with the degeneration pattern of hypocontractility. Of the remaining four patients with BOO, two had the degeneration pattern alone and two were normal. The patients from whom the six biopsies with a degeneration pattern were obtained had consistent postvoid residual volumes (PVR) of > 150 mL; the rest all had a PVR of < 150 mL. The ultrastructural patterns were localised and patchy, with areas of surrounding normal detrusor. There were no abnormal ultrastructural patterns in the control group.
Conclusions Interesting qualitative ultrastructural changes are apparent in the obstructed detrusor, but these are not consistent enough to form any reliable diagnostic potential. However, there maybe an important relationship between the degeneration pattern and PVR in BOO. Further studies, which attempt to quantify these changes and to see whether they could assist in predicting the outcome of bladder outlet surgery, are ongoing.

P161

Quantitative ultrastructural changes in detrusor muscle cells in the underactive bladder

R.D. Brierly, R.G. Hindley, E. McLarty, D.M. Harding and P.J. Thomas *The Department of Urology, The Royal Sussex County Hospital, Brighton, UK*

Introduction Previous qualitative electron microscopy studies of detrusor biopsies have shown reproducible distinct morphological patterns that correlate with impaired detrusor contractility [*J Urol* 1997; 157: 1783–1801]. The degeneration pattern was defined as the presence of disruptive muscle cell profiles in at least half of randomly studied fields (at × 4000–7000). We observed that at high power, more cells show fine disruptive features. The aim of this study was to quantify the disruptive cells seen at high power in a group of patients with an underactive bladder (UAB) compared with controls, and to study the relationship with age in our control group.
Patients and methods Fourteen patients (mean age 64.0 years) with UAB on urodynamics and 17 asymptomatic normally voiding controls (age range 19–81 years) were biopsied; 14 of the controls were age-matched with the UAB group (mean age 63.9 years). Bladder biopsies were obtained endoscopically using the cold-cup technique and processed for electron microscopy using standard methods. All specimens were randomized and studied at high power (× 12 000–24 000) by an examiner who was unaware of the urodynamic findings. All complete cells within each random grid field were counted up to a total of 500. The number of disrupted cells per 500 cells was noted.
Results Disruptive cell profiles were found in both groups. The matched control group had a mean of 29.6 cells/500 and the UAB group of 91.3 cells/500. This difference was statistically significant ($P < 0.001$). In the control group, the number of disruptive cell profiles per 500 had no statistically significant correlation with age ($r = 0.34$, $P = 0.18$).
Conclusion Disruptive cell profiles are apparent at high power in all detrusor biopsies. There were about three times as many disruptive cells in patients with a UAB than in age-matched controls. There was no correlation between age and the number of disruptive cells in control patients, suggesting that muscle cell disruption is not simply a process of ageing per se.

P162

Are 'whaling' women normal?

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Introduction A characteristic EMG signal (complex repetitive discharges, CRD, and decelerating bursts, DB) has been reported in the urethral sphincter of 58% of young women with urinary retention [*BMJ* 1988; 297: 1436–8]. The DBs have a characteristic sound on the audio output of the EMG machine, resembling the underwater recordings of whale song. Little is known about 'whales' in young women.
Patients and methods To date, 17 asymptomatic women volunteers (aged 21–43 years, with normal menstrual cycles) have been assessed. Uroflowmetry and postvoid ultrasonography were undertaken, with concentric-needle EMG of the urethral sphincter to assess the duration of 10 individual motor units; the audio output was recorded.
Results The median (range) maximum flow rate was 20.4 (10–57) mL/s and the voided volume 47–797 mL. None of the women had a postvoid residual urine volume. The median (range) mean motor unit duration (MMD) was 6.5 (5.4–9.2) ms. Seven women had widespread CRDs and DBs in the striated urethral sphincter. There was no correlation between the presence of 'whales' with age, parity, contraceptive history, flow rates, voided volumes or MMD. Six of the seven 'whale positive' women were in the second half of their menstrual cycle.
Conclusions 'Whales' can be found in the urethral sphincter of asymptomatic young women with normal bladder emptying. They were more common in women in the latter part of their menstrual cycle, suggesting that the neurophysiology of the urethral sphincter is under hormonal influence. Their presence may still be important in the pathophysiology of lower urinary tract dysfunction and this will be discussed.
Funding: Department research fund

P163

Pharmacokinetics and pharmacodynamics of oxybutynin desethyloxybutynin after oxybutynin administration by oral and intravesical routes

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Introduction A proportion of patients with detrusor hyper-reflexia who are unresponsive to, or cannot tolerate, oral oxybutynin benefit from intravesical (IV) oxybutynin instillations, whose precise mode of action is obscure. We sought to clarify this issue.
Patients and methods Twelve patients with detrusor hyper-reflexia, previously unresponsive to all anticholinergic regimens, were given oxybutynin 5 mg orally and increased dosages of 15 mg IV oxybutynin with passive diffusion and 15 mg IV oxybutynin with an associated electric current of 15 mA. Each administration mode (plus oral placebo and IV controls) for each patient was associated with a full 8 h urodynamic monitoring session, with serial measurements of oxybutynin and desethyloxybutynin (DEOB) plasma levels and IV uptake of oxybutynin.
Results Oral oxybutynin 5 mg induced no urodynamic improvement; the plasma levels area under the curve (AUC) for combined DEOB/oxybutynin being 16297 ng/8 h and the AUC ratio DEOB : oxybutynin being 11 : 1. Intravesical passive diffusion of oxybutynin resulted in 12 mg IV uptake, a significant improvement in three of eight urodynamic measurements, but the AUC for combined DEOB/oxybutynin was only 2123 ng/8 h and the DEOB : oxybutynin ratio was 1.2 : 1. Intravesical electromotive oxybutynin resulted in almost complete IV uptake (15 mg), a significant improvement in all eight urodynamic measurements, increased AUC oxybutynin levels vs those of oral and passive diffusion, and yet the AUC combined DEOB/oxybutynin was only 4574 ng/8 h and the DEOB : oxybutynin ratio was inverted, at 1 : 1.4. Oral oxybutynin 5 mg caused anticholinergic side-effects in eight of 12 patients. Neither IV administration (12 mg and 15 mg uptake) caused side-effects.
Conclusions A large proportion of intravesical oxybutynin is sequestered, probably in the urothelium, and intravesical oxybutynin administration confers therapeutic benefits through a localized direct action within the bladder wall.
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Augmentation ileocystoplasty for interstitial cystitis

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Introduction Interstitial cystitis (IC) is characterised by frequency, urgency and pelvic pain. Intractable urge incontinence (frequently a result of reduced bladder capacity) often fails to respond to more conservative measures. Augmentation cystoplasty represents one

surgical option available in the management of these patients. However, long-term outcomes from surgical interventions are seldom reported and its place in the management algorithm remains correspondingly obscure.
Patients and methods Twenty-two patients with a clinical and histological picture consistent with IC (and after failing to respond to a series of more conservative measures) underwent augmentation ileocystoplasty. All had full-thickness bladder biopsies submitted for histological confirmation at the time of ileocystoplasty. Outcome measures were assessed for all, over a mean (range) follow-up of 6 (2–12) years. An analysis of preoperative factors and subsequent clinical course of those failing to gain a durable response was similarly undertaken, with an analysis of additional surgical interventions undertaken in this group.
Results Over this long-term outcome of 22 patients, 70% were dry and asymptomatic, 13% had residual symptoms of frequency and urgency (although they were substantially improved), and 18% failed to gain significant benefit and would not have elected to have undergone ileocystoplasty again. Of those who failed to derive a durable response to augmentation, all underwent further surgical intervention, i.e. ileal diversion, subtotal cystectomy and substitution cystoplasty, cystectomy and diversion and substitution cystoplasty with continent diversion (Mitrofanoff), respectively. All those who failed to derive benefit from initial surgery were noted to have had suprapubic pain as their principal complaint before surgery.
Conclusion Augmentation ileocystoplasty provides a durable response in those patients with IC who have failed to gain significant response to more conservative measures (70%). Those in whom suprapubic pain is the predominant symptom appear to respond poorly. These patients subsequently appear to require either defunctioning of the urinary bladder (ileal conduit) or substitution cystoplasty (after total or supratrigonal cystectomy) before symptoms are resolved. It would appear that whilst frequency, urgency and urge incontinence respond well to augmentation, only removal of the diseased bladder results in amelioration of suprapubic pain in those who are most severely affected.

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Long-term outcomes with augmentation ileocystoplasty

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Introduction In those who have failed to respond to more conservative measures, augmentation ileocystoplasty has established itself as the surgical intervention of choice for detrusor instability or hyper-reflexia. Despite concerns over the sequelae of surgical intervention, there remain limited data on the long-term outcomes.
Patients and methods We reviewed 180 patients undergoing ileocystoplasty (and followed for a mean of 5 years); 18% had neuropathic bladder dysfunction (predominantly after spinal cord injury) and the remainder a combination of idiopathic detrusor instability (most), IC and small-capacity or hypersensitive bladders.
Results At a mean follow-up of 5 years, 90% of patients remain continent and dry after surgery. The main complications consisted of recurrent UTIs (10%), troublesome mucus production (10%), stone formation (5%), small bowel obstruction (1.5%), metabolic acidosis (1.5%), malignant transformation (1.5%) and rupture (0.8%). Self-catheterization rates ranged frome 38% (detrusor instability) to 87.5% (neuropathic bladder dysfunction), and 9% required further surgical intervention, ranging from cystectomy and substitution cystoplasty to re-augmentation or deconstruction and diversion.
Conclusion Ileocystoplasty provides a durable response to intractable detrusor instability and the hyper-reflexic neuropathic bladder. Whilst both safe and effective, it is associated with significant morbidity, principally related to recurrent UTI, mucus production and their sequelae. Further surgical intervention may be required for those who fail to respond to initial surgery.

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A DMSO-based 'cocktail' for interstitial cystitis

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Introduction Interstitial cystitis is a clinical-pathological condition of the bladder, characterized by frequency, urgency and pain, and associated with characteristic inflammatory appearances on cystoscopy. Bladder installation therapy is a widely accepted form of treatment for these patients, with varying results. The efficacy of a DMSO-based 'cocktail' was reviewed.
Patients and methods Over a 30-month period, 23 patients were treated (22 women and one man, mean age 55 years, range 17–85). The installation of 50 mL sodium bicarbonate 8.4%, 1 mL pentosan polysulphate 100 mg/mL, 0.25 mL hydrocortisone sodium phosphate 100 mg/mL, and 50 mL DMSO 50% (v/v) was given once a week for 6 weeks. Patients completed a questionnaire based on the IPSS symptom and quality-of-life scores, and a visual analogue pain scale in the first and sixth months of treatment.
Results Of the 23 patients, 17 (75%) had a good response to treatment. The visual analogue pain scores were reduced by a mean (range) of 5.0 (0.1–7.7) and the quality-of-life scores improved by 3.5 (1–6). However, the frequency and nocturia scores were not significantly changed. Five patients relapsed at 6–12 months and commenced maintenance therapy; they had further remission of their symptoms.
Conclusions It is encouraging that 75% of the patients benefited, with a marked improvement in the pain and quality-of-life scores. Less improvement was reported in daytime frequency and nocturia. This regimen may be an alternative to other instillation treatments for patients whose principal complaint is pain, rather than frequency and urgency. A longer-term follow-up of these patients is ongoing, plus a review of patients on maintenance therapy.