# letters

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## PERIANAL AND INTRARECTAL ANAESTHESIA FOR TRANSRECTAL BIOPSY OF THE PROSTATE: A PROSPECTIVE RANDOMIZED STUDY COMPARING LIDOCAINE–PRILOCAINE CREAM AND PLACEBO

Sir,

We read with great interest this paper by Raber *et al.* [1], which represents a well-conducted randomized trial providing new evidence in the highly debated field of pain control during prostate biopsy. At our institution a similar prospective, randomized, placebo-controlled trial, assessing the effectiveness of intrarectal and perianal lidocaine-prilocaine cream as local anaesthetic during prostate biopsy, has just closed to enrolment. Patients graded their discomfort/pain during simple TRUS at an initial clinical evaluation on a 10-point linear visual analogue scale (VAS), and were accordingly divided into three groups: high compliance (VAS score ≤2), medium compliance (VAS score 2–5) and low compliance (VAS score ≥5) to insertion/residence of the ultrasound probe. Patients of each group were then randomized to receive intrarectal and perianal lidocaine-prilocaine cream or placebo and, after a mean of 3 weeks, had a TRUS-guided prostate biopsy with a systematic 10-core sampling protocol. Discomfort/pain was again graded according to the VAS.

We therefore comment on the article by Raber *et al.* also by reporting the preliminary results of our experience on the first 98 patients (recently presented at the national meeting of the Società Italiana di Urologia [2]), waiting for the definitive data to be published soon as a peer-reviewed article. The conclusions drawn by the authors are remarkable, but we address some issues that we think deserve scrutiny. (i) At the time the paper was accepted for publication in the *BJU Int*, to the best of our knowledge anaesthesia with lidocaine-prilocaine cream for prostate biopsy was already reported in two randomized clinical trials [3,4]. (ii) It is quite striking that all men in the placebo group completed the 12-core sampling; in the four-arm randomized trial by Galosi *et al.* [5], in 10% and 15% of patients in the placebo and no-treatment group, respectively, the scheduled six-core biopsy session had to be prematurely interrupted due to intolerable pain, and in our series in 14% of the placebo group. The reason for this is probably the discrepancy in mean VAS score among the placebo groups of the studies, i.e. 1.6 during probe insertion and 3.2 during biopsy puncture in the series by Raber *et al.* [1], 5 (overall) in that reported by Basar *et al.* [4], and 5.5 (overall) in our series. The lower pain score in the series of Raber *et al.* might be due either to a less disturbing ultrasound probe or even to selection bias, but we are concerned about the representativity of the population, which could have consequently altered the real benefit of lidocaine-prilocaine anaesthesia. (iii) We agree with the authors that pain during prostate biopsy comes from both the insertion/residence of the TRUS probe into the anal canal and the biopsy punctures through the rectal mucosa, and we are convinced that the application of the anaesthetic cream should involve both locations. Accordingly, in our trial we first stratified the patients by discomfort/pain during simple TRUS at the initial clinical evaluation, and then randomized them to lidocaine-prilocaine or placebo for the subsequent prostate biopsy. Our analysis showed that in men with high compliance at TRUS, needle trauma did not significantly alter the tolerability, and that anaesthetic administration added little benefit for the subsequent biopsy; the opposite was found in patients with discomfort/pain of medium and high degree at initial TRUS, who benefited from local anaesthesia during the biopsy. On the contrary, stratification by age did not result in a statistically significant difference, unlike the result reported by Raber *et al.* Given that the studies so far addressing the issue of pain relief during prostate biopsy have resulted in controversial findings, as shown by many medical centres around the world still using or until recently using it routinely with no anaesthesia, we think that the anaesthesia should be reserved only for selected patients. These might be, e.g. the 'younger' ones (<67 years old), as suggested by Raber *et al.*, or those with high compliance (VAS score ≤2) to simple TRUS, as advised by us. Further studies aimed at seeking men potentially benefiting from pain control are, in our opinion, mandatory, before anaesthesia can be recommended as a standard procedure during prostate biopsy.

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## SURGICAL ATLAS: ANASTOMOTIC URETHROPLASTY

Sir,
Professor Mundy's crisp, incisive description of anastomotic urethroplasty [1] evoked memories of the 1970s when I was able to observe John Blandy and Richard Turner Warwick. From Blandy I learned to carve an extensive perineoscrotal skin flap. Turner Warwick introduced me to the joy of the right instrument, and to make it if it were not made. Mundy's anastomotic urethroplasty is the 'gold standard' operation for repairing a short urethral stricture. Longer strictures require substitution urethroplasty. In the presence of infection, e.g. 'watering-can' perineum, Blandy's operation is still indicated.

At the end of a Urolink presentation in Glasgow at BAUS 2005 I had suggested that buccal mucosal flap substitution is probably a better option than skin flap substitution. I had the opportunity to be part of a team of Caribbean urologists who repaired two long post-traumatic posterior urethral strictures in Trinidad. The particular difficulty is suturing down a long posterior urethral tunnel. A 'fish hook' modification of a Turner Warwick needle, described in the *Br J Urol* in 1979, was helpful. It enabled us to anchor the buccal flap proximally to the bladder neck. There was a problem delivering the needle afterwards, so we needed to improvise a retractor/director long enough and wide enough to accept an index finger (Turner Warwick's original index finger tip). Thank you, Tony Mundy.

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1 **Mundy AR.** Anastomotic urethroplasty. *BJU Int* 2005; **96**: 921–44

## PROTEINURIA ON DIPSTICK URINE ANALYSIS AFTER SEXUAL INTERCOURSE

I congratulate Domachevsky *et al.* [1] for this first study to determine that sexual intercourse (actually ejaculation itself) is one of the benign causes of proteinuria on dipstick urine analysis (DUA) among the other causes, e.g. heavy physical activity, dehydration, postural change (upright position), fever and emotional stress [2]. They assessed a small group (22 men and 11 women) of sexually active, possibly young (no data given for the ages of the group) navy personnel. No women but six of the 22 men had proteinuria after intercourse, and thus this indicated that the proteinuria was a result of residual semen, composed of various proteins, in the urethra after ejaculation, or of retrograde ejaculation to the bladder. From this theory it is possible that after the semen is washed out by the initial part of the urine stream, a mid or terminal urine sample (not used in the study) might be a simple solution for DUA to avoid further unnecessary investigations for proteinuria in men after intercourse, although this makes the DUA as a home procedure rather more difficult. This is the same principle as used in culture technique to discriminate the source of microorganisms, whether from the urethra or the bladder, by using the 10-mL initial portion of the urine stream as 'voided bladder' (VB1) and the midstream urine (VB2) [3]. In addition, I did not think that even the 12-h duration of proteinuria after intercourse could be determined from these six positive subjects with proteinuria, of whom only two were assessed with a consecutive series of urine samples, and where the proteinuria had disappeared after 1.5 h and 8 h.

This study is also reminiscent of the effect of ejaculation on serum PSA levels; while ejaculation can also increase serum PSA levels in elderly men [4], it is not a factor in serum PSA levels in younger men [5]. Moreover, clinical or subclinical retrograde ejaculation might also be affected by age, due to insufficient closure of the neck of the ageing bladder. Overall, although different physiopathological mechanisms might be possible, proteinuria after ejaculation should also be checked in different age groups.

From the results of this study physicians should consider that intercourse might be a cause of proteinuria in men on DUA used soon after coitus, and that this might precipitate unnecessary further investigations and additional stress for the patients. However, I think this result should be confirmed in a larger group of men consisting of different ages without using the initial part of the urine stream, before routinely warning patients to use overnight sexual abstinence before DUA, and to determine the precise interval for the disappearance of protein in urine.

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## A CASE FOR SCREENING FOR RENAL CANCER

Sir,
I enjoyed this Comment about screening for renal cancer [1], and broadly agree with the conclusions. However, the survival rates for RCC according to Tsui *et al.* [2] were misquoted, being respectively 83%, 57% and 42% for T1, T2 and T3, rather than 91%, 74% and 67%, as presented by the authors. Interestingly, one of the findings of the study by Tsui *et al.* was that tumour size (and hence T stage) is not a significant independent

predictor of survival on multivariate analysis, which is slightly at odds with the point that Turney *et al.* were using their article to make. However, there is little doubt that the arguments presented in the article are sound.

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1 **Turney BW, Reynard JM, Cranston DW.** A case for screening for renal cancer. *BJU Int* 2006; **97**: 220–1
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Sir,

The proposal for a pilot UK screening policy for renal cancer in elderly asymptomatic patients [1] fails to fulfil the Wilson-Jungner criteria for screening, as the natural history of the disease must be well understood, and the risks of treatment should be less than the benefits of treatment. Neither of these facts applies to renal cancer screening in the elderly. The natural history of renal cancer, infamous for spontaneous regression, recurrence many years after apparently curative resection, and wide variability in progression rates, cannot be said to be well-defined nor understood. We contest the assertion that "small tumours follow a relentless course of progression to advanced disease if left untreated". Few studies describing the natural history of small renal masses have a true observational cohort, rather than patients undergoing deferred nephrectomy. Lamb *et al.* [2] reported one of the largest series of observation in renal cancer, with 36 patients who were unfit for, or had declined nephrectomy for serendipitously detected renal masses confirmed as renal cancer. The mean diameter of tumour was 7.2 cm and the growth rates of tumours in that series were 0–1.7 cm/year, with only one patient progressing to metastases 132 months after the initial diagnosis.

The increased use of cross-sectional imaging has lead to more low-stage RCCs being identified, but it has also lead to more nephrectomies for benign lesions, e.g. oncocytoma. Results from an Austrian group, where all patients with a small (<5 cm) renal mass on CT were offered nephron-sparing surgery, reported benign histology in 32% of cases [3] and a similar value of 33% was reported from Johns Hopkins Medical Institution for laparoscopic nephrectomy [4]. The increase in the proportion of benign histology must be measured against the significant morbidity of major surgery, whether laparoscopic or by open nephrectomy. The morbidity from nephrectomy is reported as 11–40% [5] although it might be higher for elderly patients with extensive comorbidity. These risks must be accepted if we develop a screening programme which carries a 30% risk of identifying a benign lesion, and with a considerable chance that even a true malignancy might never become clinically relevant.

The true incidence of asymptomatic renal cancer in the general population is unknown but the incidence of a metachronous contralateral renal tumour is consistently reported as 2–4% [6,7]. We should focus our clinical resources on ensuring that all patients undergo annual renal ultrasonography for life after a nephrectomy, to allow early detection of second primary tumours, before we embark on a general population screening programme.

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Sir,

The authors [1] have very succinctly highlighted the perceived benefits of a screening programme to detect asymptomatic renal cancers. However, in proposing their case for screening they have made assumptions which are not necessarily substantiated by data already available. They seem to suggest: (a) that screening will have a significant detection rate; (b) most incidental renal tumours would eventually progress to become symptomatic; (c) the survival advantage of screening-detected renal cancers is primarily due to lower stage at diagnosis; (d) most if not all incidentally detected masses would require surgery; and finally (e) that renal screening can be done together with screening for abdominal aortic aneurysms (AAA) with minimal added costs and a significant detection rate.

(a) Currently, incidental tumours already comprise up to 66% of all renal cancers, thus any screening programme can only detect the remaining third of patients. Most series of ultrasonographic screening in asymptomatic patients have shown very low detection rates. Tosaka *et al.* [2] analysed >41 000 scans and showed that 2177 were needed to make each diagnosis.

(b) It is not clear whether all renal tumours will eventually become symptomatic. The age at diagnosis of symptomatic renal cell cancer is lower than for incidentally detected tumours, which are more commonly diagnosed in older patients [3]. This contradicts the concept that an incidental tumour is the pre-clinical phase of a symptomatic tumour. In a prospective study by Rendon *et al.* [4] only two of 13 incidentally detected renal tumours were found to be fast-growing. The growth rate of the remaining 11 cases was zero. They surmised that tumours that are destined to grow progressively and possibly metastasize do so early, and that most small tumours grow at a low rate or not at all. Reports from autopsy series before imaging became widely available had shown that up to 67–74% of

renal cancers remain undetected until death. Of these only 8.9–20% of undiagnosed renal cancers were directly responsible for the patient's death [5]. It follows that significantly many elderly patients might have renal tumours that never become clinically relevant. Screening runs the risk of over-diagnosing renal tumours in an increasingly elderly population, leading to greater anxiety from the need for further imaging, conservative management and surgery. Furthermore, despite the increased detection of incidental renal masses, the incidence of metastatic disease and mortality has been relatively stable.

(c) In a report by Jayson *et al.* [6], 85% of asymptomatic tumours and 77% of symptomatic tumours were stage I or II at diagnosis. This stage difference was not statistically significant and might reflect that the survival advantage of asymptomatic renal lesions has more to do with the nature of the tumour rather than the stage. Tsui *et al.* [7] found that symptomatic renal tumours not only had a higher stage but also a higher grade, and were associated with a poorer outcome than were incidentalomas.

(d) Not all renal cancers require excision and their growth rate cannot be predicted at the initial diagnosis. Studies prospectively following tumour growth showed that tumour volume doubling times can vary from <12 months to >60 months [8]. Of tumours in one series, 65% had doubling times of >1 year [5]. In these studies, 4 cm was the threshold at which intervention was usually planned. It therefore follows that a tumour that is 2 cm in diameter and therefore reliably detected by ultrasonography, growing at a fast rate and doubling in volume every year, will be >4 cm in 3 years, whereas another less aggressive tumour doubling every 60 months would take 15 years to reach this equivalent size. Several reports have shown that most patients with incidental renal cancers can be safely observed [5]. Not every incidentaloma needs to be operated upon because most are slow-growing and innocuous, and often diagnosed in elderly patients. Screening should aim to detect the fast-growing tumours, before they grow to >4 cm and become more likely to metastasize. However, just as importantly it should also detect those renal masses that do not require surgery. Scans would therefore have to be repeated at least at 3-yearly intervals. After detecting a small incidentaloma surveillance would be needed from one to several years before the progression could be accurately assessed.

(e) The authors suggested adding the screening for renal tumours to that for AAA, for which screening is advocated only once after 65 years of age; however, substantially many symptomatic renal tumours are detected at an earlier age. Therefore renal cancer screening will not only have be done at several points in a patient's life, but start at an earlier age, if it is to be effective. Unlike a history of hypertension and smoking for patients with AAA, there are no clearly identifiable risk factors for patients with renal cancer to tailor the screening programme to high-risk patients. Any attempt at risk stratification of a screening programme would potentially miss a large percentage of tumours.

Of course, the earlier detection of all renal masses is a goal worth striving for, but for the reasons we cite, a national screening programme might not be as fruitful as it appears, and the argument for it is less compelling than the authors suggest. In an analysis of 1107 ultrasonograms requested for various symptoms from a urology clinic in our region, the incidence of renal masses was 0.6% (unpublished data), providing a much higher yield than for population screening. An opportunistic renal scan to detect those renal cancers that might require intervention should be strongly advocated during every abdominal ultrasonography.

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