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Variations in PSA level following various urological procedures

F. Saadeh, C. Coker,* R. Sherwood, J. Goodall, D. Mulvin and M.J. Coptcoat *Department of Urology & *Department of Biochemistry, King's College Hospital, London*

Introduction: PSA is now recognized as the most useful marker available for prostate cancer. However, it is also raised in BPH and in acute prostatitis. Most studies on the effect of DRE on PSA have shown only small increases in serum PSA following the examination, but the data on the effect of other investigative procedures on PSA are both limited and conflicting.
Materials and methods: Serum PSA concentration was monitored using the Technicon Immuno 1 analyser, in 49 patients undergoing various procedures. Samples were taken before the procedure (Pre) and afterwards at 1, 2, 3, 7 and 14 days.
Results:

	Flexi-cystoscopy (n = 10)	Rigid Cystoscopy (n = 8)	TRUS (n = 10)	TRUS & biopsy (n = 9)	TURP (BPH = 6, CaP = 4)
Mean PSA value, ng/mL Pre Procedure	0·8	1·6	4·5	17	4·8
Mean PSA value, ng/mL Post Procedure	0·9	1·9	4·6	21	21·5

There was no change in patients undergoing flexible cystoscopy, rigid cystoscopy or following TRUS. However, ultrasound-guided prostate biopsies did result in an increase in mean PSA of 4·0 ng/mL with larger increases seen following prostatectomy (12·3 ng/mL).
Conclusion: This study showed that neither cystoscopy nor ultrasonography caused an increase in PSA and samples can safely be taken 1–2 days after these procedures. Prostate biopsy and prostatectomy produced a variable rise in PSA, with a peak rise in PSA occurring at 12 h after the procedure. In most patients, the serum PSA had returned to baseline by 14 days. Therefore, we recommend that blood is not sampled for PSA for at least 14 days after prostate biopsy.

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Free to total PSA ratio: a second screening test for prostate cancer

C. Coker, K. Walsh,* R. Sherwood, F. Saadeh, D. Mulvin and M. Coptcoat *Department of Urology & *Department of Biochemistry, King's College Hospital, London*

Introduction: PSA has recently been shown to occur in the serum both as a complex with alpha-1 antichymotrypsin and an uncomplexed smaller fraction of free PSA (FPSA). Recent reports have indicated that patients with BPH have a higher proportion of FPSA to the total serum PSA (TPSA) and this FPSA/TPSA ratio is a more useful test in identifying patients with cancer.
Patients and methods: Fifty patients with histologically confirmed prostatic disease (20 with BPH and 30 with prostate cancer [CaP] were evaluated with TPSA and the Free/Total ratio using the Delfia Prostatus™ dual-labelled immunofluorometric assay (Wallac Ltd). The statistical sensitivity was assessed at 4 µg/L and 10 µg/L for TPSA and at ratios of 0·15 and 0·2 for FPSA/TPSA.
Results:

Test	Threshold	Sensitivity, %	Specificity, %
Total PSA	4 µg/L	95	25
	10 µg/L	79	63
FPSA/TPSA	0·15	57	89
	0·2	71	75

Applying the generally accepted threshold of 4 µg/L TPSA to define a positive test result, 22/30 (75%) patients who had BPH were falsely positive and 19/20 (95%) with CaP were correctly identified. The positive predictive value was 19/41 = 46%. If the Free/Total ratio (threshold = 0·15) was then applied to the false positives, then only three of the 22 false positives remained positive, with an overall false-positive rate of 3/30 (10%). The positive predictive value increased to 90%.
Conclusion: The preliminary data suggests that the FPSA/TPSA ratio, in conjunction with TPSA, is a useful tool in increasing specificity and reducing the false-positive rate.

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Bone morphogenetic protein-6 expression correlates with metastatic prostate cancer

Pernille Autzen, Craig Robson, C.H. Wilson Horne, David E. Neal and Freddie C. Hamdy *Department of Surgery, The Medical School, Framlington Place, University of Newcastle, Newcastle upon Tyne NE2 4HH*

Introduction: Many attempts have been made to predict the metastatic potential of prostate cancer, but to date, no method can distinguish quiescent from potentially progressing tumours. Bony secondaries in prostate cancer are mostly osteosclerotic, with no clear explanation for this phenomenon. The term Bone Morphogenetic Protein (BMP) refers to an activity derived from bone that induces bone formation *in vivo*. Preliminary studies have demonstrated an association between BMP expression and the presence of skeletal metastases, with differential expression favouring BMP-6 as a potential new marker for metastatic progression. The aim of this study was to investigate BMP-6 expression by *in-situ* hybridization in malignant and benign prostatic tissue.
Patients and methods: Twenty-seven patients were investigated; 15 men had evidence of bony secondaries, eight patients had disease apparently confined to the prostate, and four patients with BPH were used as controls. Patients with cancer were studied before treatment. Tissue samples were obtained from TURP specimens or needle-core biopsies. Using the non-radioactive digoxigenin system, a specific RNA probe was generated from the human BMP-6 cDNA for *in-situ* hybridization, as described previously (Fischer *et al.*, Br J Dermatol 1991; 125:516–20).
Results: All patients with proven skeletal metastases showed a strong positive cytoplasmic signal in malignant epithelial cells for BMP-6 mRNA, whilst none of the organ-confined cancers or BPH tissue samples showed any evidence of BMP-6 expression.
Conclusions: These results confirm that BMP-6 expression may be an important factor in disease progression in prostate cancer, and may be partly responsible for the osteoblastic changes found in prostatic skeletal secondaries.

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Skeletal alkaline phosphatase in the metastatic evaluation of patients with prostate cancer

J.M. Wolff[1], T.H. Ittel[2], W. Boeckmann[1], F.K. Habib[3] and G. Jakse[1] *Department of Urology,[1] Department of Medizinische Klinik II,[2] RWTH Aachen, Germany; Department of Surgery/Urology, University of Edinburgh, Edinburgh[3]*

Objective: To compare the efficacy of two tests, PSA and skeletal alkaline phosphatase (SAP) as staging markers to discriminate patients with cancer of the prostate (CaP) with bony metastases (M+) from those without bony metastases (M0).
Patients and methods: Thirty-nine untreated patients with Mo (n = 22) and M+ (n = 17) CaP and 10 patients with BPH who served as controls were entered into this study. Serum concentrations for SAP and PSA were determined using two immunoassays. ROC curves were constructed to compare the ability of SAP and PSA to discriminate

patients with CaP with bony metastases from those without bony metastases.
Results: None of the M0 patients but 65% of the M+ patients had a SAP value above the reference range (< 19 ng/mL). A corresponding threshold of 100 ng/mL for PSA showed that 27% of M0 patients and only 65% of the M+ patients had a value > 100 ng/mL. This resulted in a sensitivity of 65% for both markers. However, SAP had a higher specificity than PSA (100% *vs* 73%). The ROC curve comparing SAP and PSA showed the superiority of SAP as a marker for bone metastases.
Conclusion: These findings suggest that SAP could become a useful marker in the evaluation of patients with newly diagnosed CaP, as it seems to provide additional information about the skeletal status of these patients.

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The effects of combining hormonal manipulation and ionizing radiation on prostatic carcinoma cells *in vitro*

Stephen A. Thomas, David Kirk and Robin Leake *Department of Biochemistry, University of Glasgow, Glasgow*

Introduction: Increasing evidence suggests that combining radiotherapy and antiandrogens in the treatment of organ-confined and locally advanced prostatic carcinoma may lead to an improved therapeutic response. This has been attributed to neoadjuvant hormonal cytoreduction, thereby reducing the prostatic target volume. However, relatively little is known about the molecular mechanisms underlying these observations. This work investigates whether ionizing radiation induces changes in cellular gene expression, in particular, alterations in the levels of expression of the heat shock protein 90 gene (HSP90) which might then modify hormonal response.
Materials and methods: Using colony formation assays, radiation cell-survival curves were established for the DU 145 and PC-3 cell lines so that radiation in combination with androgens or antiandrogens could be studied by gradient analysis. Gel electrophoresis protein separation and radioimmunoassay were used to detect HSP90 protein induction following cell irradiation.
Results: In the DU 145 cell line, cell survival following irradiation was modified by hormonal manipulation to give increased cell kill. At 2 Gy exposure, the surviving fraction decreased from 0·59 to 0·35% in the presence of 10^{-9}mol/L OH-Flutamide. This radiosensitizing effect was not seen in the PC-3 line, suggesting that the effect on DU 145 was mediated by an androgen receptor-dependent mechanism. DU 145 HSP90 levels increased after irradiation, showing a bimodal peak in induction at 9 and 18 h.
Conclusion: Our working hypothesis proposes that radiation-induced stress response proteins may interact with receptor-bound antiandrogens to increase cell death.

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Incidence and impact of incontinence and impotence following retropubic total prostatectomy

T.S. Bates, M.P.J. Wright and D.A. Gillatt *Bristol Urological Institute*

Introduction: We have studied the incidence of incontinence and impotence in patients after total prostatectomy and assessed the impact their symptoms have on their quality of life using an anonymous, validated, postal questionnaire.
Patients and methods: Between 1987 and 1994, one surgeon performed retropubic total prostatectomies on 96 patients, of which 87 were available for follow-up. Patients were sent an ICS-BPH questionnaire. Patients' ages ranged from 49·5 to 73 years (median 65). The interval between surgery and completing the questionnaire ranged from 7 to 87 months (median 22). The response rate was 95%.
Results: No patients suffered with incontinence pre-operatively. Post-operatively, 69% (57/83) of patients suffered some degree of leakage of urine and 24% (29/83) used pads. Of these, 60% used one pad per day, 15% two pads and five patients used three or more. Nocturnal incontinence was reported by 20% of patients. Urinary incontinence was considered a problem in only 34% (28/83) of patients, 65% of patients using pads considered urinary leakage to be a problem but only one considered it a serious problem. Eighty-nine per cent claimed to be potent before surgery. The overall post-operative potency rate was 41% (30/74) in those potent pre-operatively. However, 67% of patients reporting potency had severely reduced rigidity and only 12% (9/74) achieved what they considered full erections; 10% of all patients considered post-operative impotence to be a serious problem and 47% stated that it was not a problem at all.
Conclusion: The incidence of incontinence and impotence after total prostatectomy is higher than earlier reports suggest, but the impact of these complications appears to be surprisingly low. These results allow patients to be given realistic expectations when counselled before this operation.

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Is transrectal ultrasonography without biopsy justifiable?

N. Sheikh, T.H. Lynch, P.M. Cunningham, R. Gibney, D.G. Kelly and D.M. Quinlan *St. Vincent's Hospital, Elm Park, Dublin 4, Ireland*

Introduction: Concerns about the specificity and sensitivity of TRUS in detecting the presence of prostate cancer have recently been expressed.
Patients and methods: To evaluate the efficacy of TRUS, we reviewed retrospectively 150 consecutive patients, all of whom had biopsy at the time of TRUS. Patients underwent TRUS-guided biopsy because they had either palpable suspicious nodules or an elevated PSA level.
Results: Of the TRUS examinations, 15% showed a suspicious lesion. However, 95% of these lesions were positive for cancer on biopsy; 85% of TRUS examinations showed no suspicious lesions but 35% of these revealed the presence of carcinoma.
Conclusion: The sensitivity of TRUS is poor and a significant number of carcinomas would be missed in the absence of biopsy. We therefore believe that the primary role for TRUS is in needle-guided prostatic biopsy and that TRUS without biopsy has no place in the assessment of patients with a suspicion of underlying malignancy.