Polymorphisms of the Serotonin Transporter Gene

In theory premature ejaculation has been postulated to be due to increased 5HT$_{1A}$ activation. Safarinejad (page 2656) from Tehran, Islamic Republic of Iran found a well characterized population of men with lifelong premature ejaculation who share an S/S (short/short) genotype for the 5HT serotonin transporter gene-linked polymorphic region compared to individuals expressing the long arm of the allele. He postulates that with this polymorphism there is less transport of serotonin in central sites regulating ejaculation. Increased serotonin concentration at the synapse activates 5HT$_{1A}$ receptors, causing a decrease in 5HT firing. The odds of developing premature ejaculation with the S/S genotype were highest (odds ratio 2.73, confidence interval 1.78–4.24) as were the odds of the heterozygous participants with the S/LG genotype (odds ratio 1.86, confidence interval 1.12–2.46).

Renal Phosphate Control Predicts Stone Recurrence

Kim et al (page 2566) from Chungbuk, Republic of Korea report that renal phosphate absorption capacity was significantly decreased in stone formers compared to normal controls. Furthermore, reduced reabsorption of phosphate was associated with hypercalciuria and hyperuricosuria. Renal phosphate handling was an independent predictor of recurrent stone forming which suggests that it may be useful to include phosphate reabsorption in metabolic analyses of patients with urinary calculi. Individuals with a low maximum reabsorption of phosphate by the glomerular filtration rate comprised 13% of the stone forming population in this study and had a higher incidence of hypercalciuria and hyperuricosuria than individuals with a normal maximum reabsorption of phosphate by the glomerular filtration rate. Of interest, drugs such as thiazide reduced calcium and phosphate excretion.

Characteristics of Prostate Cancer at Low PSA Levels

In the Prostate Cancer Prevention Trial 15% of men with prostate specific antigen (PSA) less than 4 ng/ml had biopsy detectable prostate cancer. However, limited data exist on the features of prostate cancer associated with PSA levels less than 2.5 ng/ml. In this retrospective study by Meeks et al (page 2515) 50 of 75 men with PSA less than 2.5 ng/ml had findings suspicious of prostate cancer on digital rectal examination (DRE). Despite the low PSA, 10.5% and 26%, respectively, had a biopsy and Gleason grade 7 or greater, while 9% had extracapsular tumor extension or positive surgical margins. Mean tumor volume was significantly higher in men with than in those without a suspicious DRE (3.3 vs 1.7 cc, p=0.018). The authors conclude that there are significant cancers in this select population with low PSA and abnormal DRE, and that an abnormal DRE should prompt biopsy in appropriately selected patients.

Improved Diagnostic Accuracy for Prostate Cancer

Ouyang et al (page 2508) from Cincinnati, Ohio evaluated the urinary sediments of 43 patients with and 49 without prostate cancer collected after DRE to ascertain the potential diagnostic value of transcripts of alpha-methyl-CoA Racemase (AMACR) and PCA3, a noncoding messenger RNA expressed only in the prostatic epithelium and kidney. AMACR encodes an enzyme that regulates peroxisomal beta oxidation of phytol derived branch chained fatty acids. Results showed that the AMACR and PCA3 scores significantly discriminate patients with from those without prostate cancer. Specificity and sensitivity for prostate cancer detection was 71% and 70% for AMACR, and 59% and 72% for PCA, respectively. The combination of both in a dual marker assay increased specificity to 84%. AMACR and PCA3 are superior to PSA in predicting prostate cancer. The combined assay could be useful for surveillance as an adjunct to PSA after a negative biopsy for prostate cancer.

Measurement of Urethral Closure Function in Women with Stress Urinary Incontinence

In a randomized, double-blind, placebo controlled crossover study 17 women with stress or mixed urinary incontinence were given 4 mg esreboxetine or placebo for 7 to 9 days followed by a
washout period before crossing over to alternative treatment. Urethral opening pressure was measured with urethral pressure reflectometry. Klarskov et al (page 2628) from Hovedstaden, Denmark reported an increase in maximum urethral closure pressure of 8.4 cm H2O in the treatment group compared to placebo, which was not considered significant (p=0.06), but the frequency of weekly incontinence episodes decreased by 58%. Urethral opening pressure measured by reflectometry also increased in the treatment group vs the placebo group by 13 cm H2O. Esreboxetine is a highly selective norepinephrine reuptake inhibitor that works through the peripheral and central nervous system. Previous studies have demonstrated efficacy for the treatment of stress urinary incontinence. This study sheds light on the method of action of this drug, producing an increase in resistance.

Botulinum Toxin A for the Refractory Overactive Bladder

In this randomized prospective trial of placebo vs botulinum toxin A (BTX) for overactive bladder subjects received 1 or 2 doses of BTX at 8 to 10 sites above the trigone. Outcome measures were assessed at baseline, and 3 and 6 weeks after injection. In the first phase of the study BTX statistically improved incontinence episodes, daily pad changes and pad weights compared to placebo. Four subjects (26.6%) receiving BTX experienced post-void residual values greater than 200 cc at the 6-week evaluation and 1 patient required intermittent catheterization. Flynn et al (page 2608) from Rochester, New York conclude that BTX can reduce urinary incontinence due to refractory overactive bladder but there is a risk of urinary retention.

Sequential Treatment Approach to Myoinvasive Urothelial Cancer

A phase II trial of neoadjuvant paclitaxel, carboplatin and gentamycin (PCG) plus transurethral resection of the bladder tumor was conducted by the Southwest Oncology Group (page 2476) to evaluate clinical reversion to T0 disease (cT0) in 74 patients. A post-PCG cT0 status was achieved in 34 patients (46%). However, 10 patients with cT0 status elected to undergo immediate cystectomy after neoadjuvant chemotherapy of whom 6 were found to have residual T2 or greater disease. While this strategy may have some value for conversion to pT0, patients completing neoadjuvant chemotherapy still need to undergo radical cystectomy rather than surveillance. This study suggests that PCG does not have sufficient efficacy when used alone with radical resection to achieve cure.

Impact of Gastric Bypass on Kidney Stones

It is known that morbid obesity is a risk factor for stone urinary calculi. However, it is suspected that enteric absorption of calcium and oxalate is altered after gastric bypass surgery thereby predisposing patients to urinary calculi. Matlaga et al (page 2573) from Baltimore, Maryland identified 4,639 patients who underwent Roux-en-Y gastric bypass (RYGB) surgery and compared them to 4,639 obese control patients in a private insurance claims database who did not have surgery. Within 5 years of RYGB 7.65% of the patients had urolithiasis compared to 4.63% of the control group. The authors conclude that RYGB is associated with an increased risk of urolithiasis (odds ratio 1.71, confidence interval 1.44–2.04) and recommend that surgeons, especially bariatric surgeons, inform patients of this potential complication. They also suggest further studies be performed to evaluate preventive interventions in high risk populations.

Efficacy of Silodosin for Benign Prostatic Hyperplasia

In this report of 2 randomized, placebo controlled, phase III studies of the efficacy and safety of silodosin for benign prostatic hyperplasia Marks et al (page 2634) from Culver City, California found that this selective α-antagonist improved International Prostate Symptom Scores over baseline as well as maximum urinary flow rates 2.6 ± 4.43 ml per second for silodosin vs 1.5 ± 4.36 for placebo. Silodosin also exhibited a low rate of cardiovascular side effects. The most common adverse effect in these studies was retrograde ejaculation, which occurred in 28% of patients and resulted in discontinuation of the drug by 2.8%. In comparison tamsulosin was associated with abnormal ejaculation in up to 18.1% of patients in phase III trials.

Effect of Urinary Tract Infection on Reservoir Function

It has long been appreciated that patients with an ileal bladder substitute have an increased prevalence of urinary tract infection (UTI) but the effect of infection on function of the reservoir remains unknown. In this retrospective study Zehnder et al (page 2545) from Berne, Switzerland evaluated 48 patients for changes in continence, post-void residual and urinary retention as well as response to antibiotic therapy. Of the 48 patients 31 complained of new onset incontinence, 28 had an increase in day
and night incontinence, and 19 had emptying disturbances. Baseline status returned in all patients after appropriate antibiotic therapy. Differences in daytime/nighttime incontinence, post-void residual and urinary retention before, during and after UTI were statistically significant. The authors conclude that for patients with an ileal bladder, UTIs should be treated. Conversely, new onset of urinary incontinence or residual urine in patients with an ileal bladder warrants evaluation for a urinary tract infection.

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