Objective: To assess side effects, toxicity, and quality-of-life scores in men with advanced prostate cancer treated with either hormones alone or hormones and radiotherapy.

Methods: The Scandinavian Prostate Cancer Group Study 7 (SPCG-7) and the Swedish Association for Urological Oncology 3 (SFUO-3) was a randomized controlled trial that compared men with locally advanced prostate cancer treated with either hormone therapy alone or hormone plus radiotherapy. Urinary, bowel, and sexual function were assessed with the prostate-cancer symptom scale (PCSS; a validated questionnaire), and quality of life was assessed with the QLQ-C30 developed by the European Organization for Research and Treatment of Cancer.

Results: Patients in the combination arm (hormones plus radiation) did have statistically significant increases in overall urinary, bowel, and sexual bother scores compared to patients who received hormones alone. These increases were very small, though, and perhaps not clinically significant. Quality-of-life scores were not significantly different.

Conclusions: In men with high-risk, localized prostate cancer who are candidates for combination hormone treatment plus radiotherapy, the side effect toxicity does not appear to be significantly worse with the combination.

Reviewer's Comments: In the SPCG-7/SFUO-3 study, men with locally advanced prostate cancer were randomized to receive hormone therapy with flutamide or the same treatment plus local radiation to the prostate. The results showed that the combination could actually double prostate cancer-specific survival and improve overall survival as well. The question of increased toxicity when adding radiation is important, so it is useful that the Scandinavian group assessed this issue in their study. They used standardized questionnaires to assess urinary, bowel, sexual, and overall quality-of-life scores for each group and report on 4 years of follow-up. The questionnaires they used are different than some we are more familiar with in the U.S., such as the EPIC, but they are validated and answer the same questions. Not surprisingly, there were statistically significant increases in all domains for patients who received combination therapy, but the differences were relatively small. Specifically, for absolute differences in symptom scores, there was only 6% more moderate to severe urinary bother, 2% more dysuria, 4% more bowel bother, and 13% more erectile dysfunction. These small statistical differences did not seem to translate into clinically significant differences, because quality-of-life scores did not differ between groups. Therefore, in counseling your patients, you must weigh the benefit of significantly improved 10-year survival with the small increases in functional side effects seen, which did not appear to affect quality of life. These additional data are extremely useful in making a decision to recommend combination therapy to your patients.

print tag: () Refer to original journal article.
Molecular Markers Can Predict Prostate Cancer Mortality

Molecular Markers and Death From Prostate Cancer.
Concato J, Jain D, et al:
Ann Intern Med; 2009; 150 (May 5): 595-603

Molecular markers will likely improve our diagnostic accuracy in prostate cancer. Three such markers (bcl-2, p53, and microvessel density) have been shown to do so in a well-designed study.

**Objective:** To assess the predictive power of specific molecular markers (bcl-2, p53, and microvessel density [MVD]) on prostate cancer mortality.

**Participants/Methods:** 1313 veterans with prostate cancer between 1991 and 1995 were identified. Clinical data were collected from medical records for 1172 men through 2006. Tissue from initial diagnosis was obtained and stained for specific molecular markers, and analysis was then performed to correlate markers with clinical outcomes.

**Results:** Follow-up was from 11 to 16 years, over which time 71.8% of men died, 21.5% of whom died from prostate cancer. In addition to classic predictors of death from prostate cancer, such as PSA level and Gleason score, the markers bcl-2, p53, and MVD were all shown to be significant in predicting prostate cancer death.

**Conclusions:** Increased presence of the molecular markers bcl-2, p53, and MVD at diagnosis is associated with an increased risk of long-term death from prostate cancer.

**Reviewer’s Comments:** There have been many marker studies in prostate cancer, and the ones used in the current study are not new or novel. What sets this article apart is the study design. Commonly, marker studies compile a small series of tissue specimens and stain for various markers to find something interesting, in what can be considered a "cross-sectional" study design, which gives no information about prognosis. Instead, these authors chose to do something more ambitious. They used a cohort design, looking at just a few interesting markers, and looked at prostate cancer from 15 years earlier, so the findings would have 15-year follow-up. In addition, they powered the study well, by including >1000 men. The "cohort" design refers to how they compared 2 sets of patients. For example, they determined which patients had low MVD versus high MVD at diagnosis, 15 years earlier. Then they "followed" those patients over time to see if there were more deaths in one group or the other. This is the best way to answer a question about prognosis. Specifically, they found that the risk of prostate cancer death was increased by presence of bcl-2 (a marker for cell death, or "apoptosis") by 61%; p53 (a marker of cell-cycle regulation) by 48%, and increased MVD (a marker of blood vessel formation) by up to 320%. The bottom line is that all markers were found to be significant. While there are criticisms and limitations to this study due to its retrospective nature, it is still one of the most interesting marker studies in recent times. With this type of conclusive data, we can move forward in determining the practical, clinical utility of these markers, and they may someday show up in our offices.

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Normal-Calcium, Low-Salt, Low-Animal Protein Diet May Be Beneficial for Hyperoxaluria

_Diet to Reduce Mild Hyperoxaluria in Patients With Idiopathic Calcium Oxalate Stone Formation: A Pilot Study._


Idiopathic calcium oxalate nephrolithiasis should be treated with a normal-calcium, low-salt, low-animal protein diet.

**Objective:** To determine whether a normal-calcium, low-animal protein, low-salt diet is as effective in reducing hyperoxaluria in idiopathic calcium oxalate nephrolithiasis as compared with the traditional low-oxalate diet that is routinely recommended.

**Design:** Cohort comparison with historic controls.

**Participants:** 56 patients with idiopathic calcium oxalate stone formation with mild hyperoxaluria.

**Methods:** The treatment group consumed normal-calcium, low-animal protein, low-salt diet for a 3-month period and compared urinary parameters with free diet consumption. Results were compared with those of a historical control group of 20 patients consuming a low-oxalate diet.

**Results:** At 3 months, the mean oxaluria level in the normal-calcium, low-salt, low-protein diet had decreased from 50.2 to 35.5 mg/day compared to a decrease from 45.9 to 40.2 mg/day with the traditional low-oxalate diet (_P_ =0.005).

**Conclusions:** A normal-calcium, low-animal protein, low-salt diet can reduce oxalate excretion in hyperoxaluric patients. Randomized studies need to confer the findings and determine if a resultant decrease in stone production occurs.

**Reviewer’s Comments:** Most idiopathic calcium oxalate stone formers are counseled to increase water intake and decrease oxalate consumption. Water intake is recommended at 2 L/day during cold weather and 3 L/day during warm or hot weather, and patients should avoid oxalate-rich foods to include spinach, rhubarb, beets, nuts, chocolate, tea, wheat bran, and strawberries. The evidence showing these dietary recommendations are efficacious is lacking, and it must be remembered that a majority of oxalate intake is accounted for by bread, pasta, rice, vegetable, and sweets. Therefore, this study tried to determine if the traditional recommendation of decreasing oxalate and increasing fluids was as effective as a diet recommended to have normal calcium, low-salt, low-animal protein. They found a significantly lower amount of urinary oxalate in the study diet than in the traditional low-oxalate diet alone. We do not have any information if stone production was lower, however. As also pointed out by the authors, the study diet contained a greatly lower amount of calories, moderately lower amounts of proteins, cholesterol, and total fat, and much less sodium and more calcium. Study patients not only had lower urinary oxalate levels, but also less sodium, chloride, and calcium. Body weight decreased by an average of 2.1 kg during the 3-month period. I have no doubt that the more comprehensive dietary changes will result in a much lower urinary oxalate excretion. Calcium oxalate metabolism is very complex, and simply reducing the oxalate intake in a diet probably does very little. I would recommend that all patients follow a normal-calcium, low-salt, low-protein, and low-oxalate diet. It is heart healthy and stone healthy. We should all follow this diet and be much healthier, but it is difficult to convince ourselves and our patients to stay on such a diet.

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Recurrent UPJ Obstruction Can Be Successfully Treated With Endopyelotomy

_Ureteroscopic Holmium Laser Endopyelotomy for Ureteropelvic Junction Stenosis After Pyeloplasty._

Ureteroscopic laser endopyelotomy is a reasonable option for pyeloplasty failures.

**Objective:** To evaluate use of ureteroscopic holmium laser endopyelotomy to manage recurrent ureteropelvic junction (UPJ) obstruction after pyeloplasty.

**Design:** Retrospective chart review.

**Participants:** 15 patients with symptomatic recurrent UPJ stenosis after pyeloplasty.

**Methods:** All patients underwent ureteroscopic laser endopyelotomy. Eleven patients had stents in place prior to endopyelotomy. 7F ureteral stents were placed for 6 weeks and then ureteroscopy was repeated with possible stent removal. Patients were then studied at 3 months after stent removal.

**Results:** Patients presented at a mean of 3.2 years after pyeloplasty. Three patients required repeat incision. Those requiring repeat incision were non-stented prior to endopyelotomy. All patients were discharged home within 23 hours without complications. Symptomatic improvement was documented in all patients, as was improved drainage in all 3-month nuclear scans.

**Conclusions:** Laser endopyelotomy is an appropriate minimally invasive procedure for post-pyeloplasty stenosis. Results may be better in patients with ureteral stents prior to the procedure.

**Reviewer's Comments:** This manuscript confirms the findings of other studies suggesting that endopyelotomy is an appropriate first-line therapy for UPJ recurrence after pyeloplasty (as long as crossing vessels are not present). The current study differs from others in that the technique is a semirigid ureteroscopy from a retrograde approach (as opposed to antegrade and/or flexible ureteroscopic incision), a mandatory second-look ureteroscopy is performed at 6 weeks, and findings suggest that prior stent placement is advantageous (while most studies show better results without prior stenting). I believe a lot of the differences found in this study are due to use of the semirigid ureteroscope. Generally, most urologists find better flexibility and precision with a flexible ureteroscope. Also, it is easier to distinguish the area of stenosis if it is not previously stented to avoid the edema associated with stenting. These authors likely found better success rates with prior stenting since it passively dilated the ureter to allow easier passage of the semirigid ureteroscope. Most previous studies also did not take a ureteroscopic look at the UPJ to determine success. The success of UPJ repair doesn't necessarily depend on visual appearance but on functional drainage. Therefore, I am not sure a second look is necessary. Generally, I believe ureteroscopic laser endopyelotomy is a good first attempt at failed pyeloplasty. However, I believe having them non-stented prior to endopyelotomy to get better assessment of the narrowed area, using a flexible ureteroscope during the case, and simply removing the stent at 6 weeks and waiting for the 3-month nuclear scan may be a better approach.

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Interest in NOTES Not Exclusive Only to Urologists

**Natural Orifice Translumenal Endoscopic Surgery: Myth or Reality?**

Ponsky LE, Poulose BK, et al; 
*J Endourol;* 2009; 23 (May): 733-735

Progress is being made in the development of natural orifice translumenal endoscopic surgery, with dedicated research efforts evaluating transgastric, transvaginal, transrectal, and transvesical approaches.

Natural orifice translumenal endoscopic surgery (NOTES) involves introduction of an endoscope through a natural orifice with intentional perforation of a hollow viscus for subsequent passage of the endoscope into a body cavity, most commonly the peritoneal cavity. Natural orifices used by researchers have included the mouth, anus, vagina, and urethra. The corresponding hollow viscera that have been perforated are the stomach, rectum, vagina, and bladder. Transvaginal access allows for direct line of sight to the kidneys and for larger-caliber instruments to be used. Specimens are easily extracted intact through the vagina. Transgastric access requires retroflexion of the endoscope to see upper abdominal organs, and closure of the gastrotomy site can be problematic. Colonic bacterial colonization potential for spillage sepsis is the main challenge for transcolonic approaches. The challenge for transurethral procedures is the limitation of instrument size and requirement for specimen morcellation. Recently, significant steps have been made in reliable closure of various access sites, but further study of this hurdle is needed. The intent of pure NOTES is to perform a variety of procedures without the need for any skin incisions. Modified laparoscopic techniques with use of transvaginal access reduce the required number of trocars and takes advantage of NOTES techniques. Hybrid NOTES procedures have been described using a combination of natural orifice access sites. Hybrid procedures offer the advantage of improved triangulation over that provided by single access procedures. Strides to improve NOTES are being made in the form of new instrumentation. Endoscopes are being tailored for the unique requirements of the procedure. Deployable instrumentation such as magnetic retractors, cautery dissectors, and cameras introduced by the University of Texas Southwestern Medical Center group can be deployed into the peritoneal cavity allowing for additional room in the working channel for other instruments. Also, the role of robotics in NOTES is also under investigation.

**Reviewer's Comments:** Interest in NOTES is not exclusive only to urologists. Gastroenterologists and gastrointestinal surgeons have joined forces with urologists to form the Natural Orifice Surgery Consortium for Assessment and Research. This group encourages cooperation among the fields and continued experimentation to investigate various forms of NOTES. However, urologists will undoubtedly form a part on the crucial role in the development of NOTES. With the advancement technology, “the distinction between laparoscopy and endoscopy becomes blurred,” as Dr Ponsky points out. Endourologists are facile with both of these techniques and are at the forefront of this field.

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Operative Time, Blood Loss Reduced With Preperitoneal Robotic Simple Prostatectomy

Preperitoneal Robotic Prostate Adenomectomy.
John H, Bucher C, et al;
Urology; 2009; 73 (April): 811-815

Preperitoneal robotic-assisted laparoscopic simple prostatectomy is feasible with low blood loss.

Background: Urologists are a lot like fishermen when it comes to simple prostatectomies. We all love to tell the story about the "big one" that we encountered.

Objective: To report on the authors' encounters with big prostates.

Participants/Methods: 13 patients underwent preperitoneal robotic simple prostatectomies. The extraperitoneal space was dissected with balloon dilation, and 5 trocars were used for cases, including a 12-mm camera port, two 8-mm robotic ports, and one 5-mm and one 12-mm assistant port. A vertical cystotomy was made to the prostatic vesical junction. After exposing ureteral orifices, hot scissors were used to create the dissection plane at the dorsal bladder neck. Enucleation was assisted with a single finger in the last 3 cases. The apical dissection was performed under direct vision.

Results: Median operative time was 210 minutes. Median blood loss was 500 mL. The finger-assisted cases were shorter, with less blood loss. No transfusions were required, and there were no open conversions. Median specimen weight was 82 g (range, 50 to 150 g). Only a urethral Foley catheter was left in place for about 6 days. With a 13-month follow-up, patients had no postoperative residual urine and a urinary flow rate of 23 mL/second. One patient had a bladder neck contracture that required incision.

Reviewer's Comments: Simple prostatectomies are associated with a 30% complication rate, including an 8% transfusion rate. This paper nicely reviews the more recent laparoscopic experience with simple prostatectomies. Articles describing pure laparoscopic procedures from a transperitoneal and preperitoneal approach are referenced, and recent robotic experience is included. Just last year, Sotelo and colleagues reported a series of transperitoneal robotic simple prostatectomies, while the current series reports on the feasibility of the preperitoneal approach. In general, the laparoscopic and robotic series report an improved blood loss from 125 to 516 mL, likely due mainly to the effect of the insufflation pressure to diminish venous oozing. The authors of this article also suggest that single-finger digital dissection after starting the plane speeds the procedure along, reducing blood loss even more. More studies are needed to define the role of laparoscopy and robotics for this particular operation.

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Are All Incontinent, Overweight Women Depressed?

Association Between Urinary Incontinence and Depressive Symptoms in Overweight and Obese Women.

Sung VW, West DS, et al:
Am J Obstet Gynecol; 2009; 200 (May): 557.e1-557.e5

The frequency of urinary incontinence episodes and a degree of bother and life impact of urinary incontinent symptoms are all associated with self-reported depression among overweight women, independent of weight.

**Objective:** To determine the association between urinary incontinence and depressive symptoms, in order to improve the knowledge of the burden of incontinence.

**Participants/Methods:** A total of 338 incontinent women who were overweight or obese and had enrolled in the Program to Reduce Incontinence by Diet and Exercise (PRIDE) clinical trial were randomized to a 6-month lifestyle intervention (weight loss and exercise or a structured education program). To be enrolled, women had to be aged at least 30 years, have a body mass index between 25 and 50 kg/m2, and report >=10 urinary incontinent episodes per week. The primary outcome measure in this trial was the self-reported change in incontinent episodes on the 7-day voiding diary 6 months after being randomized. Participants also completed the self-administered Beck Depression Inventory (BDI) to assess depressive symptoms. Those who had a BDI score of >=10 were categorized as having depressive symptoms.

**Results:** Patients with depressive symptoms reported a higher mean number of urinary incontinent episodes per week (28 vs 23; \( P =0.005 \)). Urogenital Distress Inventory and Incontinence Impact Questionnaire scores were also significantly worse in patients with depressive symptoms and urinary incontinence. Consideration of other known risk factors for depression, including smoking, race, and medical comorbidities, did not affect these findings.

**Reviewer's Comments:** Because this study population included only obese and overweight women, the validity of these findings may not extend to normal weight women with urinary incontinence or to overweight or obese women who are not participants in a randomized trial for behavioral weight loss.

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How Bothersome Is Nocturia?

Bother Related to Bladder Control and Health Care Seeking Behavior in Adults in the United States.

Benner JS, Becker R, et al:
J Urol; 2009; 181 (June): 2591-2598

Symptoms due to overactive bladder increase with age. Urgency and urge incontinence are more bothersome in women in all age groups. Nocturia is the most commonly reported bothersome symptom reported by both genders.

**Objective:** To report (1) the degree of bother due to overactive bladder (OAB) symptoms and (2) patterns of physician consultation and medication use for OAB symptoms in adults in the United States.

**Participants/Methods:** 260,000 adults were selected, and 63% (162,906) responded. Of respondents, 55.0% were women and 21.8% were aged >65 years. Participants were surveyed using the Overactive Bladder-Validated 8 awareness tool. Additional questions on treatment patterns and type, consultation with health care providers, OAB diagnosis, and medications were also given.

**Results:** An Overactive Bladder-Validated 8 score of >=8, indicating probable OAB, was reported by 26.6% of the total sample (23.7% of men and 28.9% of women). The percentage reporting a score of >8 increased with age. Symptoms suggesting bother were more common in women than men up to age 65 years, at which time the trend reversed. Nocturia was the most common symptom reported as bothersome, affecting 58.2% of men and 68.7% of women. Women were more likely than men to report bother due to frequency until age 75 years, when the trend again reversed. Urinary urgency was bothersome to 38.6% of respondents. Women were more likely than men to consult a medical provider and, overall, the proportion of respondents who reported receiving treatment was 2 times higher in women than men (35.8% vs 18.2%).

**Reviewer's Comments:** The National Family Opinion Household Panel is not necessarily representative of all ethnic groups or socioeconomic strata in the United States; therefore, the findings in this study probably should be projected only to predominately white Americans of middle socioeconomic status.

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Sperm DNA Damage, Decreased Semen Parameters Weakly Overlap

Correlation Between DNA Damage and Sperm Parameters: A Prospective Study of 1,633 Patients.

Cohen-Bacrie P, Belloc S, et al:
Fertil Steril; 2009; 91 (May): 1801-1805

DNA fragmentation testing and standard semen parameters are correlative but not strongly associated. The utility of testing for sperm DNA damage remains in question.

Background: Results of a previous study of sperm DNA damage and its correlation with traditional semen parameters and outcomes of assisted reproductive techniques have been mixed.

Objective: To correlate sperm DNA damage with traditional semen parameters and computer-aided sperm analysis (CASA).

Design/Participants: Prospective analysis of 1633 men referred for infertility workup.

Methods: Single semen samples from all subjects were analyzed and correlated after semen testing with CASA and DNA damage testing using terminal deoxyribonucleotidyl transferase-mediated dUTP nick-end labeling (TUNEL).

Results: 30% of all subjects had abnormal TUNEL results (>30%). Of 21 semen parameters assessed, 7 significantly correlated with increased DNA damage: increased age, increased length of abstinence, increased percentage of abnormal forms, increased abnormal necks, increased coiled tails, decreased total motile sperm count, decreased rapid progression, and decreased vitality. The remaining 14 variables did not correlate, including semen volume and concentration, semen pH, number of motile and atypical spermatozoa per ejaculate, and presence of leukocytes and poly nuclear cells in the ejaculated sperm.

Conclusions: Sperm DNA damage and sperm parameters are weakly linked.

Reviewer's Comments: This straightforward but important study concludes that sperm DNA damage and traditional sperm parameters are complementary, rather than strongly linked. The literature is fraught with studies regarding DNA fragmentation, but what is the appropriate setting to test for sperm DNA damage? Mixed outcomes in research arguing for clinical use of sperm DNA testing, in part, likely stem from various DNA damage assays' ability to detect clinically important DNA damage from insignificant (or even physiologic) damage. The authors conclude that for infertile couples "in the case of sperm of good quality [traditional parameters and use of CASA]...a careful analysis of chromatin structure and DNA decays is mandatory." Other experts elegantly argue that further prospective studies are required before routine adoption of DNA testing is undertaken. Specific clinical scenarios support occasional use of DNA fragmentation testing such as for intrauterine insemination pregnancy prediction or in couples with recurrent pregnancy loss. However, suboptimal DNA fragmentation test characteristics (positive-/negative-predictive value) and current literature review findings should be considered and disclosed to patients before initiation of testing.

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TEMPE (PSD502) Spray Offers Hope for Premature Ejaculation

PSD502 Improves Ejaculatory Latency, Control and Sexual Satisfaction When Applied Topically 5 Min Before Intercourse in Men With Premature Ejaculation: Results of a Phase III, Multicentre, Double-Blind, Placebo-Controlled Study.

Dinsmore WW, Wyllie MG:
BJU Int; 2009; 103 (April): 940-949

PSD502 (TEMPE), a prilocaine/lidocaine spray, offers great promise for treatment of premature ejaculation.

**Background:** Premature ejaculation (PE) is estimated to affect 30% to 40% of the male population at some point. Thus far, treatments have had several shortcomings, including lack of durability, ineffectiveness, inconvenience, and unwanted side effects.

**Objective:** To assess the treatment effect of PSD502 (TEMPE) on men with lifelong PE.

**Design:** Double-blind, randomized, placebo-controlled phase III trial.

**Participants/Methods:** 300 patients with a mean age of 35 years were studied; 200 received PSD502 and 100 received placebo). The majority of patients were white, uncircumcised, and had lifelong PE with a documented intravaginal ejaculatory latency time (IELT) of <=1 minute during >=2 of the first 3 sexual encounters during a month-long evaluation period prior to randomization. Both patient groups had previously undergone some form of treatment in nearly the same proportion (roughly 25%). Over a 3-month period, men applied either placebo or 3 sprays of TEMPE 5 minutes prior to intercourse.

**Results:** Mean IELT for the treatment group significantly increased from 0.6 minutes to 3.8 minutes and from 0.6 minutes to 1.1 minutes for the placebo group. Several other variables had significant improvement for the intervention arm, including reported differences in ejaculatory control, sexual satisfaction, medication rating, and proportion of IELTs >1 minute (90% vs 54%) or 2 minutes (74% vs 22%). Localized treatment-related events were rare and similar in both arms (about 3%).

**Conclusions:** After 3 months of treatment with PSD502, a statistically significant treatment improvement was present in the majority of primary and secondary study end points, with little systemic adverse effects.

**Reviewer's Comments:** The authors are to be congratulated on a well-done study demonstrating impressive efficacy of PSD502. Of note was the significant difference in attrition rate during the study period for the treatment group compared to the placebo group (18 and 4, respectively). Previous studies on dapoxetine (a PE-tailored selective serotonin reuptake inhibitor not approved for use in the U.S.) yielded similar increases in IELT from <1 minute to about 3 minutes, but at the cost of many more side effects. Topical lidocaine has been used off-label for years but is messy, requires condom use, and can cause significant numbness in both the penis and/or vagina. Apparently, differences in keratin content of the glans penis versus penile shaft and TEMPE's unique penetrative properties allow it to be effective without causing significant hypoesthesia rates. Other recent important findings regarding lifelong PE are its moderate genetic effect (28%, Jern et al) and 2 separate investigators' implication of serotonin transporter genes polymorphisms in leading to short IELTs (Paddy et al, Safarinejad). As our rudimentary understanding of ejaculation and PE progress, TEMPE will likely play a pivotal role in management of PE.

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Reduction in LDL, hs-CRP Best Indicators of Optimum Health in Statin Users

Reduction in C-Reactive Protein and LDL Cholesterol and Cardiovascular Event Rates After Initiation of Rosuvastatin: A Prospective Study of the JUPITER Trial.
Ridker PM, Danielson E, et al; 
Lancet; 2009; 373 (April 4): 1175-1182

An low-density lipoprotein of <70 mg/dL and an high-sensitivity C-reactive protein of <1.0 mg/L should be considered one of the new gold standards for optimum health.

Background: Statins not only reduce cholesterol, but also tend to reduce markers of inflammation such as high-sensitivity C-reactive protein (hs-CRP), which may play a role in the risk of heart disease and cancer. The JUPITER trial is one of the most important cardiovascular prevention trials in medicine to demonstrate that otherwise healthy individuals with normal cholesterol (LDL, 100 mg/dL) and elevated hs-CRP levels (>2 mg/L) could reduce their risk of a future cardiovascular event by taking a low-dose statin drug (20 mg of rosuvastatin/Crestor(R)). The JUPITER trial was stopped only 1.9 years into the 5-year study because of the dramatic and rapid positive results.

Objective: To determine if there is a graded reduction in cardiovascular events with greater reductions in LDL and hs-CRP levels in the JUPITER trial.

Design/Participants: 15,548 healthy men and women that participated in the randomized double-blind placebo controlled JUPITER trial were analyzed based on their LDL and hs-CRP levels.

Methods: A cardiovascular event in this study consisted of one of the following: non-fatal myocardial infarction, non-fatal stroke, unstable angina, arterial revascularization, or cardiovascular death.

Results: Mean age of the participants was 65 years with a body mass index (BMI) of 28. Individuals with the following LDL and hs-CRP levels had the following results when taking this statin compared to placebo: LDL >=70 and hs-CRP >=1 experienced a 9% reduction in the risk of a cardiovascular event; LDL >=70 and hs-CRP <1 experienced a 35% reduction; LDL <70 and hs-CRP >=1 experienced a 50% reduction; and LDL <70 and hs-CRP <1 experienced a 79% reduction. The 20-mg statin reduced the median LDL cholesterol by 50% (P <0.0001) and the median hs-CRP by 37% compared to placebo (P <0.0001).

Conclusions: A reduction in both LDL and hs-CRP are the best indicators of a potential positive impact with a statin drug in healthy individuals.

Reviewer's Comments: This study is nothing less than remarkable in terms of the potential clinical impact of the findings. I get tired of so called "experts" telling the public that an LDL of <=130 is acceptable and hs-CRP needs more evidence before it is utilized in clinical practice. We need to remember that the alternative consequence (ie, death) of not being aggressive in terms of education and intervention is completely unacceptable. However, I am not suggesting that everyone has to achieve these low numbers regardless of cost and side effects, but at least they should be made aware of or have the right to know what the ultimate goal is today for any individual. I also believe that these are the numbers that will be associated with a potential small reduction in the risk of cancer or risk of progression with certain forms of cancer. I hope I am right, but if not, who cares, because at least it will still help to reduce the number 1 cause of death in men and women (aka cardiovascular disease) over the last 109 years in the U.S.

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Lower CRP Levels May Be Associated With Lower Risk of Cancer, Death

Baseline C-Reactive Protein Is Associated With Incident Cancer and Survival in Patients With Cancer.
Allin KH, Bojesen SE, Nordestgaard BG:
J Clin Oncol; 2009; 27 (May 1): 2217-2224

C-reactive protein may be a potential blood marker to predict risk of heart disease and/or cancer.

**Background:** C-reactive protein (CRP) is an acute phase reactant that is increased during infection, inflammation, heart attack, and perhaps even cancer. CRP is synthesized in the liver after an inflammatory stimulus, which could be a marker of the damage that is caused in the premalignant state or after a diagnosis of cancer. Regardless, the role of CRP and cancer needs further clarification.

**Objective:** To determine the role of CRP in predicting the risk of being diagnosed with and/or surviving cancer in the general population.

**Participants/Methods:** 10,408 individuals with recorded baseline CRP levels from the Danish general population were followed for up to 16 years; over 1500 individuals developed cancer and approximately 1000 died of cancer. Individuals with a cancer diagnosis at baseline were excluded from this analysis.

**Results:** Baseline CRP levels of >3 compared to <1 mg/L were associated with a 30% increase in the risk of cancer of any type, and an 80% increased risk for an early death from cancer. An increased CRP level was associated with an early death in patients with localized disease ($P =0.03$), but not in individuals with metastatic disease. CRP was not associated with the risk of being diagnosed with some cancers, such as prostate cancer, but was more associated with these cancers in terms of prognosis.

**Conclusions:** Elevated levels of CRP are associated with an increased risk of cancer, and an early death from cancer, especially in patients without metastatic disease.

**Reviewer's Comments:** What the heck are we suppose to do with this information?! Should everyone receive CRP or high-sensitivity CRP blood tests during their annual physical? The answer is "yes!" Why not? It is a very cheap blood test and is just a marker of inflammation. This blood test value is generally reduced with better and improved wellness such as exercise, better diet, and reduced belly fat, which is similar to cholesterol. In other words, the risk versus the benefit of this blood test seems to favor benefit in most cases. If this test is utilized before or after localized treatment for many cancers, perhaps this is also a good thing because it may just be an indicator of adherence to healthy behaviors.

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Ureterolithiasis Linked to Poor Follow-Up Habits

Sterrett SP, Moore NW, Nakada SY:
Urology; 2009; 73 (June): 1195-1197

A significant percentage of patients with ureterolithiasis never see a urologist.

**Objective:** To determine patterns of follow-up for patients diagnosed with ureterolithiasis in an emergency department (ED) visit.

**Design:** Retrospective chart review.

**Participants:** 130 first-time stone formers with ureteral stones and no prior urological visit within the past 5 years.

**Methods:** Follow-up visits of patients seen in a single ED over a 2-year period were retrospectively determined.

**Results:** 14 patients seen in the ER had immediate urological consultation. Of the 116 patients discharged home from the ER without urological consultation, 71 (61%) followed up with a urologist, 27 (23%) followed up with a primary care physician, 10 (9%) returned to the ED for follow-up, and 8 (7%) patients had no further follow-up. When stratified for stone size, 44 patients had ureteral calculi >=5 mm, of which 38 (86%) either had immediate urological consultation or follow-up with a urologist as an outpatient.

**Conclusions:** Most patients seen in the ED for ureterolithiasis >=5 mm follow-up with a urologist. However, a significant percentage of overall patients with newly diagnosed ureteral stones in the ED never see a urologist in follow-up.

**Reviewer's Comments:** This study is intended to provide a starting point for evaluating practice patterns and follow-up in ED visits for ureterolithiasis. It is limited by being a single institution study at a tertiary care center. However, it does demonstrate relatively poor urological follow-up of patients with ureterolithiasis. Ideally, these patients would be followed by a urologist to ensure proper medical expulsive therapy, prescriptions, eventual stone passage (avoiding silent obstruction), and counseling on stone prevention techniques to limit stone recurrence episodes. This study demonstrates that many patients don't necessarily follow ED recommendations to follow-up with a specialist, and therefore it is important that we educate our ED physician colleagues and primary care physicians on medical expulsive therapy and stone prevention techniques. The authors comment that this study may also be a platform to determine the economic burden imposed by urolithiasis. Along those lines, it would have been interesting to determine why patients did not follow-up with a urologist, and what percentage cited financial reasons and/or had no medical insurance/coverage. Many of these stone patients may have been unfounded and added even greater economic burden on all parties involved.

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Newest-Generation Piezoelectric Lithotripters Have Modest Success Rates


Urology; 2009; 73 (May): 958-963

The newest-generation piezoelectric lithotripters have inferior stone-free rates compared to earlier generation electrohydraulic and electromagnetic machines.

**Objective:** To determine stone-free, success, and complication rates for the newest-generation piezoelectric lithotripter, the Piezolith 3000.

**Design:** Retrospective chart review.

**Participants:** 139 patients with solitary kidney stones undergoing a single shockwave session with the Piezolith 3000.

**Methods:** All procedures were performed under IV sedation. Stone-free status was the absence of any fragments, and success was defined as fragments <4 mm on a 1-month follow-up KUB.

**Results:** Stone-free rate was 45% after 1 session and success rate was 64%. Stone size correlated with success rate. Overall complication rate was 15.0% with 5.8% major complication rate. Shock rate was 120 Hz. Procedure room time was 33 minutes. Adjunctive procedures were needed in 1.4%, and secondary retreatment rate was 10.0%.

**Conclusions:** The Piezolith 3000 provides modest single-treatment stone-free and success rates. It has a reasonable safety profile. The advantage is rapid and convenient lithotripsy requiring only IV sedation.

**Reviewer's Comments:** Piezoelectric machines provide shockwaves with a smaller F2 and greater peak pressure than electrohydraulic or electromagnetic machines. Piezoelectric machines were designed for treatment with no or minimal anesthesia. However, initial success rates in the 1990s were greatly inferior to the standard electrohydraulic Dornier HM3 machine and the technology fell out of favor in the United States. A newer version of the piezoelectric machines--the Piezolith 3000--has been marketed again in the United States. The authors report their outcomes using the newest-generation machine. The study itself has many flaws to include: 30% of patients having no follow-up imaging, KUB as modality to determine stone-free rate, no stone composition analysis, and treatment at 120 Hz only (due to only 60 or 120 Hz options for treatment of machine). Success rates are low at 45% for stone-free and 64% with <4 mm fragments, even excluding those without follow-up. Success rates would likely be even lower if CT imaging was used to determine success or all patients were captured. This study again demonstrates an inferior outcome of piezoelectric machines compared to other modalities. The only real advantage to these machines is performance under IV sedation alone.

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LSC Results in Subjective Cure of Prolapse Symptoms at Medium Term

Medium-Term Anatomic and Functional Results of Laparoscopic Sacrocolpopexy Beyond the Learning Curve.
Claerhout F, De Ridder D, et al:
Eur Urol; 2009; 55 (June): 1459-1467

Laparoscopic sacrocolpopexy results in good medium-term anatomic and functional outcomes.

Objective: To describe the medium-term anatomic and functional outcome of laparoscopic sacrocolpopexy (LSC).

Design/Participants: Prospective consecutive series of 132 patients that underwent laparoscopic sacrocolpopexy.

Methods: Cases were indicated by presence of symptomatic vault prolapse. At a minimum, this consisted of stage 2 prolapse of the upper posterior wall of the vagina. Using a 4 trocar technique, 2 separate meshes were sutured to the posterior and anterior aspect of the vagina. The posterior mesh was also fixed laterally to the levator muscle. The vault was positioned at the level of the ischial spines and then fixed tension-free with 3 staples to the sacral promontory. Twelve patients also underwent hysterectomy, 5 patients underwent tension-free vaginal tape for stress urinary incontinence (SUI), and 2 patients underwent rectocele repair. Anatomic cure was defined as absence of stage 2 prolapse or more. Mean follow-up was 12.5 months.

Results: Vault prolapse was cured in 98%. Anatomic failure for all compartments was 22%, with 2% at the vault, 3% anteriorly, and 18% posteriorly. The subjective cure rate was 92%, and objective failure could be seen in only 30% of these patients. Preexisting urinary incontinence and fecal symptoms were cured in about 40%. De novo SUI occurred in 7%, while de novo constipation occurred in 5%. Two patients experienced vault infections in the early postoperative course. Nine patients required reoperation due to mesh erosion or pain related to the mesh. Of patients who were sexually active, 33% considered their sex life to be impaired because of a vaginal lump and 30% reported dyspareunia.

Conclusions: LSC results in good anatomic outcome and subjective cure of prolapse symptoms at medium term. The posterior compartment was most vulnerable for recurrence.

Reviewer's Comments: The authors are to be commended for this large prospective study. While the somewhat higher than expected incidence of posterior failures may require more attention to this aspect of the technique, the study affirms the feasibility of successful repair of vaginal vault prolapse with sacrocolpopexy via laparoscopy. The rate of dyspareunia will also need to be scrutinized in future studies, but is probably related to the surgical technique of fixing the mesh laterally to levator muscles. The procedure is also being reported with robot assistance and laparoscopically via a single-port.

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Urologists in Training Should Perform Laparoscopic Ureterolithotomy Transperitoneally

Laparoscopic Ureterolithotomy: A Comparison Between the Transperitoneal and the Retroperitoneal Approach During the Learning Curve.  
Bove P, Micali S, et al: 
J Endourol; 2009; 23 (June): 953-957

Laparoscopic ureterolithotomy can be accomplished either transperitoneally or retroperitoneally depending on surgeon preference.

**Objective:** To compare the transperitoneal approach and the retroperitoneal approach of laparoscopic management of ureteral stones at 2 different urologic centers during the learning curve period.

**Design:** Prospective evaluation.

**Methods:** One surgeon performed 18 transperitoneal laparoscopic ureterolithotomies, and another performed 17 retroperitoneal procedures. Indications for procedures were >10 mm, impacted, proximal ureteral calculi that were inadequately treated with shockwave lithotripsy (SWL) or unmanageable by ureteroscopy. During the procedure, a grasper or vessel loop was placed around the ureter proximal to the stone to prevent upper migration. No ureteral stent or nephrostomy tube was left in place postoperatively unless placed preoperatively (n=11) for severe hydronephrosis or pyonephrosis, fever, septic status, acute renal impairment, or pain.

**Results:** Mean total operative time for transperitoneal procedures was 75 minutes compared to 102 minutes for retroperitoneal procedures ($P<0.01$). Times for laparoscopic access and suturing were statistically shorter for the transperitoneal approach. One major complication occurred in the combined series consisting of a venous injury requiring open conversion in the transperitoneal group. However, blood loss was minimal in all cases. Ten of 17 retroperitoneal cases had a peritoneal tear that compromised working space. The transperitoneal group had 6 cases with a postoperative fever, 2 wound hematomas, 1 ileus, and 1 persistent hydronephrosis requiring postoperative nephrostomy placement. The retroperitoneal group had 7 cases with a postoperative fever, 2 wound hematomas, and 1 retroperitoneal hematoma requiring postoperative nephrostomy placement. At 12 months' follow-up, no cases of ureteral stricture were reported.

**Conclusions:** The authors suggest that urologists in training for laparoscopy perform laparoscopic ureterolithotomy using a transperitoneal route. In expert hands, both transperitoneal and retroperitoneal approaches are feasible, and the choice depends on personal preference.

**Reviewer's Comments:** This is an informative report on a comparison between transperitoneal and retroperitoneal approaches for laparoscopic ureterolithotomy. This procedure is performed uncommonly because of the SWL success and technologic advances of ureteroscopy, but should certainly stay in the armamentarium of practicing urologists. Urologic laparoscopists more routinely perform pyeloplasties, which require similar skill sets including ureteral dissection and suturing. As with pyeloplasties, this report shows that ureterolithotomies can be safely and successfully performed by either approach, and choice of approach depends mainly on surgeon preference and experience. The authors report that one of the factors that significantly slowed the retroperitoneal operative times was lack of working space due to decompression through a peritoneal tear, which occurred in 59% of those cases. This is a relatively high rate of tear, and the key to preserving the working space is prevention of the tear. I prefer to digitally create the initial working space rather than use dissecting balloons or bluntly dissect with the laparoscope. Then, with safe placement of a working trocar posteriorly, dissection under vision anteriorly can proceed to carefully reflect the peritoneum without tears.

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OAB Symptoms Chronic, Last More Than 10 Years

The Long-Term Natural History of Overactive Bladder Symptoms Due to Idiopathic Detrusor Overactivity in Women.

Garnett S, Swithinbank L, et al:
BJU Int; 2009; April 15 (epub ahead of print):

These results suggest that overactive bladder symptoms due to idiopathic detrusor overactivity are chronic and persistent in nature, lasting at least 10 years, and are associated with a decrease in quality of life.

Objective: To assess the long-term natural history of overactive bladder (OAB) symptoms due to idiopathic detrusor overactivity in women.

Methods: The authors conducted a search of urodynamic studies done at their institution >10 years ago to identify patients who had been referred with OAB symptoms and diagnosed solely with symptomatic idiopathic detrusor overactivity on urodynamic studies. Patients with urodynamic evidence of stress urinary incontinence were excluded as were patients with diagnosed neurologic lesions or outlet obstruction. The authors then attempted to contact all patients whose records met inclusion criteria. In all, 174 women were identified and invited to participate. Fifty-three women had repeat urodynamics, 32 underwent symptom assessment, and 23 completed a mailed questionnaire.

Results: Mean age of patients at baseline was 49.3 years, and mean time to repeat urodynamic studies was 11.5 years. Of 53 patients who did undergo a repeat urodynamics study, 88% had persistent symptomatic idiopathic detrusor overactivity present on their urodynamic study. OAB symptoms between baseline and review, using the patients' urodynamic history, showed little evidence of change. Only pad use per day demonstrated a statistically significant change, with those who had repeat urodynamics showing increased pad use, and those who declined a current urodynamics study decreasing in pad use.

Conclusions: OAB symptoms have a significant effect on the quality of life of those affected. OAB symptoms due to idiopathic detrusor overactivity in women are persistent, lasting for >=10 years in 88% of this study population.

Reviewer's Comments: The personnel performing the repeat urodynamics study on these patients were aware of the purpose of the study as well as the previous diagnosis in patients who underwent the repeat urodynamic studies. These facts may have introduced some bias.

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Do Oral Contraceptives Increase Odds of Urge Urinary Incontinence?

**Oral Contraceptive Use and Incident Urinary Incontinence in Premenopausal Women.**


More research is needed to identify mechanisms by which hormone use may increase incontinence in women.

**Objective:** To investigate the association between oral contraceptive pills and incident urinary incontinence in premenopausal women enrolled in the Nurse's Health Study II.

**Participants/Methods:** >115,000 female nurses aged 25 to 42 years responded to a questionnaire in 1989. Information from these participants has been updated using biennial questionnaires. The initial questionnaire asked participants about urinary incontinence, including frequency and quantity, in 2001 and 2003. Patients were excluded from the study group if they reported any urinary incontinence in 2001. Participants were also asked to report whether they had used an oral contraceptive pill for at least 2 months beginning at the age of 13 years to present. From a baseline population of >23,000 in 2001, there were complete data on almost 22,000 patients. In 2003, 17,600 patients had no incontinence, with approximately 750 reporting incident incontinence in 2003 who had been continent in 2001. These respondents were mailed the supplementary questionnaire and ultimately responses and data were obtained on 600 women who were classified into groups according to incontinence type: stress incontinence (390), urge incontinence (89), mixed incontinence (113), and other (8).

**Results:** After multivariate adjustments, use of all oral contraceptive pills was associated with a modest odds of urinary incontinence of 1.27. However, when the odds of specific urinary incontinence types were associated with oral contraceptive use, urge incontinence had an odds ratio of 2.48 versus only 1.04 for stress urinary incontinence.

**Conclusions:** Use of oral contraceptive pills may be associated with a modest increase in the odds of urinary incontinence among premenopausal women. However, this is one of the first reports of such an association and, thus, further research is needed to confirm our findings and investigate possible mechanisms.

**Reviewer’s Comments:** Overall, the link between exogenous hormone use and increased risk of urinary incontinence is a relatively recent finding. The mechanisms that underlie the association are not completely understood. The findings in this paper, that oral contraceptive pills are associated with a significantly increased odds ratio of urge urinary incontinence may help in identifying some of the mechanisms of the disorder.

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Cigarette Smoking Does Not Affect Testosterone Levels

Evaluation of the Effects of Cigarette Smoking on Testosterone Levels in Adult Men.

Halmenschlager G, Rossetto S, et al:
J Sex Med; 2009; 6 (June): 1763-1772

Neither short- nor long-term tobacco use affects testosterone levels or any of the hormonal axes influencing its production.

Objective: To investigate the relationship between cigarette use and levels of total and bioavailable testosterone as well as pituitary gonadotropins.

Design: Cross-sectional study performed at a single center.

Participants: Of 1356 men aged 30 to 70 years, 255 qualified for the study; 90 were smokers and 165 were not. Illiterate men were excluded as were those with any of the following comorbidities: diabetes, neoplastic or liver disease, pelvic surgery for prostate cancer, psychiatric disease, and class II or III obesity. Use of mood stabilizers, anxiolytics, psychotropics, illicit drug use or alcohol abuse, and endocrine agents were also exclusionary criteria.

Methods: All participants underwent a history consisting of detailed information about current and past tobacco use as well as a physical exam including laboratory work consisting of total testosterone, sex-hormone binding globulin, follicle stimulating hormone, and luteinizing hormone. Hormone levels were compared in smoking and non-smoking men. Comparison was also done by lifelong tobacco use.

Results: No difference was found in any measured hormone level when smoking and non-smoking men were compared. In addition, no correlation between pack-years and altered levels of hormones was found.

Conclusions: Neither short- nor long-term tobacco use affects testosterone levels or any of the hormonal axes influencing its production.

Reviewer’s Comments: Several previous studies with varied methodological quality have provided dramatically different results regarding the effect of tobacco use on testosterone levels. Negative, positive, and neutral effects of tobacco on testosterone and sex hormones have all been shown, and this study endorses a neutral effect. Furthermore, this study explores the role of both short- and long-term tobacco exposure and again, it demonstrates neutral action. Although it lacks the large patient numbers of some previous studies, the great strength of this study is its strict entry criteria resulting in highly matched study groups. Multiple patient characteristics were also compared between smokers and non-smokers with no clinically relevant distinctions found. The most notable omission of comparison was quantity of alcohol use, though alcohol abuse was an exclusionary criteria. Also, the non-smoking group (never smoked or quit >6 months ago) was not analyzed by those with and without a history of smoking. A strength of this article is that it draws from the general population, whereas other studies have looked at specific populations, namely infertility clinic patients. In short, this is a small but clean study showing no relationship between tobacco use and testosterone/gonadotropin levels.

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Coenzyme Q10 Improves Sperm Motility in Men With Idiopathic Asthenozoospermia

Coenzyme Q10 Treatment in Infertile Men With Idiopathic Asthenozoospermia: A Placebo-Controlled, Double-Blind Randomized Trial.
Balercia G, Buldrehini E, et al:
Fertil Steril; 2009; 91 (May): 1785-1792

Coenzyme Q10 administration improves sperm motility. Overall fertility benefit is still unproven.

Objective: To investigate the effect of coenzyme Q10 on sperm motility in idiopathically infertile men.

Design: Placebo-controlled, double-blind randomized trial conducted at a single center.

Participants: Patients were selected from those presenting at an andrology clinic with >2 years of infertility and a detailed infertility evaluation revealing the sole finding of idiopathic asthenozoospermia. In total, 60 patients aged 27 to 39 years were enrolled. Other exclusion criteria were substance abuse, occupational chemical exposure, and systemic disease or medication use in the past 3 months; 55 patients completed the study.

Methods: Patients were randomly selected for the CoQ10 (200 mg/day) or placebo groups. Prior to treatment, and after a 1-month run-in period, asthenozoospermia was reconfirmed by semen analysis. Six months of treatment were followed with semen analysis at 3 and 6 months, and again after a 3-month washout period.

Results: CoQ10 and ubiquinol (reduced CoQ10 form) levels significantly increased in both seminal plasma and sperm cells with treatment. At 6 months, semen samples from men treated with CoQ10 demonstrated a statistically significant improvement in sperm motility with grade a+b sperm increasing from 33% to 39% and grade a sperm increasing from 10% to 15%. Computer-assisted measurements of curvilinear and straight velocities also increased from 28% to 33% and 11% to 13%, respectively. All of these parameters returned to baseline after the washout period. Partner impregnation was achieved by 3 in the placebo group and 6 in the treatment group.

Conclusions: Coenzyme Q10 treatment improves sperm motility. Although not a specific end point, a higher pregnancy rate was noted for patients on CoQ10 treatment.

Reviewer's Comments: This is a rigorous, well-designed study that assesses the effect of CoQ10 administration on asthenozoospermia in men with idiopathic infertility. Improvement in motility as a direct result of CoQ10 was convincing, given loss of treatment effect after the washout period. Interestingly, the study found a higher likelihood of motility improvement in treated men with lower motility levels at baseline. Historically, the use of multivitamins and other antioxidants such as glutathione, carnitine, and CoQ10 have been proposed as beneficial for male fertility, but optimal study design has been lacking. However, the growing body of evidence of the deleterious effect of reactive oxygen species on male fertility has led to the recommendation by many experts of a daily multivitamin in men actively pursuing pregnancy (a practice that I follow, especially in lieu of its low cost, safety, and general health benefit). Six of the CoQ10 treated patients did impregnate their partners compared to only 3 of those on placebo. This merits, and will require, further investigation to see if CoQ10 does indeed improve fertility rates.

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Sorafenib May Be Better Tolerated Than IFN-alpha-2a in Metastatic RCC

Randomized Phase II Trial of First-Line Treatment With Sorafenib Versus Interferon Alfa-2a in Patients With Metastatic Renal Cell Carcinoma.

Studies on sorafenib continue to define its utility and role as an alternate (second-line) agent in metastatic renal cell carcinoma. This study suggests a quality-of-life benefit over interferon alfa-2a but no survival benefit.

Objective: To assess the effect of sorafenib versus interferon alfa-2a (IFN-alpha -2a) on progression-free survival (PFS), tumor response, adverse outcome (AEs), and quality-of-life (QOL) scores in patients with metastatic renal cell carcinoma (RCC).

Participants/Methods: 189 patients with metastatic RCC were randomized to receive either sorafenib (400 mg twice daily) or IFN-alpha -2a (9 million U 3 times weekly) until progression was seen (period 1). After progression, patients in the sorafenib group had dose escalation (to 600 mg twice daily), and those in the IFN group were switched to sorafenib (400 mg). Tumor responses were assessed with well-accepted measurement guidelines (RECIST criteria), and AEs and QOL issues were assessed with standardized questionnaires.

Results: During period 1, comparing initial sorafenib and IFN doses, there was no difference in PFS seen (5.7 months for sorafenib, 5.6 months for IFN), but there was more tumor shrinkage seen (68.2% for sorafenib, 39% for IFN). There were more overall AEs and more severe (grade >=3) AEs seen in patients who received sorafenib than IFN, but even so, patient-reported symptoms and QOL scores appeared to favor sorafenib.

Conclusions: While no benefit in PFS was seen in this study using sorafenib as first-line therapy compared to IFN-alpha -2a in patients with metastatic RCC, there may be a QOL benefit.

Reviewer's Comments: Clearly, we have come a long way in the treatment of advanced RCC. Initially, it was unclear which of the 2 original tyrosine-kinase inhibitors, sunitinib or sorafenib, might prove to be a better first-line agent. Currently, we know that sunitinib has shown significant response and survival benefits and is now one of the first-line recommendations in this disease. The role of sorafenib continues to be determined. It currently is used as a second-line agent in most cases. This study showed no survival benefit when comparing it to IFN-alpha -2a, an immunotherapy drug with questionable benefit of its own. However, there did appear to be better QOL scores, making it a nicer choice for patients who have failed initial therapies. Perhaps a more interesting and useful finding in this study was seen in the "period 2," however, where patients progressing on sorafenib tended to respond to a higher dose, and those progressing on IFN tended to respond to sorafenib. There is already some evidence suggesting that higher doses of sorafenib may be more effective in this setting. It seems we do not really yet know proper doses of this drug to use or perhaps even which patients might benefit the most. Clearly, though, it should remain in the armamentarium.

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Urine Loss on Post-Foley Removal Day 1 May Help Predict Duration of Incontinence

An Easy Prediction of Urinary Incontinence Duration After Retropubic Radical Prostatectomy Based on Urine Loss the First Day After Catheter Withdrawal.

Van Kampen M, Geraerts I, et al:
J Urol; 2009; 181 (June): 2641-2646

Quantifying the amount of urinary leakage during the day after catheter removal may help predict how long a patient will remain incontinent after radical prostatectomy.

**Objective:** To assess the predictability of the duration of urinary incontinence after radical prostatectomy (RP) with simple postoperative measurements.

**Participants/Methods:** 104 of 140 consecutive patients at a single site underwent RP followed by strict measurements of urinary incontinence. Foley removal was performed in the hospital with 24-hour observation to record urinary output. Patients kept pad diaries 3 times weekly, and had weekly office visits for continence physiotherapy. Continence was defined by <2 g urine lost over 24 hours, which was confirmed at the weekly office visit with a 1-hour pad test and a patient-scored visual analog scale.

**Results:** On multivariate analysis, the only significant predictor for the duration of postoperative incontinence was the amount of urine lost during the day after catheter removal.

**Conclusions:** The amount of urine lost the day following catheter removal may predict the duration of incontinence after RP.

**Reviewer’s Comments:** Patients who undergo radical prostatectomy for prostate cancer understand that they will be incontinent for a period of time, and that recovery of continence may take up to a year. However, most patients expect that they will be the one to be dry in 6 weeks, and it is often hard to set realistic expectations for them. Having a reliable prediction tool for patients would be a valuable asset. The authors of this study chose to investigate the amount of urinary loss in the 24 hours after Foley removal and correlate it with duration of incontinence. To accomplish this, they kept patients in the hospital during the 24-hour period after Foley removal and carefully monitored all urine loss. Patients also recorded urine loss at home. The result was a significant correlation between amount of urine loss in the initial 24 hours and duration of incontinence. Although they attempted to show a stepwise increase in initial leakage and time to recovery, the only meaningful numbers appeared to be for very little loss in the first day (2 to 50 g), which corresponded with average recovery at day 8, and for very great loss (>500 g), which corresponded to average recovery at day 70. Confidence intervals were very wide as the initial leakage amount increased, making true prediction less reliable in this circumstance. Other issues with the study are that patients were kept in the hospital for 24 hours after Foley removal to get accurate readings—something unlikely to be popular by either patients or physicians in the U.S. Furthermore, patients all got physiotherapy or biofeedback to help speed continence—again something not widely employed in the U.S. This clever study provides a potential tool for continence prediction after RP, but it will need further study and validation in more realistic settings before it could be used practically.

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